Abstracts 1-68 Relate to the Sunday Program

Biology

1. 100 Years of Genetics

William Sofer, Rutgers University, Piscataway, NJ

Almost exactly 100 years ago, Thomas Hunt Morgan and his coworkers at Columbia University began studying a small fly, Drosophila melanogaster, in an effort to learn something about the laws of heredity. After a while, they found a single white-eyed male among many thousands of normal red-eyed males and females. The analysis of the offspring that resulted from crossing this mutant male with red-eyed females led the way to the discovery of what determines whether an individual becomes a male or a female, and the relationship of chromosomes and genes.

2. Streptomycin - Antibiotics from the Ground Up

Douglas Eveleigh, Rutgers University, New Brunswick, NJ

Antibiotics are part of everyday living. We benefit from their use through prevention of infection of cuts and scratches, control of diseases such as typhoid, cholera and potentially of bioterrorist's pathogens, besides allowing the marvels of complex surgeries. Antibiotics are a wondrous medical weapon. But where do they come from? The unlikely answer is soil. Soil is home to a teeming population of insects and roots, plus billions of microbes - billions. But life is not harmonious in soil. Some microbes have evolved strategies to dominate their territory; one strategem is the production of antibiotics. In the 1940s, Selman Waksman, with his research team at Rutgers University, began the first ever search for such antibiotic producing micro-organisms amidst the thousands of soil microbes. The first antibiotics they discovered killed microbes but were toxic to humans. Then in 1943, came pay dirt! Albert Schatz, Elizabeth Bugie and Selman Waksman found streptomycin. It attacked the agents of tuberculosis, cholera, the Black Death and other pathogens against which penicillin was ineffective. Streptomycin spurred further searching, leading to the major development of the antibiotic industry. Antibiotics are the soil microbe's gift to medicine. As Selman Waksman said "Out of the Earth shall come thy Salvation."

3. Biology Teachers (BTANJ) Program

Bunny Jaskot, Biology Teachers Association of New Jersey, Scotch Plains, NJ

The BTANJ Executive Board members will demonstrate a sample bioinformatics lesson utilizing TIGR lessons. We will take teachers step by step through the bioinformatics process to increase the level of comfort for the participants in utilizing biotech/bioinformatics in "real time" in the classroom. Resources from NABT, Detectives in the Classroom, and Biozone will be distributed. There will even be a lesson for Middle School teachers.

Chemistry III: Computers in Education

Official: Bettyann Howson Chatham HS, Madison, NJ

4. Using Simulation to Teach Chemistry

John Gelder, Oklahoma State University, Stillwater, OK

All participants will learn how to use Flash and Java-based programs that are accessed using a web browser. Lab Experiments at the molecular level will provide an interactive, molecular level view of an ideal gas,or of an equilibrium reaction. The chemical kinetics of the equilibrium reaction can also be investigated. Each program includes several guided-inquiry activities for students. Both Java-based labs and Flash simulations, along with their accompanying inquiry activities, have been tested in classrooms in universities and in high schools.

5. Powerful Powerpoint Workshop

Patricia Duncan, HIgh Point HS, Lakeville, PA

In a computer lab, we will learn how to use the Power Point program to make presentations for professional activities. Enliven your classroom teaching with this powerful computer tool.

High School Student Posters & Displays

6. Effect of Weather and Ozone Concentrations on the Occurrence of Stroke Death

Aakruti Bhalja, John F. Kennedy Memorial High School, Iselin, NJ

Effect of Weather and Ozone Concentrations on the Occurrence of Stroke Death

People all over the world are experiencing strokes and sometimes die from them. The aim of this study was to clarify whether air pollution, weather, and the incidence of stroke mortality can be correlated as some recent studies have shown. Scientists are puzzled by the occurrence of stroke daily among hundreds of people in the U.S. More research is

needed to find the possible risk factors for stroke. To begin, monthly averages of meteorological factors were obtained for the years 2001 and 2002. Furthermore, unhealthy exceedances of ozone concentrations were acquired along with stroke deaths. This data regarded six counties in New Jersey: Essex, Sussex, Morris, Bergen, Camden, and Cape May. This data was then tabulated into Excel and correlated using the Pearson Correlation. Results indicate an inverse relationship between temperature and stroke deaths. However, results also determined that a relationship between ozone concentrations and stroke deaths does not exist. Therefore, the second hypothesis is corroborated, that the fluctuation of weather will result in the fluctuation of stroke death. The study reveals that weather may be risk factors for stroke. In order to gain a better understanding of grasping such a correlation, further research should be undertaken, inclusive of studying stroke subtypes, other meteorological factors, socioeconomic factors, and a larger sample size.

7. Catch Me If You Can

Lina Zamamiri and Daria Bialik, Woodbridge High School, Woodbridge, NJ

Different black inks have been analyzed using chromotography to determine if different black inks are the same or diferent. Preliminary results show that they are different and further testing is necessary to determine which solvent system is best for each ink type.

8. Energetic Light: a Chemiluminescence Reaction

Robert Ngenzi, Monroe Township High School, Monroe Township, NJ

Chemiluminescence is an energy emission in the form of light which results when a molecule is excited and releases energy upon its drop back into its ground state. Luminol (5-amino-2,3-dihydro-1,4-phthalazinedione) and hydrogen peroxide (H202) were reacted under various conditions in order to test the effect of these conditions on the reaction's green chemiluminescence. These conditions included different concentrations of hydrogen peroxide, varied solution temperatures, and the addition of emulsifiers. Alterations to these factors were determined to affect the intensity of the light emitted, and the duration of the light emission.

9. Formation and Combustion of Acetylene

Scott M. Kaufman, Monroe Township High School, Monroe Township, NJ

The purpose of the research was to study the formation and combustion of acetylene. The percent yield of the reaction of calcium carbide and a proton donor, water, to form acetylene and calcium oxide was first determined by measuring the volume of evolved acetylene in a eudiometer. On average, the calcium carbide produced a 67% yield of acetylene. The theoretical volume of acetylene to fill a 9 in. diameter balloon was then calculated, and the required amount of calcium carbide was found to be 23 g. A technique was developed to capture the generated acetylene gas. When a lit splint was put to the acetylene-filled balloon, under controlled conditions, it quickly combusted and produced a bright flame.

10. The Chemistry of the Oscillating Clock Reaction

Simranjeet S. Sran, Monroe Twp. High School, Monroe Twp., NJ

This is an oscillating clock reaction of bromide, bromate, malonic acid, sulfuric acid, and ferroin. In this research, these components and their relationships were studied in the oscillating clock. Parameters were defined for induction time, cycles, and length of reaction. Data was collected in these areas as well as initial cycle length with the original reaction concentrations, followed by reactions with a single concentration change. An increase in bromide slowed induction time, initial cycle length, length of reaction, and number of cycles while a greater bromate concentration led to a speedier reaction with more cycles. An increase in the concentration of malonic acid resulted in a longer reaction. Ferroin, when increased, masked the oscillations. It was also found that an oscillation could be induced in the reaction vessel. The results and their relative graphs showed a distinct correlation to the equations for this specific oscillating clock.

11. The Spirit of Chemistry - The Catalytic Decomposition of Hydrogen Peroxide

Yushen Qian, Monroe Township High School, Monroe Township, NJ

Hydrogen peroxide undergoes an exothermic disproportionation to form oxygen gas and water *in situ*. Although this decomposition is spontaneous according to the Gibbs Free Energy equation, the rate of the reaction varies according to the identity and amount of catalyst present, as well as the concentration of the hydrogen peroxide itself. We have tested a variety of catalysts, including redox metal oxides such as MnO_2 and $KMnO_4$, to ionic salts such as KI and NaI, as well as elemental iodine. Furthermore, we have also varied the concentration of H_2O_2 from 3% to 30%. The goal of the project was to determine the optimal parameters with which a solution of hydrogen peroxide can catalytically decompose to release enough heat to vaporize the water of the solution, and thus produce a “genie effect” of gaseous water rushing out of the neck of a 2 liter or 20 oz. soda bottle. The most effective reaction was produced when 0.75 to 1.22 g of manganese (IV) oxide, MnO_2, was used to catalyze the decomposition of 3.48 M or 12% H_2O_2. Furthermore, catalyst effectiveness was augmented by using finely ground particles; it was determined that as the catalyst's surface area increased, its effectiveness increased as well.

Math and Science Learning Center

Official: Kathy Scott Rutgers University, Piscataway, NJ

12. Math and Science Learning Center

Kathy Scott, Rutgers University, Piscataway, NJ

The MSLC is a unique resource for students in the sciences. We are committed to providing support services for University students and outreach programs for K-12 students. Special to the MSLC are the hands-on interdisciplinary science demonstrations and activities. Instrumental to our success are the contributions made by our student managers and employees.

Pre-College Reseach Posters

13. The Effect of Different Bacterial Strains on the Lifespan of Wild-type and Mutant Nematodes

Laura Toth, John F. Kennedy Memorial High School, Iselin, NJ

The nematode C. elegans is used as a model to study the lifespan of multi-cellular organisms. In the laboratory, E. coli is the standard food source for C. elegans. This experiment focused on the effect of different bacterial food sources on the lifespan of wild-type and 2 long-lived mutants of C. elegans. Three types of plates were prepared to measure the lifespan of the 3 lines. Three plates contained the bacteria A. faecalis, 3 contained E. aerogenes, and 3 contained the standard E. coli as food sources. Twenty eggs of each line were put onto separate plates (1 strain on 1 plate). After the nematodes hatched, they were continuously transferred to fresh plates as they aged. On A. faecalis, the age-1 mutant line lived for a significantly shorter time than the age-2 mutant or the wild-type N2 lines. On E. aerogenes, the age-1 mutant lived significantly longer than the other two lines. These results suggest that the type of bacterial food source can affect lifespan length. In addition, because the long-lived age-1 line showed a shorter lifespan length on A. faecalis, I found that the food source can dominate the expected phenotype of a mutation.

14. The Effects of Various Genres of Music on the Maze-Solving Abilities of Mus Musculus

Vicky Du, John F. Kennedy Memorial High School, Iselin, NJ

The classical music of Mozart has been shown to increase a person's spatial-awareness skills and concentration when exposed for a period of time. Even so, this is still a theory, and the effects of other genres of music are yet to be tested. The results of such research would revolutionize the types of music people listen to. For the designated experiment, four types of music; classical, rap, pop, and metal, and four mice of the same sex were used. First, a mouse ran through the timed maze. Afterwards, it was exposed to fifteen minutes of the metal genre of music. Then the same mouse ran through the timed maze once more. This process was repeated with each mouse and each genre of music. Statistically, when comparing the control and experimental runs for each type of music, none of them proved to be significant. Even so, when comparing the means of the runs, the classical genre was the only type in which the mice performed better after exposure. Yet, the metal genre of music performed the worst when compared to its control, and the pop and rap genres showed little differences. The research was able to give some support to the Mozart Effect, while showing the various levels of negativity on the mice from the music. Further research could be done to retest the hypotheses with more mice, and possibly even testing a range of sounds at various decibels to show their effects on mice, and even possibly, that of humans.

15. The Effect of Grape Juice on the Adherence of Streptococcus mutans on Tooth Surfaces

Manalika Ringshia, John F. Kennedy Memorial High School, Woodbridge, NJ

Grape Juice contains an active antioxidant identified as polyphenols. These antioxidants have been known to decrease heart disease and cholesterol. One of the characteristics of polyphenols is to inhibit the glucosyltransferase of certain tooth-decay causing bacteria. In other words, it turns off an enzyme responsible for converting sugar into polysaccharoses, the binding agent of plaque-causing bacteria to teeth. One of the major decay causing bacteria is Streptococcus mutans. An experiment to analyze the effect of the polyphenols from the grape juice on the adherence of the bacteria to the teeth was conducted. Hydraxapatite pieces, structures that are composed of the same material as the outer surface of the teeth, were used, along with 100% Welch's Grape Juice. The preliminary results indicated that the polyphenols inhibited the bacteria from adhering onto the teeth. Therefore, grape juice plays an important part in inhibiting dental caries.

16. The Effects of the Magnetic Field on Primary Carrot Roots

Kruti Sanghavi, John F. Kennedy Memorial High School, Metuchen, NJ

The Magnetic Field is a factor that influences all living things. It is an environmental factor that has been important to all living organisms through out time including plants. The magnetic field is closely related to the cell metabolism of the plants (Belyavskaya, 2004). Magnets have 2 opposite poles. The effect of these different poles on root growth has not been studied. The two poles of a magnet each have a different effect on different kinds of roots. Taproots are roots that have a

positive magnetic tropism. It is not certain which pole has a more significant and positive effect on the growth of taproots. Four different groups of carrots seeds were planted and grown in four Root-Vue chambers, where the growth of the roots could be monitored and measured. Magnets were placed so that the roots were exposed to different magnetic poles. The steel bar magnet was placed in between two roots, where each root was placed 4cm away from the magnet. The control did not use a magnet. Plants were grown for 21 days and results on root growth length were calculated. The T Test was conducted for statistical analysis, and it proved to be not significant. The P values for the Control vs. North Pole was 0.4724, Control vs. South Pole was 0.4172, and the North Pole vs. South Pole was 0.9155. The results proved to be not significant, and did not have a great difference in the growth rates of the three groups.

17. The Effects of Ginkgo and Caffeine on Learning and Memory

Nina Lee, Millburn High School, Millburn, NJ

The objective of the study is to test the effects of Ginkgo biloba extract and the combination of ginkgo and caffeine on learning and memory function. Zebrafish (Danio rerio) were used in the experiments since zebrafish are vertebrates and their genome is very similar to those of humans. The fish were divided into 3 groups: a control group, a ginkgo-fed group and a ginkgo plus caffeine-fed group. Their learning behavior and memory function were examined by teaching the fish a simple spatial alternation task with food as the reward. During the experiments food was delivered on alternating sides of the fish tank at constant time intervals. The animal's achievement of the spatial learning and memory tasks was represented by its presence at the correct side of the tank at food delivery. The results from the learning experiments showed the ginkgo group's responses indicated a higher correct response rate than the control group and the ginkgo plus caffeine group. The ginkgo group had a 8.2% higher success rate than the other two groups. The correct response rate of the ginkgo plus caffeine group did not show any significant difference than the control group. From the memory experiments, all three groups indicated about the same memory retaining results. The ginkgo and caffeine appeared have no effect on the memory retention function.

18. Altering Biomineralization

Ilya Sabnani, Kent Place School, Westfield, NJ, Joanna Aizenberg, Bell Labs/Lucent Technologies, Murray Hill, NJ and Bernice Feuer, Kent Place School, Summit, NJ

Organisms always adapt to their environment to protect themselves from predators and to help themselves in getting necessary nutrients for living. One form of protection is an outer covering; sea organisms have very intricate outer coverings that protect them from prey and help in getting essential resources, such as light or food. The intriguing nature of these skeletal elements is due to the presence of various substances, including proteins. In my experiment, I will explore the role of protein in the formation of skeletal elements. I will use biological species, such as brittlestar and sea urchin, to grow calcite crystals in vitro. These crystals will then be examined under the microscope and differences in the structure will be noted.

19. Effect of pH on Mycorrhizal Plant Growth in Two P Concentrations

Mahak Jain and Joanna Kong, JFK Memorial High School, Iselin, NJ

Mycorrhizae can aid plants best in conditions of low pH concentrations. The effect of a lower pH level on the growth rate of plants in low P concentration versus high P concentration soils on mycorrhizal grass was tested. There were three hypotheses: (H1) In a neutral pH, there will be a significantly higher growth rate in soil of low P concentration versus soil of high P concentration. (H2) In an acidic pH, there will be a significantly higher growth rate in soil of low P concentration versus soil of high P concentration. (H3) The growth rate in soil of low P concentration and low pH will be significantly higher than the growth rate in soil of low P concentration and neutral pH. H1 was accepted at a 95% significance level; H2 and H3 were rejected. Overall, the research was found to be insignificant, though the results may have been skewed by the growth of one pot.

20. Link Between the Nematodes

Divya Gupta, John F. Kennedy Memorial High School, Iselin, NJ

With the completing of the Human Genome project, there has been increased interest in sequencing many other organisms such as C. remanei being one. The genes of the nematode have never been determined before; the researcher dedicated her skills to sequencing C. remanei's DNA. This researched sequenced the genome of C. remanei and attempted to examine the cause of coding introns in a non coding region. The research used various techniques from C. remanei gene in order to isolate and then sequencing those genes. Programs such as BLAST were used to link the acquired DNA of C. remanei to closely related worms such as C. elegans and C. Briggsae. RNAi was used in order to interfere with gene expression. As a result the genes tat code for basic functions for survival development and reproduction will be affected. The results showed the scientist could in tune investigate the many essential biological characteristics that are central problem of human biology and evolution and create new databases.

21. The Allelopathic Effect of Kava on Plants

Waqar Tariq, John F. Kennedy Memorial High School, Iselin, NJ

Allelopathy is defined as a way in which certain plants prevent other plants from growing too close to them; this is usually done through the use of chemicals that the plant produces and releases into its surroundings. Kava is a perennial pepper

plant from the Oceanic region that is known to have these allelopathic affects. In this experiment three different type of plants seeds were grown in containers of the same size, with the same amount of soil, water, and light exposure. Within each container of specific plant seeds, a concentration of 0.25g, 0.5g, or 1.0g of kava extract was mixed into the soil over a period of ten days. It was discovered that kava extract had little to no effect on the plants, while the extent of inhibition did vary from one type of plant to another. Except for a few exceptions, most of the data according to a T-test was not statistically significant. Thus, more research needs to be conducted in order to determine the exact effect of kava extract on plants.

22. The Antibacterial Effect of *Mimosa tenuiflora*

Andrea Hodgson, John F. Kennedy Memorial High School, Metuchen, NJ

Mimosa tenuiflora is a tree whose bark, according to literature, contains miraculous healing powers. Its antibacterial properties are 300% more effective than streptomycin (University of Ottawa, 2003). This property can be found in many of its products, most commonly used is soap. Antibacterial soap is used as a defense mechanism against the spread of bacteria, but there is controversy about bacterial resistance. Using natural products to eliminate bacteria from the body will hinder resistance. In this study, *Staphylococcus epidermis* and *E. coli* were exposed to three different soaps, antibacterial, non- antibacterial, and *Mimosa tenuiflora* soap to test the antibacterial properties. A colony count was done and results were analyzed using a T-test. Preliminary results indicate the *Mimosa tenuiflora* soap may possibly be as effective against *E. coli* as the antibacterial soap.

23. Various Sound Effects on Wisconsin Fast Plants

Charmi Shah, John F. Kennedy Memorial High School, Iselin, NJ

Research indicates that sound waves affect all living organisms. The main purpose of experimenting with plants was to scrutinize the various sounds affecting the plants growth. It is believed that the vibrations of music interact with the roots of the plants by giving different frequencies. Loud, hard music has a different effect on the plants, than Indian raga music. (Dorothy Retallack and Professor Broman, 1973) In this experiment, three groups of plants were planted and exposed to two types of music, Indian raga and rock music. One of the groups was the control (group 1), which received no music, just natural atmosphere. Group 2 received the Indian raga music, when group 3 was given rock music. Each group received music for five hours simultaneously at the same volume level, except the control. Results indicate that plants exposed to raga music showed a significant higher growth and better leaf quality. In the future, farmers and agricultural workers may use raga music to increase growth in their plants and crops.

24. A Numerical Design Simulation of a Novel Notched Airfoil

Jayanth Krishnamurthi, John F. Kennedy Memorial High School, Iselin, NJ

A novel wing design was evaluated based on the Kline-Fogleman airfoil using numerical simulation software. Unlike conventional wing designs, the Kline-Fogleman foil contains a notched, hollow pocket on the lower surface that creates a high pressure bubble capable of sustaining the foil at high angles of attack. Three replicas of the foil were created and were modified to include a conventional rounded leading edge. In addition, the height, angle, and location of the notch were varied in order to determine their effects. It was hypothesized that lift will primarily be proportional to the notch height, with notch location playing a minor role. The three designs and a baseline foil were tested under specific flight conditions. Results indicate a 12.5 % increase in maximum lift from the baseline foil, with minimal increase in drag. These modified designs have many prominent applications, especially ones where stall-resistance is important.

25. Traumatic Recall and Retention in Adolescents

Barry P. Shifrin, John F. Kennedy Memorial High School, Iselin, NJ

The aim of the study was to observe the effect that recalling details of traumatic life experiences has on retention of information in adolescents. The experiment was given in three parts, verbal-written-verbal, to a group of mixed-gender high school students. Subjects were given the Hopkins Verbal Learning Test-Revised, with a delay in which they completed an inventory of personal traumatic experiences that asked them to recall details of their trauma. Following this they completed the HVLT-R to serve as a basis of pre- and post-recall retention. Traumatic experiences, which vary from natural disasters to violent crimes to family deaths, can have a profound impact on human psychology. In mild cases, symptoms such as depression or physical sickness can persist after the experience, while severe cases can cause psychological disorders such as PTSD (post-traumatic stress disorder). In a study by Yehuda, et al., a group of Vietnam War veterans diagnosed with PTSD showed no problems in immediate recall of data, but had major problems in delayed recall of information. While there are many ways to cope with trauma, periodic exposure to stimuli connected to the event may exacerbate symptoms and force a recall of emotions. Biological repression of emotion through hormones is possible, but this natural ability may be depleted through repeated use. Mental deficits may continue for several years, depending on the severity of the event. While certain coping methods may be employed, these do not always guarantee absolute freedom from mental disruption, which may affect everyday or academic concentration.

26. Can Cruciferous Vegetables Repair Damaged Cell Cycle Checkpoints?

William J. Zupko, Woodbridge High School, Fords, NJ

Indole - 3 - Carbinol is a commonly found chemical in cruciferous vegetables such as broccoli. Many reports suggest that these vegetables provide cancer protection by correcting damaged cell cycles. I was interestied in finding out if the Indole

– 3 – Carbinol does play a role in the repair of the damged cells. I experimented with the Indole - 3 Carbinol, and tested it with mutant yeast (S pombe), which don't divide at 35 degrees Celsius, to see if the yeast would once again reproduce and divide. During my experimentations, I had found out that Indole - 3 - Carbinol is not soluble in water slightly in alcohol, and more in acetone. When I applied the Indole - 3 - Carbinol to the yeast while suspended in acetone, the yeast were killed by the concentration of acetone. After I exhausted all possible ways of applying the Indole - 3 - Carbinol to the yeast, I used a broccoli extract suspended in alcohol. First I mixied the broccoli extract into the agar plate, yet none of the yeast grew. I also tried applying 0.5ml of broccoli extract on top of the yeast and had again received no results from the yeast that were placed in 35 degrees however, those yeast that were placed at room temperature grew. These yeast cells had taken a longer amount of time to grow, and were not all rod shaped as the mutant yeast should be, but appeared shorter, and slightly rounded.

27. A Possible Role of Bilirubin In Inhibiting PKC Induced Vasoconstriction

Sarah Arshad, John F. Kennedy Memorial High School, Iselin, NJ

New food sources and substances are found every year to contain antioxidant properties. One such substance that has recently gained high interest in the scientific community is bilirubin – a bile pigment produced by the liver. Bilirubin is known to be a toxin as it is associated with neonatal jaundice but literature also shows that bilirubin has antioxidant properties. This research looked into the possible role of bilirubin in preventing vasoconstriction of coronary vessels induced by Protein Kinase C, which increases the production of reactive oxygen species. The hypothesis stated that bilirubin would inhibit vasoconstriction of the vessels by reducing the formation of reactive oxygen species. The experiment was conducted at New York Medical College physiology lab. Bovine coronary arteries were obtained and dissected into rings, which were then suspended in Krebs solution in individual tissue/organ baths. The rings were treated with a solution of HiK and then 30K to contract the vessels, while the polygraph recorded the isometric tension. The peaks obtained from the contraction of the vessel acted as a control. The rings were then treated with a Protein Kinase C activator-PDBu, which activated constriction in the vessels. Bilirubin was then added to observe inhibition properties. An average of the peaks was taken at 5-minute intervals and a t-test was performed. Results indicated a significant inhibition of contraction induced by PDBu after adding bilirubin ($p=0.05$).

28. Nutritional Basis of School Lunches and their Composistion Based on Present Requirements

Sarah Heitmeyer Jr., John F. Kennedy Memorial High School, Iselin, NJ

Obesity has become a rising problem of many children and adolescents. Most children spend large amounts of time in school and receive one to two meals there. It is important that their schools' cafeteria menus are those that meet the requirements set down by the National School Lunch Program (NSLP), which requires certain minimum quantities of each category of foods. The purpose of this experiment was to test whether the food and beverages in hot lunches at JFK High School in Iselin, NJ are meeting the requirements set down by the NSLP. While the school may offer healthy choices, this experiment will also determine if and how individual students make unhealthy ones. For one week, a sample of each daily hot meal was obtained and its components' weight was measured. In addition, ten random students who bought hot lunch were observed in their choice making each day. The results concluded that JFK follows the requirements by the NSLP, however the student body may make choices unhealthy for them, supporting the hypothesis. For future research, it is suggested that more student observations are needed. More nutritional suggestions can be made to substitute a school meal, making it as healthy and enjoyable for the student body and its benefit.

29. A Scientific Way to Determine the Most Effective Suntan Lotion

Krysten Thomas and Megan Mcdonald, Woodbridge High School, Woodbridge, NJ

Different suntan lotions have been analyzed using a light spectrophotometer at different wavelengths. Different SPF suntan lotions have different absorption spectra. Further tests will establish which is the best suntan lotion to use for sensitive skin.

30. The Effect of Emissions of Volatile Organic Compounds on Proximate Plants

Nidhi Jain, JFK Memorial High School, Iselin, NJ

Volatile organic compounds (VOCs) are emitted from wounded plants as a defensive mechanism, slowing the growth of the plant. They can also signal proximate plants that wounding has occurred and induce the production of defense-related compounds. This experiment looked at whether VOCs from wounded grass grown near bean plants slow the growth of the bean plants. The growth rate of bean plants grown next to unwounded grass was compared to the growth rate of bean plants grown next to wounded grass. This may affect where gardeners or farmers place their plants or crops so as not to stunt their growth.

31. Gender Aggression in Crayfish

Kerima Burdette, The Young Women's Leadership, New York N.Y, NY

Our team is researching gender aggression in crayfish using Procambarus sp. We will test hypotheses: 1) a higher level of aggression is demonstrated by male crayfish than by female crayfish. 2) Habitat structure plays a role in crayfish aggression in both genders. Our experimental design will include a 40 gallon control tank with a structurally complex

habitat that will allow adequate space and cover for all of our subjects. We will then set up experimental tanks, one for males and one for females. The tanks will be identical in structure. We will be observing the levels of aggression in each tank to determine whether gender is a factor in crayfish aggression. We will observe behavioral patterns in crayfish at 20 minute intervals. We will then test for aggression between genders. Using a tank with the identical habitat structure that we used in the first test we will introduce male and female subjects and observe the level of aggression compared with aggression noted between same gender subjects. Finally, we will test the effect of habitat structure on crayfish aggression. We propose to compare the effects of a densely vegetated habitat with a simple habitat. In order to accurately isolate the effect of habitat structure we will set up six experimental tanks. Three tanks will have complex vegetated structure; three tanks will have sand substrate only. Once we conduct multiple tests and analyze our data using a two way ANOVA we will propose some possible factors that contribute to aggression in crayfish.

32. High School Fitness Assessment

Alycia K. Ryan, The Health and Medical Science Academy at Morristown High School, Morristown, NJ

Ryan, Alycia HIGH SCHOOL FITNESS PROGRAM ASSESSMENT, Morristown High School

The purpose of this study was to investigate the effectiveness of high school fitness programs on the student population in order to gather data that can be used to help students design an individual fitness program. Specific protocols were designed to assist subjects in reaching personal fitness goals based upon the outcomes of the five individual fitness assessments. A body composition protocol was designed to assess body fat and body mass index. A heart rate protocol was designed to assess heart rate before, during, and after exercise. A flexibility protocol was designed to assess flexibility and range of motion. A strength protocol was designed to assess maximum muscular strength of the chest, shoulders, arms, legs, and buttocks. Lastly, an endurance protocol was designed to assess the subject's muscular endurance by having subjects perform a push-up test and sit-up test. The designed protocols were followed by subjects for a 22 day physical education cycle. The proposed outcome for student subjects was to maintain and optimal level of personal fitness, identify and evaluate personal physiological response to exercise, and demonstrate knowledge and understanding of basic physiological principles of exercise and wellness.

33. Aloe Vera: the Green Wonder Plant

Andrij O. Kuzyszyn, Woodbridge High School, Fords, NJ

Bacteria is a major problem in the medical world as many antibiotics are becoming scarse and expensive. This project was designed to test the effectiveness of certain plants such as Aloe Vera and Garlic as cheap and natural antibacterial agents.

34. The Effects of Bathroom Cleaners on Mold

Nina E. Babeu, JFK Memorial High School, iselin, NJ

The presence of chlorinated cleaners and bathroom molds are common reasons for asthma attacks. Chlorinated cleaners can eliminate the presence of molds. The non-chlorinated cleaners can also decrease the proliferation of mold. Presently there is no research that determines between the non- chlorinated cleaners. This research examined the effects of two non-chlorinated cleaners on the growth of A. Niger. A. Niger was plated on Sabouraud-Dextrose Agar. The growth was then tested on three different cleaners. The zone of inhibition was then measured. Results indicate that Scrubbing Bubbles decreases the proliferation more significantly then Kaboom. This research shows mild cleansers decrease the proliferation of mold as well as extreme cleaners.

Using Technology to Inspire Students, Teachers and Mentors

Organizer: Peter Kieselbach Pharmacopeia Drug Discovery, Inc., Cranbury
Official: Kathie Kentfield Team 173 - Rockville High School, East Hartford, CT

35. Seeing Chemistry Non-visually; Using Talking Lab Tools to Assist a Blind Student’s Ambitions in the Laboratory

Cary A. Supalo, Pennsylvania State University, University Park, PA

Using non-visual techniques and other senses to detect valuable information can lead to a successful laboratory experience for a blind person. Chemistry can be made more accessible to the blind by listening to verbal instruction from talking lab tools, paying attention to the sounds of an experiment, and receiving detailed verbal descriptions of equipment set up. The alternative skills of blindness such as Braille, use of a white cane or guide dog, and computers with speech output play integral roles in the laboratory. A speech-accessible computer interface with laboratory probes such as balances, thermometers and pH meters will open doors for blind people to obtain observational information non-visually.

For a blind person studying Chemistry, having good mentoring can lead to a career path in Science, Technology, Engineering and Mathematics (STEM) fields. A good work ethic and motivation leads to more open doors in the chemical sciences. A positive attitude, creativity, good problem solving skills, motivation can lead to success in the chemical field.

36. Robotics as a Vehicle to Achievement, Entrepreneurship and Higher Education

Peter Kieselbach, Pharmacopeia Drug Discovery, Inc., Cranbury, NJ

To meet the challenge of inspiring diverse populations of secondary school students to pursue careers in science and technology, FIRST (For Inspiration and Recognition of Science and Technology) created robotics competitions that annually attract tens of thousands of students.

Recognizing the importance of these initiatives, major corporations sponsor teams and events while universities annually award millions of dollars in scholarships to graduating students. Parents, educators and professionals volunteer as mentors and many invest hundreds of hours each year to make these programs happen. What is it about FIRST robotics that makes it so successful?

This presentation will discuss the draw of FIRST robotics programs and their impact on students, adult mentors and educators. Though robots are the 'hook' to draw students in, these programs encompass much more than just robotics. Many teams are modeled after corporate multi-disciplinary teams, with engineering, marketing, communications and manufacturing subgroups.

37. Non-Engineering Mentoring

Kathie Kentfield, Co-Founder, NEMO (Non-Engineering Mentor Organization), FIRST Robotics, Vernon Rockville, CT

Providing your club or team with a strong support non-engineerng mentor base enables your primary mentors to focus on projects that are of most interest to them. Learn how to recruit and retain parent and professional mentors to help your team with support areas such as administrative, travel, fundraising and public relations.

38. FIRST Robotics in the classroom

David Beck, Palisades High School, Kintnersville, PA

FIRST(For Inspiration and Recognition of Science and Technology)Robotics is about getting kids excited about science, mathematics and technology. It is where kids and professionals team together to work side by side in designing and building robots. This presentation will explain how one high school has been able to integrate the concept of FIRST Robotics into the high school curriculum.

39. There's No Wrong Way To Get Involved

Sabrina Marie Varanelli, Pope John XXIII Regional High School, Newton, NJ

This presentation traces the history of FIRST Robotics Team #1302, and will explain insight that we have gained and experiences that we have learned as a result of our unique and successful team management and organizational system. The presentation has been designed to cover the formation and organization of a team, and will start go over team foundation, and the recruiting of both team members and staff and school support. The presentation will cover inter and intra-team relationships and will include discussion on team building and student and adult interaction, with strong emphasis on the concept of "Gracious Professionalism." We will also include ideas for training team members and for the integration of robotics and engineering into school curriculums through the FIRST Lego League Program. The presentation will then move into the more complex topics of team organization and will include Team member organization, leadership roles, time management, meeting formats, and inter-team communication. Mentor and student roles will also be discussed, in addition to discussion on ways to work effectively with a school administration to accomplish team goals.

40. Student Mentorship of FIRST LEGO League

Rebecca Kieselbach, Palisades High School, Upper Black Eddy, PA

On mentoring a FIRST LEGO League (FLL) team as a senior in high school. FLL is the little league of FIRST Robotics; children, ages 9-14, design and build robots using LEGO Mindstorms kits. The talk will outline my experiences and challenges when managing and coaching two FLL teams this past year.

41. Life skills learned through FIRST robotics

Patrick Bogard, Johns Hopkins University, Baltimore, MD

Participation in FIRST robotics offers a variety of opportunities to learn about technology, teamwork and about yourself.

I will discuss how FIRST impacted my career and educational goals; how the skill sets learned during the FIRST season can be applied throughout your life and how they affect your interactions with peers.

42. Teambuilding - Getting Your Introverts to Work Together!

Kathie Kentfield, FIRST Robotics Team 173 - East Hartford and Rockville High Schools, East Hartford, CT

Big or small, most robotics teams find themselves populated with a group of unique, talented individuals - many of whom are glad to work individually on their own projects. It can be a challenge to get these introverts together for meetings, let alone to work together on tasks! In this interactive forum you will learn some teambuilding exercises and obtain tips for planning a fun-filled Teambuilding Weekend. Bring back some great ideas to develop your group of students and teachers into a cohesive team.

Volcanoes of the Deep Sea

Presider: Richard Lutz Rutgers university, Piscataway, NJ

43. Volcanoes of the Deep Sea: An IMAX Film

Richard Lutz, Rutgers university, Piscataway, NJ

There will be several separate showings of a video version of the title film, which will be introduced by Dr. Lutz. He was Principal Investigator on the NSF project which funded the IMAX version of the film and also served as the film's Science Director.

Dr. Lutz is one of the foremost authorities on the ecology of deep-sea hydrothermal vents. Since the first biological expedition to these unique ecosystems in 1979, Dr. Lutz has spent countless hours on the bottom exploring thermal vents throughout the world's oceans in a variety of deep-diving submersibles.

In April 1991, Dr. Lutz joined a number of his geological colleagues on an oceanographic expedition, during which they used the deep-submergence vehicle Alvin to dive, for the first time, into the caldera of an actively erupting volcanic ridge along the East Pacific Rise at a depth of 2500 meters. Dr. Lutz has returned to the site at approximately annual intervals to document events that have occurred since the eruption.

The results of his ongoing studies at the volcanic eruption site have been featured in many scientific journals and magazines, including Science, Nature, American Scientist (cover story), and three separate issues of National Geographic. Observations made during the course of Dr. Lutz's ongoing studies in this unique "natural deep-sea laboratory" are dramatically altering our views of the rates at which many biological and geological processes are occurring on the face of the planet.

Food Science

44. Food Science and Technology

Geetha Ghai and Mukund Karwe, Rutgers University, New Brunswick, NJ

Food Science is a coherent and systematic body of knowledge and understanding of the nature and composition of food materials, and their behavior under the various conditions, which they may be subject. Food Technology is application of food science to practical treatment of food materials so as to convert them into food products of the kind, quality and stability, and so packaged and distributed, as to meet the needs of consumers for safe, wholesome, nutritious and attractive foods (Institute of Food Technologists). A food scientist studies chemical, physical, and microbiological make up of food; develops ways to process, preserve and store food according to the specifications and regulations of industry and government. To get a degree in food science at Rutgers, students have to take courses in physics, chemistry, mathematics, biochemistry, nutrition, microbiology, and engineering. It typically takes 4 years to get a B.S. in food science. Students have a choice of specializing in four areas: food chemistry, food biological technologies, food operations & management, and food science & management economics. The job opportunities for food science graduates have been and will continue to be extremely good. Our strong curriculum with emphasis on science, allows our graduates to pursue careers in food industry, regulating agencies, medicine, business, or teaching.

Marine and Coastal Sciences

45. The Seascape - Then and Now

Gregory Mountain, Rutgers University, Piscataway, NJ

Our understanding of the deep seafloor was a near total mystery until the late 19th century when efforts to plumb the ocean depths were first organized. Seafloor mapping received sporadic attention in the mid- to late-20th century, spurred first by economic interests in laying trans-ocean communication cables and exploiting natural resources above, on and beneath the seafloor, and later by territorial interests in establishing ownership of the seabed. Basic research aims to understand the origin and processes that shape the 70% of Earth covered by water. A wide range of technological advances in the last 4 decades has led to an astonishing leap forward in our knowledge of the seascape hidden from ordinary view.

46. Earth System Science: In the World & In Our Classrooms

John Dobosiewicz, NJ Earth Science Teachers Association, Kean University, Union, NJ

Earth System Science is evolving at a rate faster than geologic time could ever track. With the use of various technologies such as satellites, high speed computers, and advanced field methods, we can now see Earth, its surface, atmosphere, oceans, and ecosystems with greater detail than ever before, and we now understand the universe deeper and farther in space and time than we ever have before. It is our challenge to take these advancements in Earth System Science and relate them to our students. How do we convey the excitement and energy of this evolving field of science to our students? There are a number of new resources and tools to aid an Earth System Science teacher in their quest to keep their classroom as alive and exciting as the field they're teaching about. Join us for a session of some of the best teaching practices in Earth System Science where the focus will be on the applications of Earth System Science to recent phenomena and understanding our Earth as a system.

Women in Pharmacy

47. Women in Pharmacy: The Pioneers

Geoff W. Rayner-Canham and Marelene F. Rayner-Canham, Sir Wilfred Grenfell College, Corner Brook, NF, Canada

The 1890s to 1930s were the most crucial decades for the advancement of women in science. In particular, this was the period when the profession of pharmacy opened its doors to women. We will compare and contrast the experiences of early women pharmacists in Britain and the United States and then highlight the contributions of some of the pioneers.

Chemagination Contest

Official: Allene Johnson NJACS-TA, Maplewood, NJ

48. Chemagination Poster

Allene Johnson, ACS-TA, Maplewood, NJ

Chemagination is a creative innovation and writing contest for high school science students In the contest, students are asked to imagine that they are living 25 years in the future and have been invited to write an article for ChemMatters, a magazine for high school students that focuses on the role of chemistry in everyday life. The subject of the article is: “Describe a recent breakthrough or innovation in chemistry (and/or its applications) and how it has improved the quality of people's lives today.” In addition to the article, students are asked to design a cover for the magazine. Finalists are named at three levels— local, regional and national. For more information visit the Chemagination website.

Chemistry I

49. From Willow Bark to PolyAspirin: Discovery and Invention

Kathryn E. Uhrich, Rutgers University, Piscataway, NJ

Aspirin is a drug that is broadly used by millions of Americans to treat aching joints, headaches, and prevent heart attacks. The oldest version of aspirin is the poultice prescribed by Hippocrates in the fifth century BC obtained from the bark of willow trees and myrtle. The latest version of aspirin is PolyAspirin, a plastic version of aspirin that was first synthesized by an undergraduate chemistry student in Uhrich's lab at Rutgers University. Since that discovery, several other polymer (or plastic) versions of drugs have been invented, which led to the formation of Polymerix Corporation. Polymerix works with pharmaceutical and medical device companies to enhance their products; for example, PolyAspirin-coated cardiovascular stents may be more beneficial to patients because the drug is located exactly where it needs to be – on the stent – rather than in the stomach.

50. From Banknotes to Diamonds: Applications of Micro Analytical Chemistry in Forensic Science

Gene Hall, Rutgers University, Piscataway, NJ

Counterfeiters have become more sophisticated in making products that can fool the public into thinking that their products are the same as the genuine ones. With this in mind, our laboratory has been using modern state-of-the-art micro analytical techniques to determine the composition and sources of counterfeit products. Specifically, our laboratory is using micro energy dispersive X-ray fluorescence (EDXRF) to determine the elemental content of counterfeit products. This information is supplemented with micro Raman and micro FTIR to determine the molecular content of the counterfeit samples. This meeting will focus on the use of the above micro analytical techniques to characterize banknotes, coins, baseball cards, stock certificates, gemstones, passports, and consumer products into genuine and counterfeit. This was accomplished by analyzing the pigments, paper, inks, and mineral content of the samples. In addition, the source of the counterfeit samples will be revealed and how they were produced. Detailed analytical protocols and data presentation will also be presented along with examples from our personal forensic files.

51. Chemistry Chronicles: the life and times of undergraduate and graduate

Eve L. Berger, Rutgers University, Piscataway, NJ

Join us for a panel discussion about what it's like to study chemistry at the graduate and undergraduate levels. Do you have questions about what it's like to work in an academic lab? What kinds of research opportunities are there for undergraduate and graduate students? What you can do with a degree in chemistry? Come join us for this informative and informal discussion, and get answers to these questions and more. Panel members will be undergraduate and graduate students from Rutgers University. All students are welcome: high school, undergraduate and graduate. Snacks and drinks will be served.

Chemistry Joseph Priestley in Person

52. Putting on Airs: The Life and Work of Joseph Priestley

Ronald C. Blatchley, Retired high school chemistry teacher, New Berlin, PA

Joseph Priestley was an Eighteenth Century clergyman, author, educator, political and social theorist, and scientist. He was personally acquainted with Thomas Jefferson, Benjamin Franklin, Erasmus Darwin, James Watt, and Josiah Wedgwood. He is best remembered by chemists for his discovery of oxygen.

In this first-person presentation, Priestley discusses his life and times with special emphasis on his pneumatic chemistry. The presenter wears a period costume and performs a series of chemical demonstrations illustrating the state of Priestley's chemical knowledge. He also discusses Priestley's religious and political ideas and his interactions with his famous friends.

Time will be allowed for a question-answer period during which Priestley remains in character.

53. Joseph Priestley in Person

Ronald C. Blatchley, Retired HS, New Berlin, PA

Joseph Priestley was an Eighteenth Century clergyman, author, educator, political and social theorist, and scientist. He was personally acquainted with Thomas Jefferson, Benjamin Franklin, Erasmus Darwin, James Watt, and Josiah Wedgwood. He is best remembered by chemists for his discovery of oxygen. In this first-person presentation, Priestley discusses his life and times with special emphasis on his pneumatic chemistry. The presenter wears a period costume and performs a series of chemical demonstrations illustrating the state of Priestley's chemical knowledge. He also discusses Priestley's religious and political ideas and his interactions with his famous friends. Time will be allowed for a question-answer period during which Priestley remains in character.

K-8 Science

54. Science on a Shoe String

Linda Lee Smith, Paulsboro Public Schools, Paulsboro, NJ

Open your students “Science Eyes” with these hands on, inquiry based lessons. Activities are standards based and appropriate for students grades prek-6.

55. Lakewood Prep’s 7th Grade Science Curriculum: Building a Foundation for High School Science

Christine Wiamer, Lakewood Prep, Howell, NJ

American middle school students have shown significant gains in science scores over the past eight years.1 However, there is still much work to be done if these students are to be prepared for rigorous high school science courses. Though there is no one set curriculum for middle school science, it is agreed that students at this level should be exposed to problems and questions dealing with everything from Biology to Chemistry to Physics. While most topics in the area of the life sciences are given adequate coverage in middle school, other topics in Chemistry and especially, in Physics, are often completely ignored. In the understanding of the breadth of knowledge that a middle school science student is expected to acquire in preparation for further, successful study in the sciences, I have worked to develop a curriculum that meets these needs. Covering eight units in a full school year, the new curriculum exposes the middle school student to physical science topics (electricity, magnetism, lenses/mirrors)in addition to basic biological units. Subjects as varied as weather, genetics and probability are part of these eight units. In addition to middle school textbooks, my seventh grade class discussions and activities are heavily supplemented by teacher developed worksheets, handouts and laboratory activities. It is hoped that this curriculum will help to prepare seventh grade students for rigorous high school science courses.

1. “TIMSS 2003: Eigth-Grade Performance Up, Fourth Grade Scores Flat” NSTA Reports, Feb. 2005, 16, 4 p. 1,4.

Engineering

Organizer: Norman Zabusky Rutgers University, Piscataway, NJ

56. The motion of matter and waves, computational science, digital technology and the arts

Norman Zabusky, Rutgers University, Piscataway, NJ

I will discuss how artists over the centuries have represented waves and matter in motion, from Leonardo da Vinci to contemporaries like Ned Kahn. I will also emphasize how new technology has affected the broadening of artistic expression. For example in the arts the advent of photography and now digital sculpture. In the sciences imagery from computer simulations and measuring devices, e.g.. the Hubble space telescope wide field camera and high speed cameras . These images can inspire artistic collaboration between a scientist and artist. Also included are illustrations and animations from the work of Jacob Fisher, Keith Brown, Ned Kahn and my own collaboration with Hilary Shames, all participants in the International Science and Art Symposium in New Brunswick, NJ, June 10-12.

High School Education Posters

Organizer: Anita J. Brandolini William Paterson University, Wayne, NJ

57. Can the Health Benefits of Oatmeal be Undone?

Michael Kortrey, Woodbridge High School, Woodbridge, NJ

High cholesterol levels have been connected with numerous ailments including heart disease, the leading cause of death in Americans and Western Europeans. It is now widely accepted that eating foods high in fiber will reduce the risk of heart disease, primarily because during digestion oatmeal fiber forms a gel and physically blocks the absorption of cholesterol lipids. This research project passed a mixture of bovine serum (blood) cholesterol through an oatmeal sieve. Using a spectrophotomer, at 590nm, in conjunction with an Amplex® Red assay kit, serum samples were assayed before and after sieving to check for a reduced lipid concentration. Other dietary substances such as coffee were added to the sieving process in further trials in order to study the interplay of those substances with oatmeal and cholesterol during digestion. Results from the assays determine if oatmeal is effective in blocking cholesterol absorption and whether secondary food elements interfere with the possible benefits of the oatmeal consumption.

58. The Effect of Ginkgo Biloba on Inhibiting the Growth of Bacteria (e.g. bacillus megaterium, bacillus subtilis)

Kelly A. Bramwell, John F. Kennedy H.S., Iselin, NJ

The purpose of my experiment was to test the effect of a ginkgo biloba leaf extract on the inhibition of bacteria's bacillus subtilis and bacillus megaterium growth. Previous studies have stated that ginkgo biloba may have antibacterial properties. In my experiment, I incubated the bacteria and then added circular filter papers dipped in ginkgo biloba to each Petri dish and incubated again. I then checked for rings of inhibition that would have occurred if the ginkgo biloba had antibacterial properties. My results were inconclusive, and showed that little or no inhibition of the bacteria had occurred.

59. Infrared Spectroscopic and Calorimetric Analysis of Various Fuels: Structure and Efficiency

Karan Chhabra and Mana Ameri, Northern Highlands Regional High School, Allendale, NJ

The current dependency on oil and the quest for alternative energy sources have prompted us to study this topic. We will use infrared spectroscopy and calorimetry to determine an optimal method for improving energy in America. Using molecular models and statistical data, we will also determine what makes a good fuel. We expect the fuel with the most hydrocarbon bonds to carry the most energy. After this experiment, we will have revealed the best way for America to shift its oil dependency and move on to more modern methods of obtaining energy.

This research project funded by the Young Science Achievers Program.

60. The Effect of Music on Plants Infected With TMV

Apurva B. Sanghvi, John F. Kennedy Memorial High School, Iselin, NJ

Not only has music been proven to affect humans, but also the growth rate of plants. According to previous studies, it can be concluded that two types of music, positive music and negative music, can either help plants grow faster or it can kill the plants respectively. The purpose of my project was to find out whether plants infected with Tobacco Mosaic Virus (TMV) had the same growth rate effect as healthy plants when exposed to music. Five groups of bean plants were planted. After 10 days, when plants had four true leaves, 2 groups of plants were inoculated with TMV and were then exposed to positive or negative music. 2 other groups were not infected whatsoever but were exposed to positive or negative music. The control, the fifth group, was neither infected nor received any music. The results showed that infected plants had the same outcome as healthy plants exposed to music. The plants with positive music showed that they grew

more than the control as well as the plants exposed to negative music. The plants exposed to negative music had the least amount of growth and showed signs of wilting leaves.

61. The Effects of Different Concentrations of Pesticides on Onion DNA

Payal A. Patel, John F. Kennedy Memorial High School, Iselin, NJ

Humans are susceptible to numerous diseases and disorders that can be traced back to DNA mutations. Many of these mutations can be caused unintentionally by humans themselves. One way to mutate DNA is through indirect contact. There are also numerous ways in which indirect contact can take place. Scientists have been studying food that humans eat in their structure and health. A factor that must be taken into view is the heavy use of pesticides on crops. Crops must be protected from insects and bacteria and therefore constantly have pesticides applied to them. These chemicals can cause damage to the DNA (mutations). The purpose of my experiment was to observe the changes (if any) to onion DNA that had been exposed to different amounts of pesticides. My experiment consisted of applying pesticides to two sets of variables each containing ten onion bulbs. My results showed that the control DNA was white string like and smooth, while the onion DNA from the bulbs exposed to pesticides were clumpy and yellow in color. This showed a distinct change in the DNA structure of the onion bulb. For future research, I would like to use specific pesticides, some of which that are used on real crops. Finally, I would like to make the results more accurate by broadening my variables.

Tech to Great

Organizer: Mary Virginia Orna College of New Rochelle, New Rochelle, NY
Presider: Mary Virginia Orna College of New Rochelle, New Rochelle, NY

62. Michael Faraday, Technician Extraordinaire

Mary Virginia Orna, College of New Rochelle, New Rochelle, NY

Almost everyone knows that Michael Faraday was one of the most famous and highly-honored scientists of his day. Yet his fame and his achievements belie his humble beginnings as a bookbinder's apprentice who worked his way into the profession of “natural philosopher” by the back door without any of the formal education normally considered essential for such a career. Initially Humphry Davy's technician, it was by dint of curiosity, perseverance, hard work, and native intelligence that he broke new ground everywhere he put his hand, eventually succeeding his master as Director of the Laboratory at the Royal Institution.

63. From Technician to Discoverer: the Scientific Career of Marguerite Perey

Janan M. Hayes, Merced College, Merced, CA and Patricia Perez, Mt. San Antonio College, Walnut, CA

This presentation will follow the career of Marguerite Perey (1909-1975) from her days/time as a chemical technician and assistant to Marie Curie through her discovery of the element francium to her career as a scientist at the Curie Institute in Paris and the University of Strasbourg.

Perey was trained as a chemical technician because family finances could not support higher education. In 1929 she was hired at the Institut du Radium (now known as the Curie Institute) and became personal assistant (1929-1935) to Marie Curie. She continued her career as a radiologist at the Institute until 1949, the last three years as director of research. In 1939 Perey isolated element 88, which she named francium in honor of her native country. Francium is the last element found in nature; all isotopes are radioactive; approximately one gram exists in nature at any given time. She earned her bachelor's degree and doctorate (1946) at the Sorbonne. Perey was professor of chemistry at the Universite de Strasbourg (1949-1975) as well as chairperson of the nuclear chemistry department. She was elected to the Academie des Sciences in 1962, the first woman since the organization's founding in 1666. Perey died of cancer, caused by her many years of working with radioactive materials. She was one of the last survivors of the pre-World War II Curie Institute.

64. Edward Hart, from Laboratory Assistant to Editor of JACS

Roger A. Egolf, Pennsylvania State University, Fogelsville, PA

Edward Hart began his chemical career without any formal undergraduate education as an assistant to Thomas M. Drown in his private chemical laboratory in Philadelphia. When Drown was appointed Professor at Lafayette College in 1874, Hart followed, assisting Drown in laboratory instruction. Two years later, he became Ira Remsen's first graduate student at the new Johns Hopkins University. After he received his PhD in 1878, he returned to Lafayette as a professor. Hart founded the Journal of Analytical and Applied Chemistry in 1882. This journal was merged with the Journal of the American Chemical Society in 1892, with Hart continuing as the editor of the combined publication until 1901. Hart was also a cofounder of the Baker and Adamson Chemical Company and the founder of the Chemical Publishing Company, printer of the ACS's journals for most of the 20th century.

65. Joseph X. Labovsky: a Technician at the Frontier of Polymer Chemistry

Mark Michalovic, Chemical Heritage Foundation, Philadelphia, PA

Joseph X. Labovsky worked as a personal laboratory assistant to Wallace Carothers at DuPont during the period when nylon was invented, and played an important role in developing the industrial processes for commercial production of nylon fiber. In addition, he is a valuable living resource of information on this important chapter in chemical history. His story offers an interesting glimpse into that history from a unique perspective.

66. NCTA - What Fuels all those Technician Award Winners

Elizabeth Poole, Shell International Exploration and Production, Houston, TX

This is an overview of the background and accomplishments of the National Chemical Technician Award winners. TECH(The Division of Chemical Technicians)has given this award for the last 16 years and we try to see how the award has changed their work , and what type of career path led them to this award.

Chemistry IV

67. Wizards Chemistry Show

David Lee, NJACS-TA, Succasunna, NJ

This show will demonstrate the wonders of chemistry. There will be explosions and magic that will amaze and trick even the most trained eye. David and several other "Wizards" have been performing for over 20 years at conventions and shows both locally and nationally.

Physics

68. Spectacular Physics Show

Mark C. Croft and David P. Maiullo, Rutgers University, Piscataway, NJ

In 1826, physicist Michael Faraday founded the Children's Christmas Lectures at London's royal Institution. His goal was to communicate to children the excitement of scientific discovery. Our show, which intends to carry on in that spirit, consists of a series demonstrations based on those used in Rutgers physics courses. They are designed not only to inform, but also with an eye towards humor and exciting the imagination. We want to emphasize the fun in science for children of all ages (5 to 105). Demonstrations will include an exploding hydrogen balloon, a man lying on a bed of nails, and the use of a fire extinguisher to shoot a person on roller skates across the room.

Environmental Chemistry

Organizer: Wen-Chung Shieh Novartis Pharmaceuticals, East Hanover, NJ
Organizer: Sanjay V. Malhotra New Jersey Institute of Technology, Newark, NJ

69. Greening the chemistry curriculum

Mary M. Kirchhoff, American Chemical Society, Washington, DC

One of the best ways to promote the adoption of green chemistry across the chemical enterprise is through education. But widespread adoption of this approach has been hindered by several factors, including a lack of teaching materials, an over-crowded curriculum, and, in some cases, reluctance on the part of faculty to introduce a topic with which they are unfamiliar. The activation energy for introducing green chemistry into the curriculum is being lowered thanks to the development of a variety of resources, including textbooks, experiments, and case studies, as well as the increasing availability of workshops and summer schools. This presentation will focus on resources and strategies for integrating green chemistry into the curriculum.

70. Structure-Property Relationships in Ionic Liquids: Rebuilding Chemical Intuition

Mark N. Kobrak, Brooklyn College -- CUNY, Brooklyn, NY

Room-temperature ionic liquids have generated considerable interest as environmentally benign solvents for chemical processing, but little is known about the connection between their chemical structure and their properties as solvents. We present the results of molecular dynamics simulations that indicate how ions in solution respond to the presence of a molecular solute, and develop an analytic theory that can be used to connect the chemical structure of an ionic liquid to its macroscopic liquid properties.

71. The Greening of the Chemical Engineering Curriculum: From Green Stoichiometry to Life Cycle Assessment

Daniel Fichana, Robert P. Hesketh and C. Stewart Slater, Rowan University, Glassboro, NJ

“Greening” the engineering curriculum is an important consideration for sustainable engineering education from fundamentals to design in the 21st century. This paper describes the latest advances in an educational project sponsored by the United States Environmental Protection Agency to integrate green engineering principles into the chemical engineering curriculum. The project's goal is to integrate green engineering concepts horizontally and vertically into the curriculum by taking existing courses and integrating topics as appropriate through examples, problems and case studies. Faculty from engineering schools across the country have been engaged to develop web-based instructional modules to allow for the seamless integration for green engineering principles such as risk concepts, green chemistry, mass and energy integration, life-cycle assessment into chemical engineering courses. Currently, faculty have contributed to chemical engineering core courses from stoichiometry to plant design. In addition, faculty have developed modules for multidisciplinary offerings such as freshman-level introduction to engineering and upper-level system dynamics and control. This paper will review some of the innovative modules developed and show how they can be used in the chemical engineering curriculum.

72. Large Area "Mud Batteries" to Power In-Situ Sensors

Gregory A. Konesky, ATH Ventures, Inc., Hampton Bays, NY

Long term sources of electrical power for in-situ sensors and data recorders present some difficulties. Battery life may be the limiting factor in the duration of these experiments. Electrical energy can be extracted from the metabolic activity of microorganisms in sediments by tapping into their respiratory electron flow, hence the term "mud batteries." While the energy density is relatively low, power can be accumulated and utilized periodically. Alternatively, large area electrodes, consisting of graphite fibers, can be used. The mechanism of operation of mud batteries is described, as are deployment scenarios. Experimental results with large area electrodes are presented.

73. Analysis of trace elements and heavy metals in fish otoliths as tracers of habitat use

Zikri Arslan, Jackson State University, Jackson, MS and David H. Secor, University of Maryland Center for Environmental Science, Solomons, MD

Trace transition elements and heavy metals within the calcified otoliths of fish may represent valuable tracers of environmental exposures, allowing inferences on natal origin, habitat use, and exposure to pollution. Accurate measurement of these metals in otoliths by inductively coupled plasma mass spectrometry is often precluded by low metal concentrations and the interferences of calcium matrix. We coupled a solid phase extraction procedure to an ICP-MS instrument to overcome the matrix problems and improve the limits of detection. Several trace elements were selectively extracted and preconcentrated on a mini-column of chelating resin from otolith solutions of American eel captured from six locations along the Hudson River estuary. Site specific differences were observed in the elemental composition of the otoliths indicating that some transition elements and heavy metals in otoliths show variability that are useful tracers of habitat use patterns in estuaries. Discriminant analysis yielded an overall classification rate of 78%. Samples collected at George Washington Bridge that were exposed to heavily contaminated region of the estuary showed 100% discrimination and substantially higher levels of the metals than eels collected from other sites.

74. Model Complexes of Anaerobic Sulfate-Reducing Bacteria

Karen R. Hatwell, Villa Julie College, Stevenson, MD and Jonathon Elmer, Swarthmore College, Swarthmore, PA

Sulfate-reducing bacteria are capable of the reduction of sulfate to sulfide, which strips metal ions from the aqueous surrounding to form metal precipitates. APS reductase, a flavin based enzyme, is found in the second step of this three-step reduction and has been the focus of the work thus far. Model complexes for APS reductase have been synthesized, and their reactions with various conditions will be probed with the goal of further understanding the process. The long-term goal of this research is to synthesize complexes that can reduce sulfate, allowing for reduction and precipitation of the sulfide with aqueous metal ions, in aerobic conditions. These compounds could then be used to remove trace elements from drinking water or as bio-remediation agents, precipitating out metals. The early results for this project will be presented.

75. Grass Fights Back

Yves A. Javier, Woodbridge High School, Jackson, NJ and Katherine Wysoczanski, Woodbridge High School, Port Reading, NJ

Large fields of turfgrass are often difficult to maintain. For this experiment, tests were done at the Plant Biology Department at Rutgers University to determine the tolerance of five different grasses to a newly developed herbicide, mesotrione. The five grass species used were: Tall Fescue, Kentucky bluegrass, Creeping bentgrass, Perennial Rye, and Crabgrass. Six concentrations of mesotrione were applied to the grass seed before germination, and after grass strands had established. The rates of mesotrione used (unit: lb/sq.ft) were: 0.031; 0.063; 0.125; 0.187; 0.25; and 0.5. Pre-emerge tests revealed that crabgrass and creeping bentgrass had little or no tolerance to the mesotrione. Kentucky bluegrass and

Perennial Rye did not suffer from the application of the herbicide leaving both with significant growth. Results show that all grasses, with the exception of crabgrass and creeping bentgrass, showed great tolerance to the mesotrione during their post-emerge test at lower and mid-level concentrations of the mesotrione. Creeping bentgrass showed the most damage when higher levels of the mesotrione were applied. Crabgrass showed no tolerance to the herbicide at all concentrations. Results indicate that the herbicide mesotrione is effective for controlling Crabgrass and Creeping bentgrass with relative safety to Tall Fescue, Kentucky bluegrass, and Perennial Rye.

76. Green Electrical Energy from Marine Microbial Biofuel Cells

Gregory A. Konesky, ATH Ventures, Inc., Hampton Bays, NY

Marine microbial biofuel cells operate by utilizing organic material in sediments as the fuel and dissolved oxygen in the overlying seawater as the oxidizer. Both fuel and oxidizer are naturally present and self-renewing, resulting in a very "green" biofuel cell. Microorganisms in the sediment consume nutrients and generate respiratory electrons which are collected by a graphite electrode. These electrons flow through an external circuit, developing useful electrical power, after which they flow into another graphite electrode suspended in the seawater. Dissolved oxygen in the seawater accepts these electrons, and ultimately combine with hydrogen ions from the sediment to produce water molecules. The graphite electrode material is low cost and non-toxic. Significantly, microorganisms in the sediment, some of which are obligate anaerobes, are able to use oxygen as a termnal electron acceptor through this arrangement, which they otherwise might find toxic by direct exposure to it. This suggests possible applications in areas such as enhanced bioremediation and waste treatment. Issues such as scale-up, long term stability, and biofouling are addressed.

Nanoparticles, Microparticles and Vesicles

Organizer: Kathryn E. Uhrich Rutgers University, Piscataway, NJ
Presider: Dennis E. Discher University of Pennsylvania, Philadelphia, PA

77. Stealth Polymeric Nanoparticles for Drug Delivery Devices

Emmanuel O. Akala, Oluyomi Okunola and Gaofeng Pan, School of Pharmacy, Howard. University, Washington, DC

Drug delivery systems have evolved from the first generation to the fifth generation dosage forms. The new approaches to drug delivery are based on the realization that optimum biological response occurs when the spatial placement and the temporal delivery of bioactive agents are optimized.

Parallel to the advances in drug delivery systems are the developments in the materials of formulation, especially polymers because their properties can be manipulated easily and the diffusion rates of drug molecules through polymers are very much less than the diffusion rates of the same molecules through water. The advent of biodegradable and biocompatible polymers has increased the versatility of polymers. Polymers have been used in various macromolecular architectures for the design of drug delivery systems, especially nanoparticles for targetable, modulated and self-regulated (fourth generation) and gene (fifth generation) delivery systems.

We have developed stealth hydrolyzable cross-linked PEG-MMA nanospheres capable of sustaining the release of naltrexone and anticancer drugs. Transmission electron micrograph showed a cross-linked core with polyethyleneglycol shell. Further, drug-loaded stealth PAMAM dendrimers have been investigated: a series of PEG conjugated PAMAM dendrimers with varying degrees of substitution of the dendrimer surface functional group by PEG were synthesized, characterized and used for encapsulation of an anticancer drug. IR spectra showed that many of the encapsulated drug molecules were located within the cavity of the dendrimer.

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78. Encapsulation of Drug Nanoparticles in Self-Assembled Macromolecular Nanoshells

Michael Pishko, Alisar Zahr and Cheryl Rumbarger, Penn State University, University Park, PA

A layer-by-layer (LbL) self-assembly technique was used to encapsulate core charged drug particles in a polymeric nanoshell. This approach provides a new strategy in the development of polymeric vehicles for controlled release and targeting to diseased tissues and cells specific to human illness, such as cancer. A nanoshell composed of two biopolymers, poly-L-lysine and heparin sulfate, were assembled stepwise onto core charged drug nanoparticles. The exterior surface of the nanoshell was functionalized with biocompatible and targeting functional moieties, poly(ethylene glycol) (PEG) and folic acid, respectively. Drug nanoparticles of dexamethasone, taxol, and 5-fluorouracil were fabricated using a modified solvent evaporation technique, producing particles within a range of 314.0 to 154.7 nm. Surface morphology of the encapsulated drug nanoparticles were viewed by TEM and SEM. TEM images indicated that the nanoshell was approximately 5 nm, and composed of two polyelectrolyte layers. Characterization of surface chemistry and charge of the nanoshell required the use of XPS and zeta potential, respectively. XPS data collected for PEG modified drug nanoparticles confirmed that the peak at 286 eV represented the repeat unit in a PEG molecule. Zeta potential results re-confirmed PEG's presence at the surface. Chemisorption of PEG molecules neutralizes the surface of the nanoshell and this was illustrated by the measured neutral zeta potential of the drug particles. Preliminary biocompatibility studies to study phagocytosis of PEG modified drug particles were performed using a flow cytometric

assay and suggested that the neutral charge of the nanoshell results in decreased phagocytosis after 24 hours of incubation.

79. Polymersomes & related Nanotransforming Carriers for Drug Delivery

Dennis Discher, Univ. Pennsylvania, Philadelphia, PA

A wide range of block copolymer amphiphiles been shown over the last several years to self-assemble into polymer vesicles or 'polymersomes'. The larger the molecular weight of the copolymer, the more stable the polymersome, and so to introduce controlled release mechanisms we have been developing PEO-polyester based polymersomes. With time, the polyester blocks degrade and porate the vesicles. If one starts with slightly more symmetric copolymers than the polyester-rich diblocks needed for vesicles, cylinder micelles can be formed. With time, these cylinders also degrade as polyester chains hydrolyse. We will highlight the controlled release aspects of both these 'nano-transforming' systems and describe targeting as well as interactions with cells and, in some cases, surprisingly long circulation in the body.

80. In Vivo and In Vitro Elution of NSAID and Drugs from Self-Delivering PolyNSAIDs Microspheres

Yun H. Choe, Zheng Wang, Bryant J. Pudil, Michael B. Hicks, Suseela Kanamathareddy, Stephen Goodrich and Alan Letton, Polymerix Corporation, Piscataway, NJ

The use of biodegradable polymers for drug delivery from microspheres demands a system that eliminates inflammation, pain and other side effects associated with current technology. Our approach utilizes anhydride bonds in the polymer where NSAIDs were polymerized to be part of the backbone, as first reported by K.E. Uhrich. In a continuation of this effort, we prepared microspheres from a series of PolyNSAIDs containing two well known NSAIDs, salicylic acid and diflunisal (DF), and studied their elution in vitro using several media including serum. In a rat subcutaneous PK model, we demonstrated the controlled and prolonged release of NSAIDs relative to standard oral NSAID dosing. PolyNSAIDs were prepared either by a melt-polycondensation or a proprietary solution method and the microspheres by oil in water emulsion method. When rats were administered a single subcutaneous injection of 250 mg PolyDF microspheres, containing about 192 mg DF formulated in a standard aqueous vehicle, peak plasma level of DF (35 µg/mL) were achieved within two days. Thereafter the drug level declined slowly over about two weeks. In contrast, a single oral dose (25 mg) of DF produced a drug level that declined within a few hours. We also have prepared a series of PolyNSAID microspheres where we ad-mixed several drugs, e.g. methotrexate. We have confirmed that the rate of breakdown of microspheres can be affected by the surface area of the spheres, by types of bonds between the NSAID and linker, and by types of anhydride bonds incorporated among the aromatic structures.

81. Degradable Polymersomes Foster Endosomal Release and Delivery of Cytotoxic Drugs to Cancer Cells

fariyal Ahmed, Goundla Srinivas, Michael L. Klein and Dennis Discher, Univ. Pennsylvania, Philadelphia, PA

Carrier-mediated entry of cytotoxic drugs into a cell's cytoplasm is often limited by release from the carrier as well as endosomal release after internalization. Here we demonstrate by molecular simulation and experiment that degradable, non-ionic polymersomes of PEG-(polyester) foster endosome rupture and release of cytotoxic drugs doxorubicin (DOX) and paclitaxel (TAX). These drugs are typical – soluble and insoluble – anticancer agents. We characterize the stability, delivery and intracellular toxicity of DOX- and TAX-loaded nano-polymersomes with breast and lung cancer cell lines that take up the vesicles. While degradable polymersome formulations retain their load for over a month at 4°C, they exhibit facilitated release at 37°C and low pH. Copolymer degradation fosters endosomal escape through copolymer-induced disruption of the lipid membrane, enhancing intracellular drug release and cytotoxicity up to 40-fold relative to free drug. More generally, the results show that macro-surfactants, which are increasingly being applied, will interact with cell membranes.

82. Formation of Polymersomes by Microfluidics

M. Erhan Yildiz[1], Elise Lorenceau[2], Andrew S. Utada[2], David A. Weitz[2], Robert K. Prud'homme[1] and **Douglas H. Adamson**[1], (1)Princeton University, Princeton, NJ, (2)Harvard University, Cambridge, MA

Lipid vesicles (or liposomes) are considered model membranes and are used to understand natural cell membranes and encapsulate and target the delivery of drugs, flavors and DNA. Recently, there has been considerable interest in another group of amphiphilic materials; amphiphilic block co-polymers that self-assemble into vesicles termed polymersomes. Polymersomes have several potential advantages over liposomes, including increased strength and decreased permeability. Vesicle formation procedures applicable to lipid vesicles have been used to form polymeric vesicles. These methods include rehdyration, electroformation and solvent injection. However, these methods generally yield a broad spectrum of vesicle sizes. The ability to obtain a unimodal vesicle size can be of great significance in applications as well as in fundamental property studies. The current bulk methods for vesicle formation also create local environments with variable characteristics that may be difficult to control and lead to inhomegenieties. Production of vesicles in a uniform microenvironment enables greater control over vesicle characteristics such as size and encapsulation efficiency. In a microfluidics device, flow rates can be controlled to create and maintain interfaces between different flow streams. We have developed a microfluidic device for the formation of monodisperse polymersomes from amphiphilic block

copolymers. The polymers consist of hydrophobic poly(butadiene) and hydrophilic poly(acrylic acid). The microfluidic device consists of concentric capillaries in which an inner fluid is surrounded by a polymer solution. This stream is then passed through a viscous interface and breaks up to form monodisperse drops, which, upon dialysis of the organic phase, results in polymersomes.

83. Degradable Polymeric Worm Micelles for Drug Delivery

Yan Geng, University of Pennsylvania, Philadelphia, PA, Larry Romsted, Rutgers University and Dennis Discher, Univ. Pennsylvania, Philadelphia, PA

While polymeric spherical micelles have already proven to be extremely useful for therapeutic applications, worm micelles with a much larger core volume for encapsulation show significant potential for drug delivery because they are able to flow readily through pores and circulate much longer than spherical object in blood. One seemingly novel strategy would be to generate, spherical micelles from degradable worm micelles. We have prepared giant and flexible worm micelles self-assembled from amphiphilic diblock poly(*ƒ*'-caprolactone)-block-poly(ethylene oxide) (denoted as OCL). The OCL worm micelles are observed to spontaneously shorten and generate spherical micelles, due to hydrolytic degradation of the PCL core. Molecular degradation mechanisms and kinetics were explored. The degradation rate is affected by temperature, pH as well as the molecular weight of the polymer. Initial evaluations of OCL worm micelles show that they are capable of encapsulating hydrophobic drug and achieve a prolonged release till completion. More interestingly, the release profile is affected by OCL worm micelle degradation rate, providing an useful tool to control/trigger drug release.

84. Multifunctional Non-Viral Condensing Agent for Gene Delivery

Alex M. Chen[1], Latha M. Santhakumaran[2], Sandhya K. Nair[2], Thresia Thomas[2], T. J. Thomas[2] and Huixin He[1], (1)Rutgers University, Newark, NJ, (2)UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ

In this presentation, we will report our efforts to develop multifunctional non-viral condensing agent for gene delivery. We first demonstrated that five generations of (G-1 to G-5) of polypropylenimine (PPI) dendrimers were able to effectively condense both antisense oligonucleotide (ODN) and plasmid DNA into nanoparticles. Different generations of PPI dendrimers, with positively charged amino groups surrounding the surface, can be deemed as positively charged nanoparticles with different particle size. Confocal microscopic studies of fluorescein labelled ODN showed remarkable increase in the uptake of ODN complexed with PPI dendrimers compared to that of ODN alone. Based on this, we proposed that inorganic engineered nanoparticles, such as gold with sufficient positive charges on the surface are also be able to effectively condense DNA into nanoparticles for gene delivery. Our study using atomic force microscopy demonstrated that oxidized aniline-caped gold nanoparticles effectively condensed plasmid DNA into nanoparticles. However, DNA condensation by PPI G-4 dendrimer appears to follow a different pathway compared to that by the gold nanoparticle. To our knowledge, this is the first visualization of plasmid DNA condensed into nanoparticles by inorganic engineered nanoparticles. The gold nanoparticles, with unique optical and electrical properties, naturally provide high contrast in transmission electron microscopy (TEM) and could significantly enhance Raman signals. These properties of gold nanoparticles not only allow us to visualize the condensing agent in the final condensing products, they can also allow us to study the interaction between DNA and its condensing agent at a molecular structural level.

85. Synthesis and Characterization of Collagen Mimetic Peptide Conjugated Gold Nanoparticles

Xiao Mo, Yoojin An, Allen Y. Wang and Michael S. Yu, The Johns Hopkins University, Baltimore, MD

While nanoparticle conjugates have been used in the past as immuno markers and cellular uptake tracers, applications in a broader biomedical discipline are greatly limited by their instability in aqueous conditions. Here we present a “bio-mimic” approach for generating highly stable, water-soluble gold nanoparticles that are passivated with collagen mimetic peptides (CMPs). CMPs are non-ionic peptides composed of Pro-Hyp-Gly trimer repeats, a representative peptide sequence of natural collagen molecules. The CMP-Au nanoparticle conjugates are stable in a wide range of pH and can endure saturated sodium chloride solution without aggregating. The CMP-Au can be freeze-dried and subsequently re-dissolved to yield a stable dispersion. UV-vis spectroscopy, dynamic light scattering, and transmission electron microscopy were used to characterize the CMP-Au nanoparticle conjugates. Stability of nanoparticles was evaluated with respect to the peptide length and sequence. The CMP-Au nanoparticle conjugates can be readily derivatized with other biomolecules using the carboxyl groups at the C-termini of the peptide chains. Due to the superb stability, the CMP-Au nanoparticle conjugates can be used in applications that may involve relatively harsh solvent condition such as high ionic strength, or for situations that may involve wide range of solvent polarity.

Bench Top to Pilot Plant I

Organizer: Ambarish Singh Bristol-Myers Squibb Company, New Brunswick, NJ
Organizer: Shankar Swaminathan Bristol-Myers Squibb, New Brunswick, NJ

86. Evolution of Process R&D as we enter the 21st century

Mauricio Futran, Bristol-Myers Squibb, New Brunswick, NJ

As Process R&D continues to evolve in the 21st century, process chemists and engineers at Bristol-Myers Squibb are poised to maximize generation of process knowledge using disciplined approaches ("bottom-up approach", parallel experimentation, DOE, process safety and environmental assessment) and tools (automation, PAT, integrated reactors, crystal engineering). Solutions afforded by the aforementioned approaches are systematically incorporated in the overall process design. As a consequence, the process knowledge obtained on reactions and separations makes scale-up of a process very predictable. An overview of this approach will be presented and will be illustrated with appropriate examples.

87. Synergy-Chemists and Chemical Engineers From Bench To Scaleup Operations

Raghavan Krishnan, Wyeth Research, Pearl River, NY

The pressing need to scale up and deliver Kilogram quantities of Active Pharmaceutical Ingredients(APIs) under cGMP conditions in the shortest possible time has been demonstrated by the scale up group at Wyeth. These Rapid, Safe, Scale-up operations have been successfully carried out by chemist/chemical engineers/ technicians adopting a team approach wherein their strengths have been maximized and their weaknesses made irrelevant. The presentation will focus on the science, team approach and case studies that have demonstrated the value of teamwork even under the most challenging conditions while at the same time satisfying regulatory requirements.

88. Micro Reactors: New Technology for Chemical Synthesis and Drug Discovery

Paul Watts, University of Hull, Hull, United Kingdom

Drug discovery is a very time consuming process, with one of the slowest steps being the synthesis and purification of potential candidates. Several companies have acknowledged that the miniaturisation of chemical reactors offer many fundamental and practical advantages of relevance to the pharmaceutical industry, who are constantly searching for automated, high throughput methods for the synthesis and purification of products with a high degree of chemical selectivity.

In this presentation a number of chemical reactions of pharmaceutical interest will be used to illustrate the advantages that micro reactors offer for the rapid optimisation of reactions, in which the product is typically produced in both higher yield and purity. It will be illustrated that compounds may be prepared and purified within an integrated system, in sufficient quantities for biological evaluation to be performed. Furthermore, it will be demonstrated that it is possible to generate intermediates in situ within the reactor, which may then be subsequently reacted to produce more complex products. It will also be shown that integration of the micro reactor to a highly sensitive microchannel-based biological assay system would enable rapid screening to be performed.

The use of solid supported reagents adds even greater diversity to the range of reactions that may be achieved within such systems. It will be demonstrated that the dimensions of reactors may be increased in size while maintaining the classic advantages associated with miniaturisation. In such systems significant quantities of analytically pure compound may be prepared without additional purification.

89. Bench Top Flow Reaction Optimization

Mike C. Hawes, Syrris Ltd, Royston, United Kingdom

Flow chemistry is an emerging technology with vast potential for process development. Advantages include better heat transfer, better mixing, better apparatus flexibility and a continual process. This presentation describes the ways that reactions can be optimized with on-line analysis, on the bench top before going to pilot scale.

90. Continuous Processing from Lab to Pilot Plant for Intermediates and API

Thomas La Porte, Chenchi Wang and Mourad Hamedi, Bristol-Myers Squibb, New Brunswick, NJ

Continuous processing has several advantages compared to batch processing which can be exploited under certain conditions. Smaller well-designed continuous reactors offer enhanced heat and mass transfer rates, lower inventory of hazardous compounds, less material at risk and precise control of reaction and quench times. These characteristics have a significant impact on safety, quality and economics. In our labs we have developed unique bench-top setups for screening reactions which may benefit by the continuous processing approach. We have used commercial and custom built micro- and milli-reactors for evaluating homogeneous liquid phase and gas-liquid heterogeneous reactions. We will look at scale-up issues and strategies for implementation of GMP glass plant and pilot plant campaigns. The successful implementation of several modes of operation which include plug flow, stirred tank and trickle bed reactors will also be

examined. Some examples of chemistries we have explored include a de-protection, an oxidation, a potential runaway reaction with hydrogen peroxide and an unstable reagent mediated reaction.

91. Scaling up Microwave Reactions: An Overview of the Advancer

Joseph M. Pawluczyk, Merck & Co, West Point, PA

Over the past several years, microwave technology has increasingly become a valuable tool for the synthetic chemist. Microwave technology has opened the door to faster reaction times, higher yielding reactions and in some cases success for reactions that were difficult under conventional conditions. Because of the scaling limitations of bench top microwave reactors, synthesizing large quantities has been problematic. This talk will present an overview of Biotage's latest instrument, the Advancer, which allows the chemist to process multi-gram quantities in a single run.

Spectroscopy of Biomolecules, Interfaces, and Materials I

Organizer: Edward, W. Castner Rutgers University, Piscatway, NJ
Presider: Edward, W. Castner Rutgers University, Piscatway, NJ

92. Understanding the folding mechanism of beta-hairpins

Feng Gai, University of Pennsylvania, Philadelphia, PA

Here, we describe the thermal stability as well as folding kinetics of a series of tryptophan zippers (trpzips) by static infrared (IR) and circular dichroism (CD) spectroscopies and IR temperature jump (T-jump) method. Our results support a beta-hairpin folding mechanism wherein the rate-limiting event corresponds to the formation of the turn (or loop). We find the logarithm of the folding rate depends linearly on the entropic change associated with the turn formation, where faster folding correlates with lower entropic cost. Moreover, a stronger turn-promoting sequence increases the stability of a beta-hairpin primarily by increasing its folding rate, whereas a stronger hydrophobic cluster increases the stability of a beta-hairpin primarily by decreasing its unfolding rate.

93. Wetting and Diffusion Phenomena in Hydrophobic Silica Nanotubes and Nanotube Membranes

Karthik Jayaraman, Kenji Okamoto, Sang Jun Son, Charles Luckett, Sang Bok Lee and Douglas English, University of Maryland CollegePark, CollegePark, MD

A sol-gel template synthesis process was used to prepare silica nanotubes within the pores of alumina template membranes. The pore diameter and thickness of the template membrane determines the tube diameter and length, respectively. Hydrophobic tubes are labeled with adsorbed dyes and the diffusion of the dye molecules are investigated using fluorescence recovery after photobleaching (FRAP) experiments. We employ FRAP to monitor wetting behavior as a function of solvent composition and tube diameter. Our results demonstrate that the wetting probability of silica nanotubes is a strong function of nanotube diameter, solvent composition and surface chemistry. The observed wetting behavior of the hydrophobic interiors of our nanotubes deviates significantly from predictions based on macroscopic models of capillarity. Also results from our experiments show spontaneous drying occurs when nanotubes are switched from a strongly wetting solution to pure water. We have investigated the transport properties of nanotube-based membranes and attempt to draw a correspondence between the single nanotubes and nanotube membranes under similar solvent conditions. Studying the solvent behavior inside these nanotubes will enable easy implementation of these nanotubes as tiny chemical reaction vessels and also as biomolecule delivery agents.

94. Two dimensional infrared spectroscopy of biologically relevant systems

Robin M. Hochstrasser, University of Pennsylvanie, Philadellphia, PA

Recent work on the application of two dimensional infrared spectroscopy (2D-IR) to biological systems and liquids will be discussed.

95. Microviscosity and solvation dynamics in non-ionic surfactant PEO-PPO-PEO triblock copolymer aggregates

Christian D. Grant, Karen Steege, Tania Fadeeva and Edward W. Castner Jr., Rutgers, The State University of New Jersey, Piscataway, NJ

Interior, interfacial, and exterior regions of aqueous PEO-PPO-PEO copolymer (BASF Pluronic F88) aggregates are selectively probed by choosing the appropriate hydrophilic ($C343^{-}/Na^{+}$), hydrophobic (C102), or water insoluble (C153) coumarin dye. Fluorescence anisotropy provides information on local microviscosity while time-dependent fluorescence Stokes shifts characterize polymer and solvent reorganization dynamics. $C343^{-}/Na^{+}$ probes the exterior PEO/water region in these aqueous polymers showing reorientation/solvation dynamics that are weakly temperature dependent. C153 shows substantial changes in dynamics and microviscosity over the critical micelle temperature because it strongly associates with the hydrophobic PPO micellar interiors. C102 is distributed among different aggregate regions and displays similar dynamical behavior but shifted to slightly higher temperatures relative to C153.

About the General Chemistry Laboratory I

Organizer: Rudolph W. Kluiber Rutgers University, Newark, NJ

96. Density and Coulomb's Law: Two Under-Utilized Concepts in General Chemistry

Parinbam (RAJ) K. Thamburaj, Ohio University- Zanesville, Zanesville, OH

One aspect of Chemistry is describing relationships among properties of matter. Among the relationships encountered in the first course in general chemistry, density is probably the simplest and Coulomb's law, probably the most complex. Text books available do not present the full extent of the relevance and applications of these concepts. The meaning and applications of density measurements and the application of Coulomb's Law in understanding sizes of atoms in the Periodic Table will be presented.

97. The Myers-Briggs Type Indicator (MBTI): a matrix for evaluating effective alternative teaching methods with diverse student populations

Victoria Finkenstadt, Illinois Heartland ACS, Peoria, IL and Sheryl L. Finkenstadt, Bridgeway Counseling Services, St. Charles, MO

This presentation offers basic concepts of the Myers-Briggs Type Indicator (MBTI), as it relates to the effectiveness of alternative teaching & learning styles in science education. One key to enhance comprehension, improve retention and increase student motivation is to appreciate the distinct ways people process experiences. The goal of applying the MBTI in science education is to create an optimal learning experience for the student AND the teacher. Utilization of the MBTI in a diverse population is surprisingly simple to implement in current curricula.

98. Determination of the Ionization Constant of Weak Carboxylic Acids Using Computer Interface Freezing Point Depression Measurements

Imranul Haque, Paris Svoronos and Pedro Irigoyen, Queensborough Community College, Bayside, NY

The use of computer interface freezing point measurements has enabled the approximate calculation of the ionization constant of weak carboxylic acids at 0oC using the van't Hoff factor. The quantities used were as a low as 0.05g of the acid in 4mL of water. The acids used included maleic, oxalic, trifluoroacetic and dichloroacetic.

99. Microscale Experiments for the General Chemistry Laboratory

Arden P. Zipp, Marcia Bonneau and Irene Maffetore, SUNY College at Cortland, Cortland, NY

Microscale experiments possess many characteristics that make them attractive to chemistry educators at all levels from pre-high school to university. This paper will describe the specific advantages that microscale experiments offer to large introductory college or university chemistry courses. In addition, details will be provided on several of the microscale experiments that have been developed for the science majors general chemistry at SUNY Cortland. (These experiments include microscale activities for acid-base, buffers, electrochemistry, intermolecular forces, kinetics, oxidation-reduction and stoichiometry.)

100. A Freshman Level Capstone Experiment with an Environmental Forensic Twist

Liina H. Ladon, Laurence J. Boucher, Alan J. Pribula and Joseph J. Topping, Towson University, Towson, MD

For the past few years, our department has made an initiative to improve student learning in the chemistry curriculum by introducing innovative guided-inquiry experiments into the freshman level laboratory courses. One of the experiments we developed is a capstone experiment that is scenario based and centers around a fictitious fish kill in an estuarine environment. Students, working in groups, play the role of a consultant firm hired by a law firm representing a company that has been accused of contributing to the fish kill. The environmental mystery is solved by a group effort involving the entire class. The project involves laboratory work, web searching, cooperative learning and a class presentation. We will present the development of such an experiment and the successes and failures of conducting the experiment over the past few years.

101. Using Software to Simplify Grading Labs and Making Pre-Labs

Charles H. Mahler, Lycoming College, Williamsport, PA

Students in the General Chemistry laboratory can learn more when they work individually, but it is more work for the instructor to make individual pre-lab assignments and to grade individual lab reports, especially when each has many calculations.

Widely available spreadsheet and word processing programs can be used to generate individual pre-lab assignments for each student for most experiments in the General Chemistry laboratory, as well as the grading keys for these.

Lab reports for experiments with many calculations are traditionally difficult to grade. Database and spreadsheet programs allow students to enter their experimental data in lab, followed by quick generation of an accurate grading key for each student's data.

Examples of pre-lab assignments and their grading keys will be given. A sample database for a thermodynamics experiment where students each enter over twenty different data points will be shown. This and a spreadhseet are then used to calculate over thirty results for each individual grading key, which will also be shown.

102. Economies of Scale: Bio, Materials, and Environmental Sections of General Chemistry Lab

Joseph T. Keiser, Penn State University, University Park, PA

When it comes to undergraduate lab instruction, large research-oriented universities are often at a disadvantage compared to small universities and colleges. But, there are cases in which larger is better. In the case of Penn State, our general chemistry lab program has eight lab rooms that run simultaneously, involving 216 students. This fact has made it easier for us to offer several versions of general chemistry lab. In the spring semester of 2005, biological (B), materials (M), and environmental (E) sections of general chemistry lab were offered, in addition to the mainstream courses. This approach has a number of benefits. First, students become more interested in general chemistry lab when it relates to their interests. Second, it enables us to take advantage of another aspect of large universities - instrumentation facilities run by full time professionals. Details will be presented.

Bioinformatics

Organizer: Nichols Murgolo Schering-Plough Research Institute, Kenilworth, NJ
Presider: Nichols Murgolo Schering-Plough Research Institute, Kenilworth, NJ

103. Ezetimibe mechanism of action: what did we learn from gene chips?

Jeffrey Yuan[1], Diane Shevell[1], Peter S. Linsley[2], Patricia A. Detmers[1] and John R. Thompson[1], (1)Merck and Co., Inc., Rahway, NJ, (2)Rosetta Inpharmatics, a wholly owned subsidiary of Merck & Co., Inc, Seattle, WA

The molecular processes involved in cholesterol uptake from the intestinal lumen by enterocytes are not well understood. Ezetimibe, a cholesterol absorption inhibitor, prevents this specific transport activity. To gain a better understanding of ezetimibe function and how cholesterol absorption is controlled, a series of microarray studies were conducted. The experiments focused on two aspects of intestinal cholesterol absorption: How intestinal gene expression in mice is affected by ezetimibe treatment, and can tissue specific expression profiling be used to identify components of the cholesterol uptake pathway. In the microarray studies, mice fed a high cholesterol/cholate diet had an intestinal gene expression signature that was anticorrelated with that of animals only receiving ezetimibe, which caused upregulation of genes involved in cholesterol synthesis. Since cholesterol uptake occurs predominantly in the duodenum and jejunum, expression profiling of these tissues was performed and compared with other tissues to identify genes specifically involved in this uptake function. Among the genes identified from this dataset was NPC1L1. Mouse knockout studies conducted concurrently with the microarray experiment identified NPC1L1 as a candidate gene for the molecular target of ezetimibe with NPC1L1 deficient mice demonstrating a severe deficiency in cholesterol absorption and unresponsiveness to ezetimibe (Altmann, et al. 2004 Science, 303:1149-1150.). Thus, the microarray experiments showed that NPC1L1 was not only expressed in the appropriate tissue types for intestinal cholesterol absorption, which is consistent with the mouse knockout data, but ezetimibe treatment can affect the expression of cholesterol synthesis genes.

104. Phylogenetic Analysis and Classification of Human Protein Kinases Targeting the ATP Binding Site

Philip W. Mui, Glaxo SmithKline, King of Prussia, PA

One of the major impediments in targeting the inhibition of kinases as therapeutic regimens concerns the associated potential side effects, and the identification of drug candidates with acceptable selectivity profiles remains a major challenge to discovery efforts in this area. Since the vast majority of drug candidates bind to the ATP binding pockets of kinases, we targeted this critical site as a basis for our phylogenetic analysis. Using available x-ray complex structures of representative kinases as a guide, residues which underlie the formation of the ATP binding pocket were mapped. Phylogenetic analysis and classification based on sequence regions corresponding to the ATP binding site was performed to afford classification of all kinase genes into major groupings (tree branches) in order to provide a representation of all kinases in this sequence space, and results so obtained will be compared to those derived from targeting the entire catalytic domain. Such information will be used as an aid to the selection of candidate genes for the construction of an "idealized" panel of kinases for selectivity profiling of compounds.

105. Phenotype Mapping of Genes

Qing Zhang, Schering Plough Research Institute, Kenilworth, NJ

Annotated genomes of human and rodents provide an unprecedented opportunity for mining drug targets for diseases, especially when combined with disease-susceptible loci (chromosome regions that carry disease-susceptible genes)

obtained from traditional genetics studies. While databases such as Online Mendelian Inheritance in Man (OMIM), Mouse Genome Informatics (MGI), and Rat Genome Database (RGD) provide query tools to search for disease-susceptible loci in human, mouse or rat, direct cross-species comparison is not available from these sites and nor are druggable genes highlighted.

A phenotype mapping tool has been developed in-house that provides easy access to druggable genes (such as GPCRs and protein kinases) in human and their rodent homologs, chromosome location of these genes, and if there are disease-related loci in the chromosome region these genes reside in. Strain-specific mouse SNP data have also been integrated so that users can quickly find out if SNPs exist between the two strains used in genetics study that characterized the disease-susceptable locus. The tool is equipped with search capabilities for gene, phenotype or chromosome region. Examples of using this tool to compile drug target candidates will also be presented.

106. Identification of tumor associated SNPs based on EST analysis

Wei Ding[1], Mitch Kostich[2], Luquan Wang[3], Ping Qiu[1], Jonathan Greene[1] and Marco Hernandez[1], (1)Schering-Plough Research Institute, Kenilworth, NJ, (2)Environmental Protection Agency, Cincinnati, OH, (3)GenScript Corporate, Piscataway, NJ

Carcinogenesis occurs, at least in part, due to the accumulation of mutations in critical genes that control the mechanisms of cell proliferation, differentiation and death. Expressed Sequence Tags (ESTs) are derived from cDNA libraries generated from a vast number of normal and disease tissues. By statistical analysis of human ESTs, we detected 176,207 candidate Single Nucleotide Polymorphisms (SNPs). We manually curated and catalogued EST cDNA tissue libraries into non-tumor libraries and tumor libraries and examined the association between individual SNPs and tumor tissues. A total of 5152 SNPs were identified which were present at higher allele frequencies in tumor compared to normal tissues. A subset of 1955 (37.9%) SNPs induce amino acid changes to the protein coding sequences. This approach identified many SNPs which have been previously associated with carcinogenesis, as well as a number of SNPs that now warrant further investigation. This genome-wide in silico approach can assist in detection of tumor associated SNPs and help to elucidate the genetic mechanisms underlying the development of cancer

Biomarkers: Quantification, PK/PD Correlation and Bioanalytical Issues

Presider: Michael Hayes Novartis Pharmaceuticals, East Hanover, NJ

107. Navigating the Shoals of Biomarker Assays

Brian Swanson, Sanofi Avantis Pharmaceuticals, Bridgewater, NJ

Text Not Available

108. Discovery, Identification and Quantitation of Biomarkers using iTRAQ™ Reagent Technology

Lynn Zieski, Applied Biosystems Corporation, Foster City, CA

Text Not Available

109. Development and validation of analytical methods to measure biomarkers in drug development

Francois Legay, Novartis Pharma AG, Basel, Switzerland

Text Not Available

110. Probing Aging in Zucker Rats Using Ultra Performance Liquid Chromatography Coupled to Time of Flight Mass Spectrometry

John Shocklor, Waters Corporation, Milford, MA

Text Not Available

DNA Gadgets: Making Novel Use of the Physico-chemical Properties of DNA

Organizer: Nadrian C. Seeman New York University, New York, NY
Organizer: Wilma K. Olson Rutgers University, Piscataway, NJ
Presider: Wilma K. Olson Rutgers University, Piscataway, NJ

111. DNA: Not Merely the Secret of Life

Nadrian C. Seeman, Shiping Liao, Baoquan Ding, William B. Sherman, Tong Wang, Pamela E. Constantinou, Jens Kopatsch, Ruojie Sha and Philip S. Lukeman, New York University, New York, NY

DNA nanotechnology uses reciprocal exchange between DNA double helices or hairpins to produce branched DNA motifs, like Holliday junctions, or related structures, such as double crossover (DX), triple crossover (TX), paranemic crossover (PX) and DNA parallelogram motifs. We combine DNA motifs to produce specific structures via sticky-ended cohesion. We have constructed DNA stick-polyhedra, such as a cube and a truncated octahedron We have built a DNA nanomechanical device by linking DX molecules with a segment that can be switched between Z-DNA and B-DNA. A sequence-dependent device has been made from PX DNA and one of its variants, using hybridization topology as the driving force for the motion. This device is a component of a translation machine. Another device walks on a sidewalk. A central goal of DNA nanotechnology is the self-assembly of periodic matter. We have constructed micron-sized 2D DNA arrays from DX, TX, and parallelogram motifs. We can produce specific designed patterns visible in the AFM from DX and TX molecules. We can change the patterns by changing the components, and by modification after assembly. The key challenge in the area is the extension of the 2D results obtained so far to 3D systems. We aim to produce high resolution crystals of DNA host lattices with heterologous guests, leading to well-ordered bio-macromolecular systems for diffraction analysis and to 3D integration of nanoelectronics. We have prototyped the use of DNA to scaffold heterologous materials. Supported by grants from NIGMS, ONR, NSF and Nanoscience Technologies, Inc.

112. DNA Machines

Chengde Mao, Yi Chen, Ye Tian and Seung-Hyun Lee, Purdue University, West Lafayette, IN

DNA has been extensively studied for supramolecular self-assembly towards structural control at the nanometer scale. The essential concept is to construct well-defined structures by integration of stiff branched DNA motifs and predictable intermolecular interactions. DNA conformational changes provide means for introduction of nanomotions. Building on previous works, we have designed and assembled a various DNA nanomachines, and started to explore their potential applications. Our works contain four sections:

i) an autonomous DNA machine;

ii) a proton-fueled DNA machine;

iii) a pair of molecular gears;

iv) switching chemical reactions by a DNA machine.

113. Engineering DNA Motors and Sensors

Niles A. Pierce, California Institute of Technology, Pasadena, CA

Single-stranded DNA is a versatile construction material that can be programmed to self-assemble into nanoscale devices driven by the free energy of base pair formation. This talk will describe the computational design and experimental demonstration of DNA systems including a synthetic walker and biosensors based on hybridization chain reaction (HCR) mechanisms.

114. Nucleation and Stability of Nanotubes from DNA Tiles

Ashish Kumar, Axel Ekani-Nkodo*, Armand Vartanian and **Deborah K. Fygenson**, University of California, Santa Barbara, Santa Barbara, CA

Nucleation and Stability of Nanotubes from DNA Tiles

DNA self-assembling systems are poised to play a major role in nanotechnology. One particularly versatile approach consists of building small DNA structures called tiles, which can be programmed via single stranded overhangs (i.e. sticky ends) to assemble into larger structures (e.g., 2D crystals) with well-defined architectures. Little is known, however, about the kinetics of the assembly process and how it might be controlled via sequence design to yield larger or more perfect assemblies. We measured kinetic and thermodynamic parameters of DNA tile assembly in the context of a DNA nanotube. To do this, we monitored the fluorescence of a dye molecule located at the base of a sticky end, which increases upon hybridization of the sticky end. This provides a versatile and sensitive means for monitoring assembly as a function of temperature, time and tile concentration. Results indicate the presence of nucleation barrier to assembly and a critical nucleus of >4 tiles.

*present address: Unilever R&D, UK

115. DNA-crosslinked gels

Bernard Yurke[1], David C. Lin[2] and Noshir A. Langrana[2], (1)Bell Laboratories/Lucent Technologies, Murray Hill, NJ, (2)Rutgers University, Piscataway, NJ

Various DNA-based devices which can perform mechanical work have been constructed that can be cycled through a set of states by the sequential application of DNA strands. Hybridization energy powers these machines. Strand displacement via competitive binding allows the completion of the machine cycle. A question of interest is whether such devices imbedded in materials could be used to give materials new functionality. To address this question we have studied the behavior of DNA-crosslinked polyacrylamide hydrogels. We have constructed DNA-crosslinked gels which can be converted from sol to gel or from gel to sol at any temperature between the freezing point of water and the melting temperature of DNA-crosslink structures. We have also demonstrated that the stiffness of polyacrylamide gels can be changed, reversibly, by a factor of three, through the use of DNA-hybridization motors imbedded as crosslinks in the gel. The gels were produced by first copolymerizing acrylamide with two types of Acrydite-modified DNA oligomers (which we refer to here as A and B) in order to produce polymers with DNA side chains. Gel is formed through the application of crosslinker strand C which consists of an oligomer whose nucleotide sequence has regions that are complementary to both A and B. The crossslinker strand may also possess single-stranded regions that serve as toeholds for the removal of the crosslinker or as motor domains for reversible stiffening of the gel. Potential biological and medical applications of these materials will be discussed.

116. DNA as the Raw Material for General-purpose Electrical Biosensors

Dipankar Sen, Richard Fahlman, Carlo Sankar and Edward Leung, Simon Fraser University, Burnaby, BC, Canada

We have recently reported on the design and properties of two related classes of “universal” biosensors made out of DNA (“Deoxyribosensors”), which generate electrical signals in response to the binding of designated ligands/analytes (small molecules or macromolecules). The original biochemical methodology has now been transferred to chips, and should be useful for the detection of a variety of analytes. In addition, this technology is being adapted to develop electronic logic gates, and for the development of a novel structure-probing method for complexly folded nucleic acids. This latter method, “Charge Flow and Quenching Mapping” (CFQ), is able to map base-stacking connectivities to yield information about the global/axial stacking relationships of two or more helical arms within specific folded DNAs/RNAs, as well as on the location of specific guanines within helices or at defined extra-helical sites. We expect that CFQ will provide structural information not easily obtained using other techniques.

Inorganic and Organometallic Polymers I

Organizer: Frieder Jaekle Rutgers University, Newark, NJ
Presider: John B. Sheridan Rutgers University, Newark, NJ
Presider: Bhanu P. S. Chauhan Nanomaterials Laboratory of Center for Engineered Polymeric Materials, City University of New York at CSI, Staten Island, NY

117. New Hybrid Polymer Systems and Materials

Harry R. Allcock, The Pennsylvania State University, PA

The incorporation of inorganic elements into polymers offers the prospect of properties that combine the advantages of ceramics, semiconductors, metals, or optical materials with the characteristics of classical organic polymers. The polyphosphazene system allows this to be accomplished in two different ways. First, the use of organic or organometallic side groups linked to a polyphosphazene chain allows property tuning in ways that are almost unprecedented, and this has led to the synthesis and study of more than 700 different polymers. Second, recent research has provided ways to link polyphosphazenes to classical organic polymers such as polystyrene, poly(ethylene oxide), or polynorbornene, or to polysiloxanes (silicones) via block copolymer or comb architectures, a method that permits a genuine hybridization of the inorganic and the organic systems. This talk will discuss both the synthetic and polymer design aspects of this field.

118. Design, Syntheses and Materials Applications of Organodecaborane Polymers

Larry G. Sneddon, Xiaolan Wei, Mark Pender, Kersten Forsthoefel, Upal Kusari and Chang Won Yoon, University of Pennsylvania, Philadelphia, PA

The use of polymeric or molecular precursors which are initially formed into a desired shape then decomposed to a final material with retention of this shape, is an important new route for producing film, fiber and nanostructured solid-state materials. Our recent work directed at the syntheses, characterization and applications of new decaborane-based polymeric and molecular precursor systems will be presented with a focus on the use of these precursors to generate technologically important nonoxide ceramic materials, such as boron carbide and metal borides, in processed forms.

119. New Routes to Boron Containing Polymeric Lewis Acids

Frieder Jäkle, Rutgers University, Newark, NJ

New synthetic routes to boron-containing polymers including the use of living polymerization techniques will be presented.

Their applications as polymeric Lewis acids, the effect of coordination of nucleophiles on physical and photophysical properties, and the formation of new luminescent organoboron polymers will be discussed.

120. Polycarbosilanes – Hybrid Inorganic/Organic Polymers

Leonard V. Interrante, Rensselaer Polytechnic Institute, Troy, NY

Polycarbosilanes, polymers that contain Si and C in their backbone structure, exhibit many of the characteristics of polysiloxanes {(Si-O)n backbone polymers}, in particular, low Tgs and ease of structural modification through reactions involving Si-X groups; however, they also provide some of the more useful features of certain organic polymers, such as high thermal stability in inert atmospheres and resistance to attack by strong base and acids, due to the essentially non-polar character of the Si-C bond and its reduced tendency to undergo depolymerization through backbiting reactions. Moreover, we have found that, unlike the polysiloxanes, one can isolate and employ in synthetically useful nucleophilic substitution reactions, polymers having one or two Si-Cl groups per repeat unit. This talk, which is based on our research on polycarbosilanes over the past ca. 20 years, will provide illustrations of the chemistry and properties of this novel class of polymers. Our efforts to employ polycarbosilanes as precursors to SiC and as a source of low-k dielectric materials will also be described

121. Silsesquioxane based Inorganic Organic Hybrid Copolymers

E. Bryan Coughlin, University of Massachusetts Amherst, Amherst, MA

The ability to tune assembly processes of organic polymers and inorganic monoliths from the nano-scale to meso-scale remains a considerable challenge. To explore the competitive, or cooperative, effects of self-assembly in hybrid systems novel inorganic-organic random and block copolymers are being prepared to facilitate investigations of the inherent ability of one component in the hybrid systems to aggregate and thus direct the assembly of the other. Polyhedral oligomeric silsesquioxanes (POSS) are molecularly precise isotropic particles with average diameters of 1-2 nm. A typical T8 POSS nanoparticle has an inorganic Si8O12 core surrounded by eight aliphatic groups (eg. cyclopentyl or cycylohexyl) attached to the silicon vertices of the polyhedron promoting solubility in conventional solvents. The incorporation of POSS macromonomers in both semi-crystalline and amorphous polymers is readily achieved using a range of synthetic methodologies. Analysis of the copolymers using WAXD reveals that the pendant POSS groups off the polymer backbones aggregate and crystallize as nanocrystals. The limitation on POSS particle aggregation and crystallization due to their incorporation along the polymer backbone serves to limit crystallization to anisotropic shapes. The self-assembly process of ordering isotropic nano-scale sub-units into anisotropic layered structures will be discussed as a design strategy, a 'bottom-up' approach, for generating long range order in hybrid organic-inorganic copolymers.

Kinase / Virtual Screening

Organizer: Robert Goodnow Jr. Hoffmann-La Roche, Nutley, NJ
Presider: Dorothy Kominos Sanofi-Aventis, Bridgewater, NJ
Presider: Paul Cox Sanofi-Aventis, Bridgewater, NJ

122. Development of Aniline amides Containing Alternative Cores as Orally Active P38 MAP kinase Inhibitors

Katerina Leftheris, John Hynes, Jr., Alaric Dyckman, Tianle Li, Shuqun Lin, Stephen T. Wrobleski, Hong Wu, Rosemary Zhang, Kathleen M. Gillooly, Derek Loo, Kim W. McIntyre, Sidney Pitt, Ding Ren Shen, David J Shuster, Arthur Doweyko, John Sack, Joel Barrish, John Dodd and Gary L. Schieven, Bristol-Myers Squipp, Princeton, NJ

Overproduction of cytokines such as TNF-alpha and IL-1beta regulated by the p38alpha pathway are implicated in a wide variety of inflammatory diseases, including rheumatoid arthritis (RA). Recently, we described out initial efforts in developing potent, selective triaminotriazine and cyanopyrimidine aniline amides as inhibitors of p38alpha MAP kinase. Herin, we describe further development of the aniline amide class of p38 inhibitors to include alternative core structures. A description of the SAR development, in vivo activity, AMDE profiling and X-ray cyrstallography will be presented.

123. Inhibitors of mitogen-activated protein (MAP) kinases synthesized by parallel solution- and solid-phase methods

Jeremy Green, Vertex Pharmaceuticals, Cambridge, MA

Inhibitors of mitogen-activated protein (MAP) kinases have been developed through the application of parallel solution- and solid-phase methods, in conjunction with a structure-guided approach. Rapid development of structure-activity relationships, and a clear structural understanding of the interactions between the inhibitors and their respective targets

was enabled. This will be illustrated with inhibitors of p38 and SAPK3 prepared by parallel methods using both solid- and solution-phase chemistries.

124. Design, Synthesis and SAR of Pyrimidopyrimidines, Dual KDR/FGFR TyrosineKinase Inhibitors

Pamela Rossman, Hoffmann-La Roche, Nutley, NJ

The pyrimidopyrimidine moiety represents a core structure that is a useful template for the design of a variety of tyrosine kinase inhibitors. From high throughput screening, a pyrimidopyrimidine analog was identified as a dual inhibitor of the growth factor receptors KDR and FGFR-1. The crystal structure of the src-family tyrosine kinase LCK with a closely related analog bound was determined, elucidating the binding mode of the pyrimidopyrimidine. From these data, the ligand was docked into a model of the ATP binding pocket of KDR and a simplified binding model was established. This model guided the design of analogs and the investigation of the structure-activity relationships. These compounds showed excellent activity in the in vitro kinase assays and also in the growth-factor stimulated HUVEC proliferation assays. In vivo experiments demonstrated significant inhibition of angiogenesis in the corneal pocket assay and tumor inhibition in xenograft models for a number of these compounds.

125. Discovery of BMS-354825, a dual Src/Abl kinase inhibitor with potent anti-tumor activity in preclinical assays

Louis J. Lombardo, Francis Y. Lee, Ping Chen, Derek Norris, Joel C. Barrish, Kamelia Behnia, Amy Camuso, Stephen Castaneda, Lyndon A. M. Cornelius, Jag Das, Arthur M. Doweyko, Krista Fager, Christine Flefleh, Craig Fairchild, John T. Hunt, Ivan Inigo, Kathy A. Johnston, Amrita Kamath, David Kan, Herbert Klei, Roger Luo, Punit Marathe, Suhong Pang, Russell Peterson, Sidney Pitt, Gary L. Schieven, Robert J. Schmidt, John Tokarski, Mei-Li Wen, Robert Wild, John Wityak and Robert M. Borzilleri, Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, NJ

Targeted therapies represent the state-of-the-art in oncology research. The use of imatinib (Gleevec^{TM}), a selective inhibitor of Bcr-Abl kinase, in the treatment of chronic myelogenous leukemia (CML) serves as validation of the concept that therapeutic agents that target cancer-specific pathways can offer significant improvements over traditional chemotherapeutic agents. Substituted 2-(aminopyridyl)- and 2-(aminopyrimidinyl)-thiazole-5-carboxamides have been identified as potent dual Src/Abl kinase inhibitors with excellent antiproliferative activity against hematological and solid tumor cell lines. BMS-354825, a 2-(aminopyrimidinyl)-derivative of this series of compounds, was identified as having good oral bioavailability in pharmacokinetic assays. Structure-activity relationships leading to the selection of BMS-354825 for in vivo evaluation, and the activity of the compound versus wild-type and imatinib-resistant preclinical models of CML, will be discussed.

126. Discovery of novel p38 MAP kinase inhibitors:

Gulzar Ahmed, Pharmacopeia Drug Discovery Inc., Princeton, NJ

A member of mitogen-activated protein (MAP) kinase is p38, which is responsible for the overproduction of cytokines such as interlukin-1 (IL-1) and tumor necrosis factor alpha (TNF-ƒnƒÑ). These cytokines are associated with a wide variety of diseases such as rheumatoid arthritis, endotoxin shock, inflammatory bowel disease, osteoporosis, multiple scelorsis, psoriasis, Alzheimer's disease, and many others. Here, we describe the discovery of potent and selective inhibitors of p38ƒÑ through the high-throughput screening of our internal ECLiPS (Encoded Combinatorial Libraries on Polymer Support) compound collection. Details on the synthesis, structure and activity relationship, kinase selectivity and cellular activity will be presented.

Pharmacetical Profiling I

Organizer: Edward H. Kerns Wyeth Research, Monmouth Junction, NJ
Presider: Edward H. Kerns Wyeth Research, Monmouth Junction, NJ

127. Overview of Pharmaceutical Profiling in Drug Discovery

Edward H. Kerns, Wyeth Research, Monmouth Junction, NJ

The field of Pharmaceutical Profiling has rapidly expanded over the past decade and has become an integral part of the drug discovery strategy of most pharmaceutical companies. This short presentation will introduce the origins, development and future prospects of Pharmaceutical Profiling. The close tie with Medicinal Chemistry and drug discovery project teams will be examined.

128. In Silico Model for CYP Inhibition

Roy J. Vaz, Sanofi Aventis Pharmaceuticals, Bridgewater, NJ

Presentation will discuss an in silico model for CYP inhibition.

129. Deciphering the Role of Drug Transporters in Early Drug Development: Cell Culture Models and Approaches

Patrick Sinko, Rutgers University, New Brunswick, NJ

In recent years drug transporters are being increasingly implicated in the Absorption, Distribution, Metabolism and Excretion (ADME) of pharmaceutical drugs. Drug transporters have been shown to alter the bioavailability (i.e., the rate and extent of drug absorption) of orally administered drugs. Although many of these effects are considered to be a liability, "controlled" drug interactions involving metabolizing enzymes and drug transporters have become increasingly popular in the clinical setting (e.g., AIDS "boosting" using ritonavir and various regimens in cancer therapies). In early drug development, it is critical to gain an assessment of the potential for drug interactions with transporters so that proper preclinical and clinical evaluations can be made, proper dosing regimens can be established, and drug-drug and drug-nutrient interactions that may alter efficacy can be identified. A variety of methods can be utilized to identify drug interactions with membrane transporters. These methods principally vary in throughput and sensitivity. In addition, due to the constraints of in vitro and in situ methods, data interpretation can be tricky when one considers experimental format and species differences. Therefore, the proper use of experimental models in conjunction with in silico models is required in order to gain a more accurate understanding of the role of drug transporters in early development. The major methods, their use, interpretation of results will be discussed.

130. Biochemical and Molecular Assays In Early Toxicity Assessments: A Tier Approach

Prathibha S. Rao, sanofi-aventis, Bridgewater, NJ

Although drug safety assessments are pursued throughout all phases of drug discovery and development, it is imperative to assess safety/toxicity liability in parallel with efficacy during the early stages of development. Within DSE, the concept of toxicity profiling was developed using a Tier approach. Using rat primary hepatocytes as an in vitro model, Tier I provides cytotoxicity information for rank-ordering compounds to select the best of the series. Tier II utilizes a multi-endpoint approach and provides mechanistic information in addition to cytotoxicity information. This paradigm was implemented with the purpose of reducing attrition of compounds early in the value chain and to provide mechanistic investigation of toxicities and thus help in improving the prediction of human risk. This paper presents the strategic implementation of the Tier approach for assessing toxicity profiles for selection of the best candidate of the series and thus providing feed-back to the chemist in order to impact chemistry-enabling activities.

131. Prediction of P450 Mediated Reactive Intermediate Formation

Ken Korzekwa, Merck Research Laboratories, West Point, PA

The majority of drug compounds interact with the cytochrome P450 (CYP)-containing microsomal enzyme system. These interactions are usually detoxifying in that they result in more polar molecules that have greater water solubility and are more susceptible to conjugation and elimination from the body. However, metabolism by P450 enzymes can also activate a compound by introducing into the compound highly reactive and toxic functionalities. One measure of reactive intermediate formation is to quantitate the covalent binding of a compound to microsomal protein. Predictive models for reactive intermediate formation could be useful for both identifying problems pre-synthesis and interpreting experimental results when covalent binding is detected. However, developing predicting reactive intermediate formation is complicated by diversity in enzyme affinities, regioselectivities, and rates. We will discuss previous and current efforts to develop predictive models for reactive intermediate formation.

Solid State and Materials Chemistry I

Organizer: Jing Li Rutgers,The State University of New Jersey, Piscataway, NJ
Organizer: Martha Greenblatt Rutgers, The State University of New Jersey, Piscataway, NJ
Presider: Jing Li Rutgers,The State University of New Jersey, Piscataway, NJ
Presider: Martha Greenblatt Rutgers, The State University of New Jersey, Piscataway, NJ

132. Chemistry and Physics of Semiconductor Nanocrystals

Louis E. Brus, Columbia University, New York, NY

This talk describes in broad terms several aspects of nanocrystals: the critical importance of organometallic chemical synthesis, self-assembled materials made from nanocrystals, the simple quantum size and electrostatic model of size-dependent electrical properties, recent DFT advances in understanding electronic structure, the luminescence and "blinking" of single nanocrystals, and EFM (Electric Force Microscopy) determination of the charge of individual nanocrystals.

133. Solid state chemistry of biological glass fibers

Joanna Aizenberg, Bell Labs/Lucent Technologies, Murray Hill, NJ

Even the most advanced man-made materials are often primitive relative to the biomaterials that have evolved in Nature. I will describe fiber-optical systems produced by a deep-sea sponge Euplectella. The organism synthesizes an array of silica fibers whose hierarchical architecture and hybrid character offer outstanding optical and mechanical properties. We

demonstrate that these glass fibers are remarkably similar to commercial silica optical fibers: they have a characteristic chemical composition that encompasses a high refractive index core composed of Na-doped silica, with the refractive index higher than that of vitreous silica; and a low refractive index cladding composed of an organic-containing glass cylinder wrapped in organically glued, multiple layers of hydrated silica. The presence of a protein filament that controls the condensation of silicic acid into glass, the distribution of index-raising dopants and high fracture toughness arising from the fibers' composite hybrid structure suggest advantages of the ambient temperature synthesis favored in nature and provide new ideas for a bottom-up synthesis of improved optical materials.

134. Wide bandgap II-VI nanostructures for intersubband devices

Maria C. Tamargo, The City College of New York, New York, NY

The wide bandgap II-VI materials family Zn(x)Cd(y)Mg(1-x-y)Se grown lattice matched to InP substrates offers many new properties and unique advantages for device applications. Among them, intersubband devices, such as quantum cascade lasers (QCLs) and quantum dot infrared photodetectors (QDIPs) are particularly of interest because of the high crystalline quality and large band offsets available in this materials system. We have investigated lattice-matched Zn(x')Cd(1-x')Se/Zn(x)Cd(y)Mg(1-x-y)Se quantum well (QW) structures and CdSe/ZnxCdyMg1-x-ySe self assembled quantum dots (SAQD) using contactless electroreflectance. By this technique, multiple transitions within the QWs and QDs are observed, which allows us to accurately estimate intersubband transition energies, as well as conduction band offsets. Conduction band offsets as high as 1.12 eV and intersubband transitions in the 1.55 micron range are predicted from our measurements. With these materials room temperature continuous wave QCLs in the mid-infrared and QCL and QDIPs operating in the near infrared region can be fabricated.

135. Optimized Synthesis, Elucidation of Structures, and Properties for Porous Materials

John B. Parise, State University of New York, Stony Brook, NY

Synthesis of novel microporous and nano-porous materials, synthesis optimization, elucidation of crystal structure and properties such as ion exchange benefit from synchrotron-based time-resolved studies. For example $Na_2Ti_2O_3SiO_4 \cdot 2H_2O$ (TS) is highly selective towards cesium and strontium, and may be an appropriate inorganic ion-exchanger to replace the in-tank precipitation procedures for cesium removal from radioactive waste solutions. We studied the crystallization process of TS and its ion-exchange mechanism in the H- and Na-forms. A combination of ex- and in-situ synchrotron X-ray and neutron powder diffraction experiments revealed a pH-dependent pathway to the formation of TS. Further, Rietveld refinements using time resolved data, collected in situ during ion exchange of Cs^+ into H-TS, reveal an interdependence of replacement at two competing sites with in the 1-D channels and enhance site-selective exchange upon distortion of the framework from circular to elliptical channels.

Work supported by NSF CHE-0221934

136. High Porosity TiO2 via Inorganic- Salt Porogens

Charlie C. Torardi[1], C. Roger Miao[1], C. Ed Greer[1] and John Gavenonis[2], (1)DuPont Central Research and Development, Wilmington, DE, (2)DuPont Titanium Technologies, Wilmington, DE

The ability to control particle microstructure of bulk solids is important in catalysis, electronics, optics, photovoltaics, and energy absorption applications. This talk will discuss novel chemistry for producing high-porosity metal-oxide compounds, with the emphasis on TiO_2. The high refractive index and visible light scattering power of TiO_2 make it a good pigment for paints and coatings that require a high level of opacity. However, TiO_2 is also an active photocatalyst for the decomposition of organic waste materials because it can strongly absorb ultraviolet light and use the absorbed energy for oxidation-reduction reactions. If the TiO_2 particles are very small (typically less than about 100 nm), transparent films and coatings can be made that offer UV protection. Therefore, TiO_2 is a versatile material with many existing, as well as potential, commercial applications. Several solution-based processes have been reported that use titanium tetrachloride ($TiCl_4$) as a starting source of titanium. Acidic, aqueous $TiOCl_2$ solutions are often neutralized with a base, such as NH_4OH or NaOH, to precipitate a titanium-oxide solid that is washed to remove the salt byproducts, such as NH_4Cl and NaCl. For the reaction between $TiCl_4$ or $TiOCl_2$ and NH_4OH, there have been no reports describing the intentional inclusion of the salt byproduct, NH_4Cl, in the precipitated solid in order to control the physical properties of the titania product. This “inorganic-salt porogen” chemistry leads to nanocrystalline products having very high mesoporosity. The high porosity can be useful in catalyst and catalyst-support applications

Strategies for Growth: How a “Small” Company can become a “Big” Player

137. IP Assets – Springboards for Success

Mary Catherine DiNunzio, Stroock & Stroock & Lavan LLP, New York, NY

It has been estimated that the value of most of the Fortune 500 companies resides within each company's IP Assets. It follows therefore that strong IP assets yield successful businesses. This talk will provide practical advice for strengthening your company's IP assets. Topics to be addressed include sufficiency of patent protection, freedom to operate and ownership considerations. This talk is a “must see” for anyone contemplating an IPO, financing round or a corporate partnership deal. By solidifying your company's IP assets, you will provide the means necessary to take your company to the next level.

138. Growing Your Business by Partnering with Industry

Matthew L. Wotiz, Lundbeck, Inc., New York, NY

Partnerships in the biotechnology and pharmaceutical industries can provide the necessary means for achieving success. This talk will discuss typical partnership mechanisms, technology and product licensing and the concept of strategic investing. The importance of specific partnerships in Lundbeck's development as a USA "specialty pharma" company will be discussed in detail. This talk will conclude with the speaker's predictions regarding the future of pharma/biotech partnerships and the evolution of the "specialty pharma" industry.

139. Venture Capital – Securing Needed Funds

Matthew R. Rothman, EuclidSR Partners, New York, NY

This talk will focus on the processes of securing venture capital investment and realizing exits. Desirable characteristics of a company from a venture capitalist's point of view will also be discussed.

140. Attracting Investment from Large Pharma

Todd Burns, Johnson & Johnson, New Brunswick, NJ

One means by which start-ups obtain funding is through equity investments made by large pharmaceutical corporations. This talk will focus on equity investing by Johnson & Johnson (J&J) and the factors J&J considers when deciding whether to invest in a start-up company. Specific topics to be addressed include the process of obtaining equity investments, a brief review of the mechanics of such investments and what steps a company could and should take to make its business an attractive target for equity investments. Obviously a significant factor that J&J considers when reviewing smaller companies for potential investments are barriers to entry, including IP. The second part of the presentation will examine the ways a company can improve its IP position to become more attractive to a larger company.

141. Growing Your Business by Partnering with Universities

Kathleen W. Scotto, The University of Medicine and Dentistry of New Jersey, New Brunswick, NJ

Facing rapid advances in technology and increased competition in the international marketplace, mutually productive liaisons between industry and universities are rapidly becoming more of the rule than the exception. While research partnerships between academics and industry have traveled a rocky road, recent changes in economics, scientific culture and government regulations have fueled a new determination to make these relationships both seamless and mutually beneficial. This talk will present a brief overview of the history of industry/academic relationships, including some examples of well-known successful interactions as well as discussion of some of the “perils and pitfalls” faced by both partners when establishing and undertaking these collaborative efforts. The primary focus will be on the current opportunities for successful collaborations between industry and university partners and discussion of the future of industry/academic relationships with respect to the changes in both infrastructure and philosophy that may be required to create an optimal partnership.

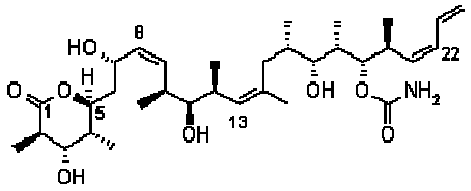
Total Synthesis/Synthetic Methodology

Organizer: Cecilia H. Marzabadi Seton Hall University, South Orange, NJ
Presider: Michael James Konkel Lundbeck Research, USA, Paramus, NJ

142. From deep-sea sponge to pilot plant: The large scale total synthesis of the marine natural product (+)-Discodermolide

Stuart J. Mickel, Novartis Pharma AG, 4002 Basel, Switzerland

A small, but structurally diverse collection of naturally occurring non-taxane microtubule stabilizing agents (MTS) has been discovered over the last decade. These include the epothilones (EPO), eleutherobin, laulimalide, and discodermolide. (+)-Discodermolide (**1**) is a novel polyketide natural product first isolated from extracts of the marine sponge *Discodermia dissoluta* by researchers at Harbor Branch Oceanographic Institution (HBOI). Discodermolide stabilizes microtubules faster and more potently than any of the other known MTS agents, is a potent inhibitor of tumor cell growth *in vitro* including paclitaxel- (PTX) and EPO-resistant cells. Discodermolide also demonstrates significant human tumor growth inhibition in hollow fiber and xenograft mouse models (including paclitaxel-resistant tumors). Discodermolide is currently undergoing Phase 1 clinical trials. This presentation will discuss in some detail the strategy and tactics that lead to a large scale synthesis. Several of the key steps in the synthesis will also be presented with respect to scalability and problems encountered. Some workable solutions to the difficulties will be presented.



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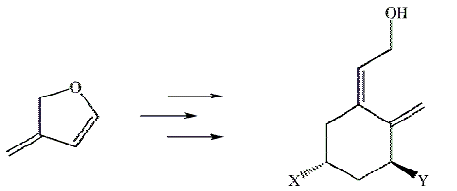
143. The Furan Approach to the Synthesis of the A-rings of Vitamin D and Calcitriol

William H. Miles, Katelyn B. Connell, Gözde Ulas, Hannah H. Tuson, Elizabeth A. Dethoff, Varun Mehta and April Thrall, Lafayette College, Easton, PA

We have synthesized the A-rings of Vitamin D_3 and calcitriol. The key steps in the synthesis of calcitriol were the asymmetric ene reaction of 3-methylene-2,3-dihydrofuran with 3-(tert-butyldimethylsiloxy)propanal and a highly diastereoselective intramolecular Friedel-Crafts hydroxyalkylation. The conversion of the bicyclic furans into (*Z*)-dienols was accomplished in four steps.



X = OTBDMS, Y = H

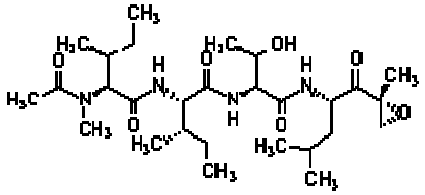
or

X,Y = OTBDMS

144. A Total Synthesis of Epoxomicin

Sreenivas Katukojvala, Kristin N Barlett, Stephen D Lotesta and Lawrence J Williams, Rutgers University, Piscataway, NJ

This talk will discuss a total synthesis of Epoxomicin. Epoxomicin, a sensitive peptidyl epoxy-ketone natural product, is a potent proteasome inhibitor. We have recently completed a total synthesis of epoxomicin using reactive spirodiepoxides as the key intermediate. This is the first application of chiral spirodiepoxides in total synthesis.



Epoxomicin

145. Preparation of Enamides via Palladium-Catalyzed Amidation of Enol Tosylates

Artis Klapars, Kevin R. Campos, Cheng-yi Chen and Ralph P. Volante, Merck & Co., Inc., Rahway, NJ

Abstract not available.

146. Chelation-Controlled Diasteroselective Reduction of 2-Fluoroketones

Pramod K. Mohanta, Todd A. Davis and Robert A. Flowers II, Lehigh University, Bethlehem, PA

The replacement of hydrogen or heteroatoms with fluorine can provide an enormous impact on the biological activity of substrates. There is currently great demand for the development of new synthetic methodologies to obtain optically active pure isomers of fluorine containing substrates and in particular stereoselective approaches to 2-fluoroalcohols are important in numerous drug targets. In recent decades considerable progress has been made in controlling the stereochemistry of newly formed chiral centers by aid of interactions between carbonyls and polar neighboring groups (e.g. alkoxy, amine, thioethers etc.) with Lewis acids through chelation. In the present work, a series of 2-fluoroketones were synthesized and reduced with common reductants in the presence of $TiCl_4$ and $Ti(O\textit{i}Pr)_4$.The data shows two important features: (1) The identity of the Ti-based Lewis acid has a large impact on the diastereoselectivity of reduction

and (2) NMR (^{1}H, ^{13}C, ^{19}F) data are consistent with the presence of chelation between $TiCl_4$ and 2-fluroketones under conditions utilized in synthetic studies.

147. Sequential Birch reduction-allylation/Cope rearrangement for the enantioselective construction of carbocyclic quaternary stereogenic centers

William Malachowski, Bryn Mawr College, Bryn Mawr, PA

The enantioselective synthesis of carbocyclic quaternary stereogenic centers remains an important challenge in organic chemistry. We have developed a method for the efficient, enantioselective construction of carbocyclic quaternary stereocenters. The method combines the previously reported asymmetric Birch reduction-alkylation with the stereospecific Cope rearrangement. In sequence, the two reactions permit the efficient transfer of chiral information to enantioselectively create a new carbocyclic quaternary stereogenic center. Modifications of the o-anisic acid Birch reduction substrate or the alkylation group allows access to a range of carbocyclic quaternary centers with extremely high levels of stereocontrol.

148. Improving the Value of HTS

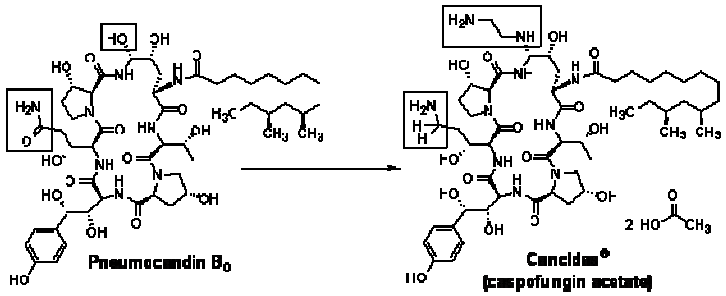
Peter Kotsonis, Novartis Institute for Biomedical Research, Cambridge, MA

Data generated from high throughput screening often needs to be integrated into meaningful information in order to effectively guide drug discovery. This involves interactions amongst a multi-disciplinary team of statisticians, modellers, screening biologists and, therapeutic area chemists for effective hit-lit provision and lead candidate identification. Here i will discuss some of the issues facing HTS and strategic ways of increasing the value HTS provides in drug discovery at Novartis.

149. Process Development and Synthesis of the β-1,3-Glucan Synthase Inhibitor Cancidas®

Kevin M. Belyk, William R. Leonard Jr., David A. Conlon, Ji Liu, Dean Bender and David L. Hughes, Merck Research Laboratories, Rahway, NJ

The echinocandins are a class of natural compounds that show potent activity against many pathogenic fungi by inhibition of the enzyme b-1,3-glucan synthase. Chemical modification of fermentation derived echinocandin Pneumocandin B_0 produced the antifungal drug Cancidas® that was found to be both well tolerated and efficacious in man. The synthesis requires chemical modification at two sites of the peptide core, a reduction of the primary amide to an amine, and condensation of the hemiaminal moiety with ethylenediamine. These two transformations presented significant synthetic challenges due to the need to control the chemo-, regio- and stereoselectivity while maintaining the integrity of the peptide core. The highlights of the synthesis include the stereoselective formation of a phenylthioaminal; a remarkable high-yielding one-step, directed, chemoselective borane reduction of the primary amide; and the stereospecific incorporation of ethylenediamine directly on the unactivated phenylthioaminal producing Cancidas® in a 45% overall yield.



Transition Metal Chemistry and Catalysis

Organizer: Alan S. Goldman Rutgers University, Piscataway, NJ

150. Steric Effects on the Kinetics of the Reductions of some Tetrakis(arylisocyanide)cobalt(II) complexes by pyridine in Trifluoroethanol Medium

Olayinka A. Oyetunji, Banyaladzi D. Paphane and Clifford A.L. Becker, University of Botswana, Gaborone, Botswana

The reductions of tetrakis(arylisocyanide)cobalt(II) complexes, $[Co(CNC_6H_3Me_2\text{-}2,6)_4(ClO_4)_2]$ (**A**), $[Co(CNC_6H_2Me_3\text{-}2,4,6)_4(ClO_4)_2]$ (**B**), $[Co(CNC_6H_3Et_2\text{-}2,6)_4(ClO_4)_2]$ (**C**), and $[Co(CNC_6H_3Pr_2\text{-}2,6)_4(ClO_4)_2]$ (**D**) by pyridine have been investigated in trifluoroethanol medium. Each complex is reduced to the corresponding pentakis(arylisocyanide)cobalt(I) complex as the final product. At 298.15K, **A**, **B**, **C** and **D** are reduced via similar mechanisms with observed rate constants, k_{obs} (in s^{-1}), being 12.4 x 10^{-4}, 6.7 x 10^{-4}, 2.9 x 10^{-4}, and 0.08 x 10^{-4}, respectively, at pyridine concentration of 3.30 x 10^{-3} M. The second order rate constants follow a similar trend. A proposed inner sphere electron transfer mechanism for these reactions involve fast ligand exchange followed by reduction of the cobalt(II) complexes. In each

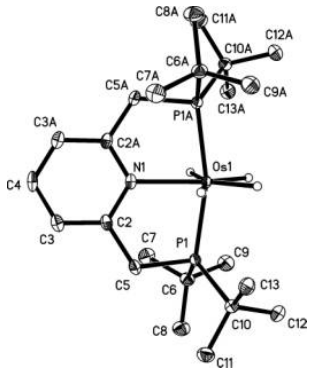
case, characterization of the final product show no evidence of coordinated pyridine. The relatively large activation parameters, enthalpies of activation, $\Delta H^{\#}$, and entropies of activation, $\Delta S^{\#}$, are also discussed for these reactions. Preliminary investigations on the reduction of a similar tetrakis(arylisocyanide)cobalt(II) complex, $[Co(CNC_6H_4Me\text{-}o)_4(ClO_4)_2]$, exhibited a rather different kinetics where the observed rate constant, k_{obs} , decreased with increasing concentrations of pyridine.

Key words: Reduction, kinetics, tetrakis(arylisocyanide)cobalt(II), pyridine, mechanism.

151. A Series of Iron and Osmium Pincer Complexes

Elizabeth M. Pelczar, Thomas J. Emge and Alan S. Goldman, Rutgers, The State University of New Jersey, Piscataway, NJ

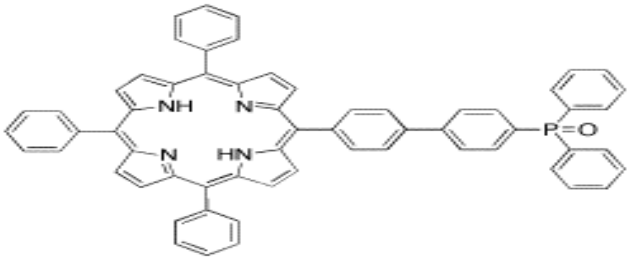
Pincer-ligated complexes of iridium (e.g. $(PCP)IrH_n$; PCP = 2,6-$C_6H_3(PR_2)_2$) are the most effective catalysts to date for the homogeneously catalyzed dehydrogenation of alkanes. We have begun an investigation of the isoelectronic group 8 PNP series (PNP = 2,6-bis(dialkylphosphinomethyl)pyridine). Toward this end, two new paramagnetic complexes ($(^{tBu}PNP)MCl_n$ (M = Fe, n = 2; M = Os, n = 3) have been synthesized as potential catalyst precursors. $(^{tBu}PNP)FeCl_2$ has been converted to $(^{tBu}PNP)Fe(CO)_2$ in the presence of CO and excess NEt_4BH_4. Reduction of $(^{tBu}PNP)OsCl_3$ with $NaEt_3BH_4$ yields the tetrahydride complex, $(^{tBu}PNP)OsH_4$. Investigations of the structure and catalytic activity of the osmium tetrahydride will be discussed.



152. Selective cleavage of the C-C bond of aminoethyl groups by a pincer iridium complex

Xiawei Zhang[1], Thomas J. Emge[2], Rajshekhar Ghosh[2] and Alan S. Goldman[2], (1)Cornell University, Ithaca, NY, (2)Rutgers University, Piscataway, NJ

The ability to cleave “unactivated” C-C bonds, particularly with regioselectivity in a functionalized organic molecule, remains a major challenge to organic and inorganic chemists. We report the reaction of a pincer-ligated iridium complex (PCP)Ir with N-ethyl-amines, HN(Et)R (R = cyclohexyl, t-butyl, ethyl), to give the corresponding iridium isocyanide complexes $(PCP)Ir(CH_3)(H)(CNR)$ (PCP = □^{3}-2,6-($^tBu_2PCH_2)_2C_6H_3$). This novel, regioselective, C-C bond cleavage reaction occurs readily under mild conditions (25 - 45 °C). The reaction is shown to proceed via initial dehydrogenation of the amine to give the corresponding imine (N-ethylidene-alkylamine). The ethylidene sp^2 C-H bond then undergoes oxidative addition to iridium, followed by methyl migration. The latter step is an unusual example of an isocyanide deinsertion to give a new M-C bond.



153. Mechanistic study of acetylene dimerization: insertion of phenylacetylene into Ir-H versus Ir-C bonds

Rajshekhar Ghosh, Xiawei Zhang, Thomas J. Emge and Alan S. Goldman, Rutgers University, Piscataway, NJ

The pincer-ligated iridium fragment (PCP)Ir (PCP = k^3- $C_6H_3[CH_2P^tBu_2]_2$) undergoes oxidative addition of the acetylenyl C-H bond of phenylacetylene to give [(PCP)Ir(CCPh)H] (**1**). This complex reacts with a second equiv of phenylacetylene to give the (PCP)Ir-pi-bound phenylacetylene dimer (enyne), [(PCP)Ir{PhCC-C(H)C(H)Ph}] (**2**). At least two different

pathways are, a priori, plausible for this dimerization: (a) 1,2-insertion of the second equiv of phenylacetylene into the Ir-H bond, followed by C-C elimination to release the enyne, or (b) 1,2-insertion into the Ir-acetylide bond, followed by C-H elimination. Mechanistic study reveals that {(PCP)Ir(CCPh)[C(Ph)=CH_2)]} (**3**) is formed rapidly (presumably via 2,1-addition of the Ir-H bond), but *reversibly*, as a side product. The reverse reaction is a very rare example of a vinyl complex liberating an acetylene (via beta-H elimination). The enyne that would result from C-C elimination from **3** (H_2C=C(Ph)-CCPh) is *not* observed. A product which appears to be that expected from the 1,2-insertion of the second phenyl acetylene into the Ir-H bond, [(PCP)Ir(CCPh)(CH=CHPh)], is observed to form *subsequent* to the formation of the complex **2**; this stable complex therefore cannot be an actual intermediate in the formation of **2**. We propose that the enyne complex **2** is formed by insertion of the second equivalent of phenyl acetylene into the Ir-acetylide bond of **1**.

154. Selective activation of aryl and vinyl C-H bonds adjacent to coordinating groups. Not chelation-assisted

Xiawei Zhang, Patrick D. Achord, Thomas J. Emge, Mira Kanzelberger, Karsten Krogh-Jespersen and **Alan S. Goldman**, Rutgers University, Piscataway, NJ

The site-directed functionalization of C-H bonds includes perhaps the most useful results to date in the field of organometallic C-H bond activation. This reaction class has been particularly well developed by the group of Murai and Chatani, and important new developments are appearing at an increasingly rapid rate. It is widely assumed that site-directed C-H bond functionalization involves chelation-assisted C-H bond activation. We present experimental and theoretical results, however, indicating that this is not necessarily the case. The "pincer" complex (PCP)Ir oxidatively adds the aromatic C-H bonds of substrates such as acetophenone and nitrobenzene to give cyclometallated products, with an apparent 100% selectivity for the position ortho to the coordinating group. Structural and mechanistic studies reveal, however, that the “directing” group coordinates to iridium *subsequent* to C-H addition. Theoretical studies support this conclusion and extend it to ruthenium (Murai/Chatani-type) complexes. Calculations (DFT) also shed light on the surprisingly high stability of the cyclometallated products and, in the case of the ruthenium catalysts, on the subsequent functionalization chemistry. In particular, metalloaromaticity appears to play a key role, stabilizing the cyclometallated products yet activating them with respect to C-C elimination.

155. Metalloaromaticity: Novel examples and an unexpected role in the site-selective functionalization of C-H bonds by ruthenium complexes

Patrick D. Achord, Xiawei Zhang, Karsten Krogh-Jespersen and Alan S. Goldman, Rutgers University, Piscataway, NJ

The site-directed functionalization of C-H bonds, typically aromatic or vinylic hydrogens adjacent to a coordinating group, is an area of rapidly growing importance. This reaction class has been particularly well developed with ruthenium catalysts by the group of Murai and Chatani. It is widely assumed that such site-directed C-H bond functionalization involves chelation-assisted C-H bond activation. Our group has obtained both computational and experimental results demonstrating that the formation of cyclometallated C-H addition products can proceed via C-H addition prior to functional group coordination. The resulting cyclometallated species are surprisingly stable and there is strong evidence that this stability is due, at least in part, to metalloaromaticity. Catalytic functionalization requires that any such intermediates undergo secondary reactions; in spite of their very favorable thermodynamics of formation, the putative metalloaromatics are particularly susceptible to C-C elimination, as predicted by calculations in which the Murai/Chatani ruthenium system is modeled.

156. Coordination Structural Shifts and Oxidation State Control in Dinuclear Complexes

Yilma Gultneh[1], Yohannes, T. Tesema[1], Teshome B. Yisgedu[1], Raymond J. Butcher[1], Guang-bin Wang[2] and Gordon Yee[2], (1)Howard University, Washington, DC, (2)Virginia Polytechnic Institute and State University, Blacksburg, VA

The dinuclear complexes of the ligand 2,6-bis{[(2-(2-pyridyl)ethyl)(2-pyridylmethyl)-amino]-methyl}-4-methylphenol) (LOH) [Mn2(II,II)(LO)(m-OOCCH3)2]ClO4 (1) and [Mn2(II,III)(LO)(m-OOCCH3)2](ClO4)2 (2) have been characterized structurally, electrochemically and magnetically. The structural parameters show evidence of an extended pi-bonding system involving the phenolate ring, C-Oph-Mn(II)-Npy. In addition, on one-electron oxidation of 1, the coordination rearrangements that stabilize the Mn(III) formed, are transmitted via the bridge which cause coordination rearrangements at the second manganese ion that make the +3 state of the latter unstable to reduction to Mn(II). Variable temperature magnetic susceptibility measurements of 1 and 2 over the temperature range of 1.8 K to 300K can be modeled with magnetic coupling constants -J /k = 6.2 cm-1 and 5.8 cm-1 showing the weak antiferromagnetic coupling between the two manganese ions in each dinuclear complex.

Transporters

Official: Jerome H. Hochman Merck and Co., West Point, PA

157. Perspectives into the Molecular and Functional Characteristics of Intestinal Oligopeptide Transporters

Gregory T. Knipp, Rutgers, the State University of New Jersey, Piscataway, NJ

Peptide-based drugs are increasingly being utilized for the therapeutic intervention of many disorders including AIDS, hypertension, and cancer. The gastrointestinal absorption of small peptide-based agents may be significantly influenced by their affinity for proton-coupled, oligopeptide transporters (POT). Considerable focus has been traditionally placed on Peptide Transporter 1 (PepT1) since it was the first identified human POT and is expressed in the intestine. Recent evidence suggests that Peptide/Histidine Transporter 1 (PHT1) may also play a role in the intestinal absorption of peptides. Results from preliminary investigations into the mRNA and protein expression of PepT1 and PHT1 in the human intestine will be discussed. In addition, the development and characterization of stably transfected MDCK/hPepT1-V5/His clonal cell lines with varying expression levels (low, medium and high) of epitope-tagged hPepT1 have been utilized to quantify the relationship between hPepT1 expression and its functional kinetics. Uptake and transport kinetics of glycylsarcosine, carnosine, benzylpenicillin, aminolevulenic acid and valacyclovir were determined to delineate hPEPT1-mediated kinetics for each substrate. These studies demonstrated that the MDCK/hPepT1-V5/His clonal cells may be a more useful model for screening hPEPT1 affinity of peptide-based. Finally, human PHT1 transiently transfected into COS-7 cells demonstrate a sodium independent, proton dependent affinity for histidine and carnosine, but no affinity for glycylsarcosine. These results provide new insights into the molecular and functional significance of POT members in the human gastrointestinal tract and provide a framework for future studies focused on elucidating the interplay between their physiological expression and substrate-structure relationships necessary for the absorption of peptide-based agents.

158. Application of drug transport studies to drug discovery and development

Masayo Yamazaki, Merck and Co., West Point, PA

Recently, carrier-mediated transport pathways and specific transporters have been recognized as important determinants of drug disposition and potential targets of drug-drug interactions (DDIs). In the past decade, the availability of in vitro P-glycoprotein (P-gp) overexpressing cells and P-gp deficient mice has paved the way for the investigation of P-gp's role in pharmacokinetics and certain DDIs. P-gp appears to play a major role in the brain penetration of many CNS-acting compounds. In acknowledgment of the importance of P-gp, many pharmaceutical companies have incorporated P-gp assays into early drug discovery and development processes. This presentation will describe our experience using in vitro and in vivo P-gp assays and show how the data from these studies are interpreted with focus on two fundamental questions: (1) Can animal data be directly scaled up to humans? (2) Can in vitro data be accurately extrapolated to the in vivo situation? Application of in vitro drug transport studies to address clinically significant DDIs will also be presented. We examined the effects of fibrates (antilipidaemic) on human organic anion transporting polypeptide 1B1 (OATP1B1), multidrug resistance protein 2 (MRP2), and P-gp to determine if fibrates have the potential to cause DDIs by inhibiting these transporters. Our results showed it is unlikely that fibrates cause any significant DDIs by affecting either MRP2- or P-gp-mediated transport. Some fibrates showed concentration-dependent inhibition of OATP1B1; however, considering the plasma protein binding and IC50 values on OATP1B1 only gemfibrozil appears to have a potential to cause DDIs by inhibiting OATP1B1 at clinically relevant concentrations.

159. Role of Hepatic Transporters in the Disposition of Rosuvastatin

Liyue Huang, AstraZeneca, Wilmington, DE

Drug transporters expressed in the liver play a significant role in the drug disposition of statins, HMG-CoA reductase inhibitors. Rosuvastatin is mainly excreted into bile as parent. It has been shown that rosuvastatin is taken into liver by a carrier-mediated uptake mechanism and has been identified as a substrate for OATP-C/OATP1B1 and other OATPs. However, it is unknown if rosuvastatin is transported by ATP-dependent transporters MDR1/ABCB1, MRP2/ABCC2 and BCRP/ABCG2 expressed at the canalicular membranes. In the present study, we demonstrated that ATP dramatically stimulated rosuvastatin transport in membrane vesicles expressing BCRP. BCRP appears to have two binding or transport sites for rosuvastatin with Km = 14 μM for the high affinity site. In contrast, no directional transport of rosuvastatin across MDR1-MDCK cell monolayers and no ATP-dependent transport in the membrane vesicles isolated from the same cells were observed. No MRP2-mediated transport of rosuvastatin in Sf9 membranes was observed. Pharmacokinetic drug-drug interactions between statins and gemfibrozil or cyclosporine have been reported. We further evaluated the effect of selected drugs from clinical drug interaction trials on rosuvastatin uptake in rat hepatocytes and ATP-dependent transport of rosuvastatin in membrane vesicles expressing BCRP. The results suggest that (1) BCRP may contribute to rosuvastatin disposition; and (2) the inhibition of transporters by gemfibrozil and cyclosporine may contribute to the drug-drug interactions observed in the clinic.

160. Functional Characterization of a Hepatic Organic Anion Transport Model; OATP1B1 and MRP2 Double Transfected MDCKII cells

Kelly Bleasby, Richard Edom and Raymond Evers, Merck and Co., Rahway, NJ

Elimination of compounds from blood into bile is a two-step process; after being taken into the hepatocyte across the sinusoidal membrane, they are effluxed across the canalicular membrane, into the bile. For lipophilic compounds this process may be achieved by passive diffusion, however for amphipathic compounds, with low diffusion rates, transporters are thought to be involved.

Previous studies suggest that recombinant cell lines differentially expressing transporters in apical and basolateral membranes are useful for the study of hepatic vectorial transport. In the present study, one such model was developed. MDCKII cells were stably transfected with OATP1B1 (SLCO1B1, OATP2, OATP-C) and MRP2 (ABCC2) and grown on semi-permeable supports, to form polarized cell monolayers expressing OATP1B1 in the basolateral membrane and MRP2 in the apical membrane.

Bidirectional transport studies demonstrated that compounds with very low passive permeabilities, e.g. E217βG, were efficiently transported by MDCKII-OATP1B1+MRP2 monolayers, but not by cells transfected with OATP1B1 or MRP2 alone. In contrast, rifampicin and cyclosporine A, which have moderate passive permeabilities, were transported across MDCKII-MRP2 and MDCKII-OATP1B1+MRP2 monolayers at similar rates, despite being previously identified as substrates and inhibitors of OATP1B1 respectively.

In conclusion, this doubly transfected MDCKII-OATP1B1+MRP2 cell line will serve as a useful tool in the identification of substrates and inhibitors and in assessing the role these transporters play in the hepatic elimination of drug candidates. Furthermore, based on a number of compounds tested, our data suggest that uptake transporters are likely to be rate determining only for compounds with a relatively low passive permeabilities.

161. Towards an understanding of organic anion transporters: structure-function relationships

Guofeng You, Rutgers University, Piscataway, NJ

Organic anion transporters (OAT) play essential roles in the body disposition of clinically important anionic drugs, including anti-viral drugs, anti-tumor drugs, antibiotics, anti-hypertensives, and anti-inflammatories. The activities of OATs are directly linked to drug toxicity and drug-drug interactions. So far, four members of the OAT family have been identified: OAT1, OAT2, OAT3 and OAT4. These transporters share several common structural features including 12 transmembrane domains, multiple glycosylation sites localized in the first extracellular loop between transmembrane domains 1 and 2, and multiple phosphorylation sites present in the intracellular loop between transmembrane domains 6 and 7, and in the carboxyl terminus. The impact of these structural features on the function of these transporters has just begun to be explored. Dr. You will summarize recent progress made from her laboratory as well as from others, on the molecular characterization of the structure-function relationships of OATs, including particular amino acid residues/regions of the transporter protein ("molecular domains") that potentially determine transport characteristics.

Undergraduate Poster Session

Organizer: Susan Ensel Hood College, Frederick, MD

162. Saliva of Humans and Animals as an Alternative Biofluid for NMR-Based Metabonomic Investigations and Diagnostics

Teresa A. Soroka[1], István Pelczer[1], Sarah Ralston[2] and Elissa Lappostato[2], (1)Princeton University, Princeton, NJ, (2)Rutgers University, New Brunswick, NJ

Urine, blood, and cerebrospinal fluid are the primary biofluids for metabolic fingerprinting of higher level organisms. Saliva is mentioned in metabonomic reviews as an alternative biofluid but there are few publications to demonstrate its possible applications. We recognize saliva as an attractive alternative-biomaterial that is specific and easy-to-access. It can reliably reflect an organism's overall condition and has the potential to provide insight into different physiological and pathological states. Our pioneering research program is using NMR and horse saliva to test our perspective that the alternative biomaterial can be used for early diagnosis of various conditions including onset of infectious disease. The focus is on parallel metabolic analyses of the full saliva and low molecular weight (LMW) extracts. A well documented set of twelve weanlings have allowed us since September of 2004 to assess the various technical details of collecting, handling, and analyzing saliva.

163. Determining the Preferential Interaction Parameter: A Study of Salt Effects on DNA Oligonucleotides

Erica R. Bush and A. P. Williams, Princeton University, Princeton, NJ

DNA is a polyelectrolyte, a long-chain polymer with many ionizable sites. According to polyelectrolyte theory, over limited distances along the DNA chain, electrical charges are modeled as a linear array of a well-defined charge density. By *definition*, if the axial charge density parameter of a molecule becomes greater than 1, counterions will condense on the polyelectrolyte to lower the effective value of the charge density parameter to 1. The preferential interaction parameter

(PIP) is a parameter that is proportional to the axial charge density of the polymer chain. We report PIP values for a series of oligonucleotides of varying lengths. Equilibrium dialysis, UV spectroscopy, and capillary electrophoresis of solutions of 14, 20, 28, 34, and 160 base single strands and duplexes in 1.0 mM Na+ were performed to determine PIP as a function of DNA length. Results show that as the oligonucleotide length increases, the value of the average axial charge density increases as well. This observation is consistent with predictions based upon counterion condensation theory.

164. DNA Oligonucleotide Functionalized γ-Fe_2O_3 Core/Au Shell Nanoparticles as a Means of Selective Magnetic Separations of Mixtures of DNA

Rebecca A. Grimme[1], John N. Richardson[1] and Mary Elizabeth Williams[2], (1)Shippensburg University of Pennsylvania, Shippensburg, PA, (2)The Pennsylvania State University, University Park, PA

At present, both colloidal gold and magnetite (γ-Fe_2O_3) nanoparticles are of use in biological applications. The unique ability for gold nanoparticles to undergo many different surface modifications, including the binding of DNA oligonucleotides (oligos), lends to their use in biological sensing techniques. γ-Fe_2O_3 nanoparticles are susceptible to external magnetic fields and thus have been used in site-specific inactivation of cancerous cells, magnetic cell sorting, and immunoassays. However, the use of γ-Fe_2O_3 particles is limited due to their instability in solutions of physiological pH. γ-Fe_2O_3 core/Au shell nanoparticles have been synthesized yielding the benefits of both γ-Fe_2O_3 and gold nanoparticles. This paper discusses our efforts toward the use of γ-Fe_2O_3 core/Au shell nanoparticles with DNA oligo surface modifications as a means of selectively separating a biological solution comprised of complementary and half complementary fluorescently tagged DNA oligos with detection via fluorescence spectroscopy.

165. Interaction of N-methylmesoporphyrin IX NMM with Quadruplex DNA formed from S.cerevisae Telomeric Sequences

Erum Azeez and **Mahrukh Azam**, West Chester University, west chester, PA

Telomeres are part of the DNA present at the end of chromosomes and are shown to form the secondary structures, called as G- Quadruplex DNA, that are different than the conventional duplex form of DNA. It is suggested that telomeres may play a role in the normal aging process through the formation of these structures. We have explored the formation of G-DNA from telomeric sequences in S.cerevisiae and their interaction with N-methylmesoporhyin IX NMM. NMM is highly specific to G-DNA and has been used as a probe for G-DNA formation in yeast cells. Although it is specific to G-DNA only and has provided the evidence for potenital G-DNA existence in vivo, its mechanism of interaction with G-DNA is not clear yet. Here we explore the nature of such a mechanism.

166. Liposomes within Giant Vesicles: Methods of Preparation and Characterization

Laura Elbakry, Shaila Zaman, Dwight Campbell and Sergey V. Kazakov, Pace University, Pleasantville, NY

Living cells and their organelles contain a developed membrane system consisting of the single, double, and network membrane compartments. Nowadays, there is no reliable and reproducible technology for preparation of membrane structures mimicking various functions of biological membrane systems. The objective of this research is to examine one of the lipid membrane/membrane structures: liposomes within giant vesicles. In the framework of this work, it is important to have practical and reproducible methods of preparation and characterization of both large unilamellar liposomes (LUV, ~50-300 nm) and giant unilamellar vesicles (GUV, ~20-150 um). Different procedures for the preparation of giant vesicles are analyzed and examined in terms of the reproducible size distributions. A feature of the membrane system is a possibility of independent variation of the LUV and GUV stability. Factors affecting the lipid membrane stability are analyzed and tested. Microscopic and light scattering methods are used for characterization of the liposomal systems. Three ways of introducing LUVs into a GUV are discussed and compared experimentally.

167. Time Resolved Exchange of Protons in Polymer Networks

Korki M. Miller and Sergey V. Kazakov, Pace University, Pleasantville, NY

The hypothesis that cell function resembles gel function and the concept of a gel-like cytoplasm have been more and more recognized nowadays. Since a cytoplasmic protein-ion-water matrix and an ordinary gel operate by the same working principle of an ionic reservoir, the kinetics of ion exchange in the artificial polymer hydrogels can be used to model some cell biological functions. Moreover, the ion-sensitive polymer networks themselves are of great potential for a new generation of environmentally responsive elements. The time-resolved measurements of the ion concentration in the exterior to the hydrogel particles of different sizes were carried out to study the mechanical and electrochemical behavior of the pH-responsive polymer networks. The kinetics of establishing an equilibrium pH in external suspension of macrogels and microgels was recorded and the size-dependent parameters of protonation/deprotonation in the studied polymer network were analyzed.

168. Probing the Interactions of a Guanidinium Ion with Water

John Landers and Margaret Mandziuk, Manhattan College, Riverdale, NY

Guanidine is of prime importance in biochemical applications. It is very often used as a 'cold' denaturant of proteins. As an arginine residue it plays an important role in molecular recognition, catalysis, and bonding of protein domains. Guanidinium ion is known to be one of the strongest bases, with a pK_a of 13.6. This high pK_a value, however, is not accounted for by the stabilization due to the Y-conjugation of the ion. It has been suggested that the high pK_a value of guanidinium ion is due to its solvation shell. Solvation of the guanidinium ion has been studied only at the classical level, with continuum solvation models or simulated with classical force fields. These methods, however, are not capable of representing the exchange of guanidinium protons with the solvent. Unfortunately, the size of the ion precludes at the moment ab-initio or DFT calculations at a sufficiently high level to reliably represent intermolecular interactions with enough water molecules to credibly represent its solvation shell. A step-wise procedure of sampling the interaction of the guanidinium ion with an increasing number of water molecules must be adopted.

We probe the interactions of a guanidinium or protonated guanidinium ion with a water molecule using the B3LYP density functional with the cc-pVTZ and aug-cc-pVTZ basis sets. Several stationary points on the potential energy surface are characterized. Our results suggest a reason for the unexplained peak at 1.8 A in the neutron diffraction studies by Mason et al. [PNAS 100 (2003) 4557].

169. Mycotoxin: An FDA Concern

Jian Yang[1], Paris Svoronos[1], Kathryn Emanuele[2] and Vincent DiProssimo[2], (1)Queensborough Community College, Bayside, NY, (2)Food and Drug Administration, Jamaica, NY

Mycotoxin, a poisonous substance produced by a fungus or mold, has been a major FDA concern over the past several decades. Its tendency to cause cancer and many adverse health effects such as damage to the vascular, digestive, respiratory, nervous, cutaneous, urinary, reproductive, and immune systems, had led the scientists to test and place regulations on all foreign and domestic food products that may contain illegal concentrations of mycotoxin, which will cause serious health problems to consumers. Out of more than eighty types of mycotoxins, five of the major FDA concerns include Aflatoxin, Patulin, Fumonisin, Ochratoxin A, and Deoxynivalenol (DON), also known as Vomitoxin. Some of the food products that the FDA had been testing include many types of grain, flour, nuts, edible seeds, fruits, milk, and any other food products that contain these things. Since mycotoxin is a very toxic substance, precautions had to be made and followed while working with them. In this presentation the procedure for the isolation of the various Mycotoxins will be presented.

170. Exploring Protein Structure in a Biochemistry Laboratory Experiment

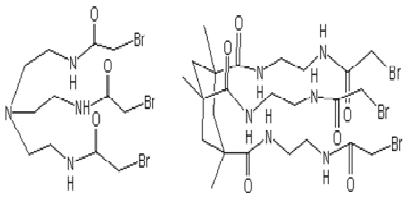
Lisa Christadore[1], Dean Del Geurcio[2] and Amber Flynn Charlebois[2], (1)Loyola College, Baltimore, MD, (2)William Paterson University, Wayne, NJ

In an effort to explore the effect of changes in the three-dimensional or tertiary structure of a protein we are developing an advanced biochemistry laboratory experiment. Specifically we are looking at the separation of a relatively small protein (bovine pancreatic tripsin inhibitor, BPTI) in its native state and in its modified state where all the disulfide bonds are reduced. We have compared the two forms of the protein using SDS polyacrylamide gel electrophoresis (PAGE) and plan to explore the differences using reverse phase liquid chromatography (HPLC). Preliminary results indicate that the two forms of BPTI migrate differently by SDS PAGE and it is expected that they will also be distinguishable by HPLC. Using these two methods of separation as investigative tools will demonstrate to the students the importance of disulfide bonds in protein structure, the techniques used to break disulfide bonds, and give them experience using HPLC instrumentation and SDS gel electrophoresis.

171. Synthesis of Amino Acid Derivatives of Flavins

Karen R. Hatwell, Anthony A. Debraccio, Jeanette M. Krug and Kimberly L. Still, Villa Julie College, Stevenson, MD

Flavins are found in the active site of APS reductase, an enzyme involved in the dissimilatory sulfate reduction of sulfate to sulfide used by sulfate reducing bacteria in the terminal electron step of their energy production pathway. To mimic this process, our group has synthesized and analyzed several flavin derivatives with amines and amino acids in the R positions, as pictured below. These derivatives will be tested with APS and compared kinetically to the APS reductase found naturally. In this poster, we will present our preliminary results.

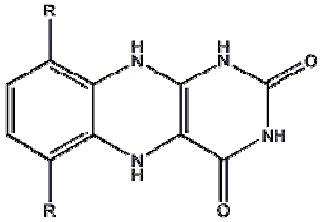


1. TREN-Br 2. KTA-Br

172. Amination of a Flavin Compound

Karen R. Hatwell, Tamara C. Ford, Nicole A. Hammerbacher and Justin W. Young, Villa Julie College, Stevenson, MD

Flavins are found in the active site of APS reductase, an enzyme involved in the dissimilatory sulfate reduction of sulfate to sulfide used by sulfate reducing bacteria in the terminal electron step of their energy production pathway. To mimic this process, our group has synthesized and analyzed several flavin derivatives with amino acids in the 6,9 positions. The amino acids are attached to an amine precursor using a BOC coupling. To improve this reaction, several catalysts have been tested to attempt to improve on the synthesis of the 6,9-diaminoisoalloxazine compound, pictured below. In this poster, we will present our preliminary results.



173. Computational Prediction of Spontaneous Thermal Resolution in Racemic Biaryl Atropisomers

Japeth Demetria, **King Tse** and Dale E. Vitale, Kean University, Union, NJ

The torsional energy barriers and dimer dissociation energies for the racemic compounds and conglomerates of fifteen (15) biaryl atropisomers were calculated by extrapolation at the PM3 level of theory. Of the compounds studied II-IV, VI, VIII, IX, X, XIII and VX had computed torsional energy barriers within 1.3 kcal/mol of that of 1,1'-binaphthyl (I, experimental, 22.5kcal/mol). The calculated conglomerate and racemic compound dimer dissociation energies for 1,1'-binaphthyl were 1.71 kcal/mol and 2.53 kcal/mol, respectively at 298.15 K. Qualitatively, compounds I, VI, VII, VIII, IX and X had similar values.

174. Electronic and Geometric Effects of the Cyclopropyl Group in Liquid Crystal Formation

Gretchen E. Repaal and George Lorenzo, Eastern University, St. Davids, PA

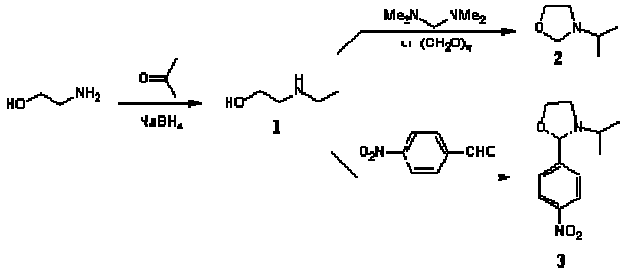
Electronic and geometric effects of cyclopropane with regards to liquid crystals were studied by varying the position of the cyclopropyl group in the terminal chain of some simple model aromatic Schiff base compounds. The terminal cyclopropylbenzene group was compared to the terminal benzene group to the electronic affects of the cyclopropyl group on the extended conjugation of the system. To consider geometry effects 1,1-disubstituted cyclopropane and a 1,2-trans-cyclopropane end groups in a conjugated system were compared. The liquid crystalline properties determined were used in conjunction with computer modeling to possibly use the information as a predictive tool for new, more complex, liquid crystals containing the cyclopropyl moiety.

175. Reductive Isopropylation of Ethanolamine Followed by Condensation with Aldehydes: Observation of Enantiotopic and Diastereotopic Nuclei in the ^{1}H and ^{13}C NMR Spectra of Achiral and Chiral Oxazolidines

Shahrokh Saba, **Jennifer Espinal**, James A. Ciaccio and Courtney E. Aman, Fordham University, Bronx, NY

2-Isopropylaminoethanol (**1**) was prepared in 75% yield by reductive isopropylation of ethanolamine using acetone and $NaBH_4$. Treatment of **1** with paraformaldehyde or *N,N,N',N'*-tetramethylamionomethane afforded 3-isopropyoxazolidine (**2**) in quantitative yields. Similarly, 3-isopropyl-2-(4-nitrophenyl)oxazolidine (**3**) was prepared quantitatively by condensation

of **1** with 4-nitrobenzaldehyde. The ^{1}H and ^{13}C NMR spectra of compounds **2** and **3** clearly display the enantiotopic and diastereotopic nuclei of the methyl groups in these compounds, respectively.



176. Synthesis and Solution Property Study of Amphiphilic Star-shaped Macromolecules

Anthony A. Argenti, Kelly Chang, Jinzhong Wang and Kathryn E. Uhrich, Rutgers University, piscataway, NJ

The Amphiphilic Star-shaped Macromolecules (ASMs) were synthesized from an alkyl based core and Poly (ethylene glycol) (PEG) corona. The hydrophobic core was prepared by Michael addition of pentaerythritol Tetraacrylate with 4-aminothiophenol, then coupled to acylated mucic acid. Methoxyl and carboxylic acid terminated PEGs were then attached as hydrophilic arms. The ASMs form micelles in aqueous solution. By changing the length of the PEG and size of alkyl chain in the core, we alter the Hydrophilic-Lipophilic balance of the micelle. Amphiphilic star shaped macromolecules in water solution were then tested for a number of physical properties. Dynamic laser scattering was used to detect the particle sizes of ASMs in varied pH solutions. Critical micelle concentration was used to investigate aggregation behavior by spectroflourimeter using a pyrene probe molecule. Solubility studies were also completed using UV in PBS buffer solution. Amphiphilic star-shaped Macromolecules can potentially be used as drug transports systems, to enhance solubility and control release.

177. Alternate Method for the Synthesis of Salicylate-Based Poly(Anhydride-Ester) Precursors

Kelly Chang and Kathryn Uhrich, Rutgers University, Piscataway, NJ

In the hydrolytic degradation of salicylate-based poly(anhydride-esters), the monomer precursor or diacid is produced, which further breaks down into salicylic acid and a carboxylic acid. Current protocol for the preparation of a diacid, the monomer precursor, involves coupling of two salicylate molecules with an acyl chloride in the presence of a base (pyridine). This method requires an acyl chloride, which is synthesized when not commercially available.

This work investigates a new synthetic pathway to prepare salicylate-based diacids directly from dicarboxylic acids. This approach eliminates the need to prepare the acyl chloride, thereby reducing the overall number of steps. The new method involves the formation of a reactive intermediate in situ, which is produced when the dicarboxylic acid reacts with dicyclohexylcarbodiimide (DCC) and dimethylaminopyridine (DMAP). The reactive intermediate reacts with the free phenolate in a single step to yield the desired monomer precursor.

By exploring an alternate synthetic method to prepare salicylate-based diacids, the coupling capabilities of salicylates and carboxylic acids are broadened. Therefore, a wider range of salicylate-based poly(anhydride-esters) can be obtained for drug delivery applications.

178. Reactivity of Tri(trimethylsilyl)phosphite: Reaction with alpha-lactam

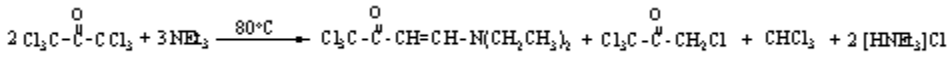
Jian Yang[1], Ralph Stephani[2] and Luis Vargas[1], (1)Queensborough Community College, Bayside, NY, (2)St. John's University, Jamaica, NY

1,3-di-tert-butyl alpha-lactam was synthesized and the reaction with Tris(trimethylsilyl)Phosphite (TMSP) is reported. The identification of the products will prove the type of cleavage of alpha-lactam, and the possibilities of having medicinal activities.

179. The Reaction of Triethylamine with Hexachloroacetone: Synthesis, Structure, Characterization and Mechanistic Study of *trans*-1,1,1-Trichloro-4-N,N-Dimethylamino-3-Buten-2-One

Ji In Kang and Jun H. Shin, Queensborough Community College, Bayside, NY

Carbon-hydrogen bonds of triethylamine were activated by hexachloroacetone to give trans-1,1,1-trichloro-4-N,N-dimethylamino-3-buten-2-one, $Cl_3CC(O)CH=CHNEt_2$. The compound has been characterized by spectroscopic methods, and the molecular structure has been determined by X-ray diffraction. A mechanism for the reaction has been proposed, and it may involve 1,1,1,3-tetrachloroacetone, chloroform and triethylammmonium chloride as side products.



180. Selectfluor Mediated Rearrangements of Azabicyclic Halides: Ring Size, Halide, and Positional Effects on Neighboring group Participation

Ryan A. Centafont, Grant Krow and Deepa Rapolu, Temple University, Philadelphia, PA

The utility of Selectfluor to facilitate neighboring group participation in 6-*exo*-7-*anti*-diheteroatom-functionalized-2-azabicyclo[2.2.1]heptanes and 4-*exo*-8-*anti*-diheteroatom-functionalized-6-azabicyclo[3.2.1]octanes was investigated. In selected cases Selectfluor was found to be a nonmetallic alternative to mercury or silver salts.

181. Neighboring Group Carbamate Participation in the Synthesis and Reactions of Dibromo- and Bromo-hydroxy-2-azanorbornanes

Kevin C. Cannon[1], Asha Mathews[1], Nini L. Garcia[1], Chirdeep K. Patel[1], Ryan A. Centafont[2] and Grant R. Krow[2], (1)Penn State Abington, Abington, PA, (2)Temple University, Philadelphia, PA

Stereoselective syntheses of novel 6-*exo*-7-*anti*-difunctionalized-2-azabicyclo[2.2.1]heptanes containing hydroxy and bromo substituents have been carried out by addition/rearrangement of dihalides or halohydrins to 2-azabicyclo[2.2.1]hept-5-enes. Subsequent substitution of bromo substituents by hydroxyl groups with retention of configuration was accomplished using Selectfluor and HgF_2.

182. Carbamate Pesticide Decomposition Using UV-Vis Spectroscopy

Christopher Divito and Clare N. Muhoro, Shippensburg University, Shippensburg, PA

Carbamates are esters of carbamic acids and receive widespread agricultural use as fungicides and insecticides. Under aqueous conditions and ambient temperature, we have found that the carbamate formetanate hydrochloride is robust in acidic media, partially stable under neutral pH and unstable under basic conditions. We have identified the products of decomposition under basic conditions and propose a tentative pathway for their formation. Kinetic data are consistent with a mechanism involving base-catalyzed hydrolysis of the carbamate. We report our findings on formetanate hydrochloride degradation monitored via UV-Vis spectroscopy over a range of basic pHs.

183. Solvent-Free Malonic Ester Synthesis by Mechanochemical Methods

Tristan E. Colestock and Joel M. Ressner, West Chester University, West Chester, PA

A method for reacting malonic ester with alkyl halides at room temperature under mild conditions and in the absence of solvent using mechanochemical action has been developed. Rates of reaction have been found to depend on the efficiency of grinding. The effect of other variables (temperature, amount of phase-transfer catalyst, amount of grinding media) will also be presented.

184. Using NMR Spectroscopy to "Discover" Organic Chemistry

Megan James, Holly Haley and Susan Ensel, Hood College, Frederick, MD

Organic chemistry labs typically take students through a series of well-planned steps, allowing for little thought or creativity. Discovery-based, guided inquiry pedagogy removes the cookbook and forces the student to examine and discover the underlying chemical principles. The general chemistry course at Hood College has been inspiring students for years with this methodology and we will now present organic chemistry lab experiments that have been designed in this manner. The new labs presented on this poster take advantage of our NSF-funded Anasazi 60 MHz NMR spectrometer to determine product identity. One experiment utilizes DEPT spectroscopy to help uncover Markovnikov's Rule while another experiment incorporates ^{13}C NMR spectroscopy to investigate substituent directing abilities in EAS reactions.

185. Determination of the Isoelectric Point of Various Amino Acids in Aqueous Solutions Using ^{13}C NMR Spectroscopy

Sabrina M. Song[1], Jun H. Shin[1] and Gopal Subramaniam[2], (1)Queensborough Community College, Bayside, NY, (2)Queens College, Flushing, NY

The isoelectric points (pI) of amino acids have been determined by ^{13}C NMR spectroscopic method using Anasazi EFT 60 MHz FT-NMR Spectrometer. All spectroscopic data have been obtained in aqueous solutions under various pHs. The isoelectric points of amino acids determined by ^{13}C NMR spectroscopic method have been compared with the corresponding literature values.

186. Computation of Organic Carbon Acids

Daqing Gao, Paris Svoronos, Tianchu Xu and Debbie Maddelena, Queensborough Community College, Bayside, NY

The pK_a value of acetate in water was calculated by using a series of state-of-the-art methods. The computated results were compared to the experimental value.

187. Investigation of the Composition of a Prescription Brand Drug vs. Its Generic Using HPLC

Elizabeth P. Crowe, Sarah Crowe and **Kathryn A. Lysko**, Immaculata University, Immaculata, PA

The purpose of this investigation is to develop an undergraduate laboratory experiment that would address the question of whether or not a selected prescription drug contains exactly the same components and concentrations as its generic version. This study has practical implications in the healthcare industry, where generic drugs are substituted for more expensive brand-name drugs. Healthcare insurance companies claim generics are equivalent to brand-name drugs; however, critics note that there have been reports of formulation inconsistencies in generics obtained especially from sources outside the US. This investigation uses HPLC (high pressure liquid chromatography) to compare the name-brand prescription drug Prozac® to its generic equivalent fluoxetine hydrochloride. Comparison of the retention times, peak heights, and peak areas of the components of both Prozac® and fluoxetine hydrochloride, allows for an evaluation of equivalence. A separation methodology using HPLC is developed from published literature sources for use in the undergraduate laboratory.

Using a separation technique, the components of a brand-name drug and its generic are analyzed for equivalence.

188. Comparison of the Degree of Hotness of Various Hot Peppers using HPLC (High Pressure Liquid Chromatography)

Tolulope Falope, Paris Svoronos and Pedro Irigoyen, Queensborough Community College, Bayside, NY

Various peppers are classified according to how “hot” they are. The comparison of the degree of “hotness” of various hot peppers using High Pressure Liquid Chromatography measurements of capsaicin present has been achieved using acetonitrile as the solvent.

189. Free Radical Chlorination of Benzylic Hydrogens

Hector Mavromatis[1], Sasan Karimi[1], Pedro Irigoyen[1], Paris Svoronos[1] and David Locke[2], (1)Queensborough Community College, Bayside, NY, (2)Queens College, Flushing, NY

We report the free radical chlorination of benzylic hydrogens in p-cymene (4-isopropyl toluene)and p-ethyl toluene using two different chlorinating agents: NCS (N-chlorosuccinimide)and sulfuryl chloride. The ratio of the mono-chlorinated products were studies by GC/MS, and the relative reactivity ratios were determined for primary:secondary:tertiary hydrogens. Reaction of p-cymene or p-ethyl-toluene with NCS led to the formation of the expected benzylic substitution products. On the other hand, treatment of the same substrates with sulfuryl chloride afforded ring chlorination as major products.

190. Synthesis of New Types of Quaternary Ammonium Ionic Liquids

Heidi Martinez[1], Hughton Walker[2], Vanessa Hernandez[1], Robert Engel[2] and Sharon Lall-Ramnarine[1], (1)Queensborough Community College, CUNY, Bayside, NY, (2)Queens College, CUNY, Flushing, NY

We have previously reported on several categories of poycationic quaternary ammonium ionic liquids containing bis(trifyl)imide and phosphate anions. These unique cations were symmetrical and yielded very viscous ionic liquids. We report here on the synthesis of new types of phosphate and bis(trifyl)imide ionic liquids containing asymmetrical quaternary ammonium cations. Preliminary results indicate that these new species exhibit lower viscosity and melting points.

191. Synthesis of ionic liquids containing ether and hydroxyl substituted cations

Kijana Kerr[1], Hughton Walker[2], Vanessa Hernandez[1], Robert Engel[2] and Sharon Lall-Ramnarine[1], (1)Queensborough Community College, CUNY, Bayside, NY, (2)Queens College, CUNY, Flushing, NY

We have previously reported on a series of ionic liquids based on mono- and polycationic quaternary ammonium, Dabco and pyridine species, bearing phosphate and bis(trifyl)imide anions. However many of these liquids were high melting and extremely viscous. We report here on a new series of ionic liquids where the cations including Dabco, pyridinium, pyrrolidinium and imidazolium have been derivatized with ether and hydroxyl substituents. Preliminary results indicate that these liquids exhibit decreased melting points and viscosities when associated with the same anions.

192. Synthesis and characterization of chiral ionic liquids

Marie Thomas[1], Jasmine Hatcher[2], Leah Rothman[1], Sharon Lall-Ramnarine[2] and Robert Engel[1], (1)Queens College, CUNY, Flushing, NY, (2)Queensborough Community College, CUNY, Bayside, NY

Ionic liquids have generated much interest due to their potential green chemistry applications. Chiral ionic liquids maybe useful as solvents for asymmetric synthesis and/or separations. We have synthesized and characterized a series of chiral ionic liquids based on the racemic form of 3-chloro-1,2-propanediol. These include LIPs (liquid ionic phosphates), PILS (polyammonium ionic liqiuid sulfonamides), dicyanamides and tetrafluoroborates. We report here on their synthesis, water content and conductivities.

193. Investigation of the Structure/Property Relationship of New Ionic Liquids

Hughton R. Walker[1], Marie Thomas[1], Vanessa Hernandez[2], Sofiya Penkhasova[2], Heidi Martinez[2], Kijana Kerr[2], Jasmine Hatcher[2], Robert Engel[1] and Sharon Lall-Ramnarine[2], (1)Queens College, CUNY, Flushing, NY, (2)Queensborough Community College, CUNY, Bayside, NY

We have previously reported on the synthesis and characterization of several types of ionic liquids. We report here on an investigation of the effect of structural variation of the cation on the physical properties of ionic liquids. In addition the effect of variation of the anion on the physical properties is also being studied. Physical properties including conductivity and viscosity are reported.

194. Investigation of the effect of anion variation on physical properties of new ionic liquids

Vanessa Hernandez[1], Hughton R. Walker[2], Sofiya Penkhasova[1], Robert Engel[2] and Sharon Lall-Ramnarine[1], (1)Queensborough Community College, CUNY, Bayside, NY, (2)Queens College, CUNY, Flushing, NY

Variation of the anion in ionic liquids leads to a variation in their physical properties. We have previously investigated ionic liquids based on phosphate anions (Liquid Ionic Phosphates - LIPs)and bis(trifyl)imide anions (Polyammonium Ionic Liquid Sulfonylimides - PILS). LIPs were found to be hydrophobic and PILS were found to be hydrophilic. We report here on our continued investigation of anion variation on the properties of ionic liquids, in particular conductivity, melting point and viscosity.

195. Characterization of the physical properties of new ionic liquids

Sofiya Penkhasova[1], Hughton R. Walker[2], Heidi Martinez[1], Jasmine Hatcher[1], Vanessa Hernandez[1], Robert Engel[2] and Sharon Lall-Ramnarine[1], (1)Queensborough Community College, CUNY, Bayside, NY, (2)Queens College, CUNY, Flushing, NY

Several series of new ionic liquids have been prepared. The structure of these species have been confirmed using H-1, C-13 and P-31 NMR. In addition the water content has been determined using Karl Fischer titration. Further the conductivity and viscosity have been investigated. We report here on our preliminary results of the physical properties of these new species.

196. Synthesis of G3 PPI Dendrimer Encapsulated Ag Nanocomposites and Their Potential Applications in the Condensation of DNA

Jowairia Chaudhry Jr., Alex Chen and Prof. Huixin He, Rutgers University, Newark Campus, Newark, NJ

Gene therapy relies on the efficient transport of oligonucleotides (ODNs) and plasmid DNA through cell membrane by mechanisms that are presently not well defined. Many studies have shown that DNA nanoparticle formation is a critical

initial step in the uptake of oligonucleotides and plasmid DNA into cancer cells. Intense research has been done in developing novel formulations and materials for delivering ODNs to cellular targets in vitro and in vivo.

In this presentation, we will show the fabrication of highly stable dendrimer protected silver nanoparticles with a narrow size distribution. We have chosen Ag nanoparticles as potential multifunctional condensing agents due to their natural high contrast in TEM and their ability to significantly enhance Raman signals. These properties can potentially allow us to visualize the condensing agent in the final condensing products, permitting us to study the interaction between DNA and its condensing agent at a molecular structural level. The fabrication method used is a one-step, one-pot method; silver nanoparticles are directly yielded via heating a third generation poly (propyleneimine) (G3 PPI) dendrimer/AgNO3 aqueous solution, where G3 PPI dendrimer serves as a mild reducing agent as well as an excellent protective agent. Their application in the compaction of DNA into nanoparticles will be studied using atomic force microscopy and transmission electron microscopy (TEM).

197. Thermal and Infrared Analysis of Cyanogels

Kristin Lammers[1], S. A. Gould[2], A. B. Bocarsly[2] and G. A. Arbuckle-Keil[1], (1)Rutgers, The State University of New Jersey, Camden, NJ, (2)Princeton University, Princeton, NJ

Cyanogels are prepared via classic sol-gel methodology. These hydrogels are synthesized by an aqueous reaction of tetrachlorometalates with transition metal cyanometalate complexes. The cyanide ligands bridge between the metals in a Prussion Blue-like structure. After drying by oven or microwave methods, the composition of the gels have been evaluated by TGA-IR. Infrared (IR) analysis of the evolved gases from the thermal gravimetric analyzer (TGA) is used to determine the gaseous decomposition products generated during heating. The gas phase IR spectra are compared with IR literature spectra. The TGA-IR results will be discussed with regards to different drying methods and sample preparations.

198. Origin of Fine-structure in Absorption Spectra of Cyanine Dyes

Anna Zarow and Yeung-gyo Shin, Kean University, Union, NJ

Absorption spectra were studied for two series of 3 cyanine dyes with varying lengths of conjugated hydrocarbon chains. As the concentration of dyes were changed up to 10,000 fold, fine sturcture in absorption spectra were analyzed to determine its concentration dependence. In all 6 dyes studied, ratios of minor peaks to the major peak remained constant within the experimental error. These results indicate that the origin of the absorption fine structure is the electronic coupling, an intramolecular process, rather than the dimerization, an intermolecular process. Effort to identify the vibrational mode responsible for the fine structure will also be described.

199. Detecting Phase Transitions in Triblock Copolymers Using Solvatochromic Dyes

David J. Sierra Jr., Edward W. Castner, Jr., Christian D. Grant and Hideaki Shirota, Rutgers, The State University of New Jersey, Piscataway, NJ

We will report on a novel method for detecting aggregation phase transitions of triblock copolymers using solvatochromic dyes. Aqueous solutions of PEO-PPO-PEO triblock copolymers are known to form complex aggregates with increasing temperature. We will study the hydrophobic phase transitions of random coil polymer chains at low temperatures to micellar aggregates at higher temperatures. Across the phase transition the dye will undergo a spectral shift as the aggregates form, which we will detect by absorption spectroscopy.

*DJS is a Raritan Valley Community College student and charter member of the NSF funded Rutgers Undergraduate Research Center.

200. Ultra-sensitive Detection of a Neurotransmitter (Dopamine)

Shah R. Ali, Yufeng Ma and Huixin He, Rutgers University, Newark, NJ

Dopamine is a biogenic amine that acts as a neurotransmitter in the brain. It is suspected that a decrease in dopamine levels below 10 nM is an indication of neurodegenerative diseases, such as Parkinson's disease and schizophrenia. However, it remains challenging to detect dopamine in nanomolar concentrations, and methods are being actively pursued.

Dopamine concentrations as low as 1 nM can be detected by modifying the gold electrode surface with a thin layer of poly (aniline boronic acid)/carbon nanotube composite. The composite was fabricated by electrochemical polymerization of aniline boronic acid monomers in the presence of potassium fluoride and single-walled carbon nanotubes (SWNTs), which are wrapped with single-stranded DNA. Cyclic voltammetry demonstrated that polyaniline (PANI) in the composite is electrochemically active even in pH=7.4 solutions, making it suitable for in vivo measurements. Dopamine chemically binds to the boronic acid moiety, which greatly influences the electrochemical activity of the PANI backbone due to steric effects. The DNA-wrapped SWNTs in the composite not only increase the effective electrode surface area, they also greatly increase the stability of the film. Dopamine concentrations as low as 1 nM were detected with cyclic voltammetry, and the electrochemical current decreased as the concentration of dopamine increased from 1 nM to 10 nM, and leveled off for higher concentrations for some films. The sensitivity is four orders of magnitude greater than the current dopamine sensors and is in the right range of Parkinson's disease patients. Thus, this sensor holds great potential for improved diagnosis of Parkinson's disease.

201. Surface-Enhanced Raman Scattering Studies of Molecules Adsorbed on Gold, Silver and Copper Nanoparticles

Boon Loo[1], Steve Tse[1], Wendy Mays[1], Nicole Loo[2] and Nordulf Debye[1], (1)Towson University, Towson, MD, (2)Rice University, Houston, TX

Surfaces play a critical role in many chemical processes such as energy conversion, environment cleaning, information processing, corrosion inhibition, bio-detection and bio-fingerprinting, etc. Information such as molecular identity, structure, orientation and nature of bonding of the surface adsorbed species may provide essential clues on the efficiency of these processes. The surface-enhanced Raman scattering effect, discovered in 1977, has been a valuable tool for surface and interfacial research. Surface-enhanced Raman spectroscopic measurements were performed on pyridine, thiourea and selenourea adsorbed on gold, silver and copper nanoparticles (2-500 nanometers) on a Solution Raman 633 spectrometer equipped with a He-Ne laser. The silver and copper nanoparticles were made according to an established procedure (Chemical Physics Letters 297, 1998, 83-89), whereas the silver and gold nanoparticles were prepared according to the Journal of Physical Chemistry 103 (1999) 870. Pyridine molecules adsorb on the gold, silver and copper nanoparticles in the similar fashion, that is, bonding through the N atom on the ring. Thiourea adsorbs on the gold, silver and copper nanoparticles via its C=S group, rather than via the N atom on the amide group. The predominantly C=S stretching bands for the free molecules were shifted to lower wavenumbers by about 10-20 cm^{-1} upon adsorption on the nanoparticle surfaces. Likewise, selenourea also adsorbs through its C=Se group, rather than via the N atom on the amide group.

202. Reaction pH and the Evolution of Polyaniline Nanofibers

Erika Feldeshi and David M. Sarno, Queensborough Community College / CUNY, Bayside, NY

The conducting polymer polyaniline (PANi) is conventionally prepared by oxidative polymerization of aniline and ammonium peroxydisulfate in aqueous acidic solution (e.g. HCl). Recent reports show that the uncontrolled growth of morphologically irregular bulk PANi can be easily suppressed, in favor of high yields of self-assembled nanofibers (diameter < 100 nm). The reaction produces sulfuric acid, causing the pH of the reaction medium to decrease. We have investigated the relationship between the changing pH and the growth of PANi nanofibers. While monitoring the pH, aliquots of the polymerizing material were removed and the reaction quenched by exposure to base. We obtained a sequence of pH-dependent “snapshots” by scanning electron microscopy. The earliest times reveal an unusual “flake” morphology that is not polyaniline. This material rapidly evolves to nanofibers of PANi as characterized by UV/Vis and FTIR spectroscopy. Ongoing studies are focused on how morphology and molecular structure are affected by maintaining a constant pH throughout the reaction.

203. Effect of Dopant Cycling on Polyaniline Nanofiber Morphology

Adina Hodes and David M. Sarno, Queensborough Community College / CUNY, Bayside, NY

Numerous reports on the simple preparation of polyaniline (PANi) nanofibers show that the fields of conducting polymers and nanomaterials have been successfully combined. PANi is unique in that electrical conductivities comparable to metals can be achieved by chemical doping with a variety of inorganic and organic acids. Subsequent exposure to base de-dopes the polymer to the insulating form. This reversibility has made PANi attractive for applications such as organic electronics and sensor materials. The original dopant determines many properties of the initially-prepared material. However, the potential exists to tailor properties such as nanofiber diameter, conductivity, and solubility by doping the insulating form with a different acid than used in the initial synthesis. We have investigated changes in morphology and the resistance of nanofibers to repeated dopant cycling using the same acid (e.g. HCl) and different acids (e.g. HCl, then camphorsulfonic acid). Stability of the molecular structure has been characterized by UV/Vis and FTIR spectroscopy. Scanning electron microscopy images show nanofibers of 30-80 nm in diameter and up to several micrometers in length, with fiber quality highly influenced by the method of sample processing.

204. Degradation Media Composition Analysis of Salicylic Acid-Based Poly(Anhydride-Esters)

Vivian Ng, Almudena Prudencio and Kathryn Uhrich, Rutgers University, Piscataway, NJ

Salicylic acid-based poly(anhydride-esters) have been hydrolytically degraded in vitro in pH 7.4 phosphate buffered solution and the degradation media periodically analyzed by UV (l=205 nm) to monitor salicylic acid release. The hydrolytic degradation of salicylic acid-based poly(anhydride-esters) initially produces oligomers, and these oligomers break down into diacids, which finally yield salicylic acid. To understand the degradation media, solubilities of the degradation products, that is, diacid and salicylic acid, were measured. It is necessary to determine if the degradation media analyzed by UV is composed of only salicylic acid or a combination of salicylic acid and other polymer degradation products.

To achieve this goal, several salicylate-based diacids containing various linkers were synthesized. The linker is the compound connecting the two salicylic molecules in the diacid. Diacids were produced by direct reaction of two molecules of salicylic acid with an acyl chloride in the presence of a base (pyridine). The solubility of the diacids and salicylic acid in pH 7.4 phosphate buffered solution was evaluated by using UV-Visible spectroscopy (l=205 nm). Diacid solubility data was affected by changes in the molecular structure of the linker, in that the measured solubilities of diacids in phosphate buffered solution were lower than that of salicylic acid.

Due to the low solubility of the other polymer degradation products compared to salicylic acid, it can be concluded that the major component of the degradation media is salicylic acid.

205. The PolymIR Library: Development of a Web-Based Resource

Anita J. Brandolini, Noelle DeStefano, Betsy Huerta and Kevin Lemire, William Paterson University, Wayne, NJ

Libraries of spectra, such as infrared (IR) or mass spec, are very useful for identifying unknown samples and for teaching spectroscopy. Traditional print-format collections of data have been largely supplanted by computer-based libraries, but the cost of these resources can be prohibitive. We are currently compiling a library of IR spectra of polymers, which will be published on the Web to allow open access. When completed, the PolymIR Library is expected to contain spectra of over 200 polymers, additives, and related materials, and to be searchable by material name and structure.

206. An Indirect Determination of Sulfate by Back-Titration of Barium with EDTA

Gregory S. Kowalczyk and **Christopher P. Simpson**, Southern Connecticut State University, New Haven, CT

A procedure for the quantitative determination of sulfate was devised using a back-titration method. The sulfate in the sample was dissolved and precipitated as barium sulfate by the addition of a known excess of barium ions. After digestion and filtration, the filtrate and precipitate washings was titrated with a standardized EDTA solution. Results were verified with use of Thorn Smith Laboratories sulfate unknowns. Relative error for replicate determinations was less than 0.30%. This procedure can be easily adapted to any quantitative analysis course.

207. SPE and HPLC Method for the Determination of Aspirin, Acetaminophen, and Caffeine in Aqueous Environmental Samples

Scott LeFevre and Stephen C. Waller, Fairleigh Dickinson University, Madison, NJ

A major concern today is the presence of pharmaceuticals in common water sources. Some of the most common compounds found near developed areas include aspirin, acetaminophen, and caffeine. In order to properly quantify the amounts of the target compounds with acceptable separation, a reverse-phase HPLC method was developed and validated using an organic gradient with pH 3.00 aqueous acetate buffer and acetonitrile as mobile phases A and B, respectively. Using acetanilide as the internal standard, relative response factors were calculated for each analyte and used in the quantification of drug concentrations. Linearity plots for all compounds were used to determine the proper concentration detection range for the compounds, which fell between 1□g/mL to 500□g/mL. Aqueous environmental samples (500-mL) were passed through solid phase extraction cartridges (SPE C-18), and the organics were eluted with acetonitrile. These organic solutions were spiked with the internal standard and analyzed using the newly developed validated HPLC method.

208. Statistical Evaluation of Acid Indicators

Seth A. Elwood, Carolyn Supplee, Jenna Case, **Marie Ineus** and Lisa Salvemini, Monmouth University, West Long Branch, NJ

Typically in the sophomore level analytical chemistry laboratory, strong acid solutions are standardized against sodium carbonate with bromocresol green as the overwhelming indicator of choice in the literature. The endpoint occurs between pH 4 and 5 with a color change of light blue to pale green. The transition between blue and green is often difficult to detect and does not allow the desirable level of accuracy and precision to be obtained readily. Often novice chemists titrate beyond the endpoint to an irreversible yellow solution. However, bromocresol green remains the overwhelming indicator of choice in the chemical literature and not methyl red. Preliminary studies indicate methyl red provides superior results. The statistical data (mean, standard deviation, Q-test and t-test) comparing bromocresol green with methyl red for standardization of hydrochloric acid solution will be presented herein.

209. Using Differential Scanning Calorimetry (DSC) in a General Chemistry Laboratory Course

Ronald P. D'Amelia, **Thomas Franks** and William F. Nirode, Hofstra University, Hempstead, NY

In the first year general chemistry undergraduate courses, thermochemistry and thermodynamic properties are very frequently discussed. In addition, calorimetry and calorimetric techniques are taught as an experimental method to determine these thermodynamic properties. However, usually only classical calorimetric methods of analysis are discussed. There is infrequently any mention of other modern methods of thermal analysis that are commonly used. Furthermore, instrumental techniques that are routinely and easily used for thermal analysis are rarely mentioned. Today, it has become increasingly important to incorporate more modern techniques and instrumentation into the general chemistry curriculum in order to provide a more hands-on and applicable learning environment for the general chemistry students. It is extremely beneficial to introduce students to instrumental techniques early in the curriculum to prepare them for more advanced courses and expose them to techniques used in the real world. Differential scanning calorimetry (DSC) is a rugged, easy to use instrumental method for thermal analysis determination of many different properties. DSC has

become more commonly used in the chemistry curriculum finding its way into physical chemistry, analytical chemistry, and even in some general chemistry courses. The work described herein discusses the use of DSC in general chemistry.

210. Correlation of the van't Hoff Factor with the Concentration of Inorganic Solutes Using Computer Interface Freezing Point Depression Measurements

Jorge Ubillus, Pedro Irigoyen and Paris Svoronos, Queensborough Community College, Bayside, NY

The use of computer interface freezing point depression measurements has enabled the correlation between the van't Hoff factor and the concentration of inorganic solutes. The quantities used were as a low as 0.05g of the salt in 4mL of water. The salts used were sodium chloride, magnesium nitrate, aluminum nitrate, sodium sulfate and sodium carbonate.

211. A Computational Chemistry Research Program at Community College Level

Daqing Gao, Sanwal Mushtaq, Hilda Dan-Archibong and Pochou Chen, Queensborough Community College, Bayside, NY

An undergraduate computational chemistry research program was established at Queensborough Community College-CUNY. Research projects including the calculation of bond energies, the study of mechanisms of the Menshutkin, S_N2 reactions and other processes will be presented.

212. Philadelphia CSI vs. CBS CSI

Stacy A. Gibbs, Community College of Philadelphia, Philadelphia, PA

An students look at Philadelphia Police Department's Crime Lab versus the dramatized CBS show CSI. Reality is nothing like TV.

213. Why College Freshman Believe Biology Is Easier Then Chemistry and How to Debunk the Myth

Stacy A. Gibbs, Community College of Philadelphia, Philadelphia, PA

Out of 2000 College freshman surveyed, a large majority believe that biology courses are easier than chemistry courses which could be the reasons for low enrollment in chemistry courses currently in addition to the low number of those under the age of 30 in the ACS. Research was done to determine the reasons for this belief and how to debunk the belief.

214. Student Affiliate Chapters at Community Colleges

Stacy A. Gibbs, Community College of Philadelphia, Philadelphia, PA

A look at student affiliate chapters at Commmunity Colleges. Explores the benefits and disadvantages of the chapters.

215. Reviving an Ailing Student Affiliate Chapter: Community College of Philadelphia

Stacy A. Gibbs and Christa Nolsoe, Community College of Philadelphia, Philadelphia, PA

A look at an ailing student affiliate chapter that revived itself through hard work and dedication. Explores the events that interested the students the most and increased their membership base.

Chemistry Outreach

Official: Julius M. Johnson Rutgers University Chemistry Society, New Brunswick, NJ

216. Student Affiliate Outreach -Chemical Demonstration Forum

Julius M. Johnson, Rutgers University Chemistry Society, New Brunswick, NJ

Student Affiliate Outreach Program Chemical Demonstration Forum

Are you a teacher or student affiliate who is interested in or already doing chemical demonstrations for younger students? For student affiliates, doing outreach is a good way to get involved with the community and a rewarding activity for all involved. For teachers it is a great way to engage your students in hands on learning that can be fun!

If you are interested, then you might want to stop by and participate in our chemical demonstration forum. If you want to actively participate then you should prepare a five minute lesson that you have presented or are thinking about presenting. The demonstration should contain a lesson, and you should say what grade or age group it is appropriate for. The active participators are going to present their demonstration and afterward there will be discussion about how you can improve your demonstration and what is good about your demonstration. The discussion will be lead by David Lee, who is a veteran when it comes to chemical demonstrations. This is a constructive way to improve your demonstrations. The inactive participants are welcome and encouraged to watch because in addition to refining your presentation this forum

will also be a place to get ideas if you want to start doing outreach in your community. So come on over and start or continue to spread the message that chemistry is interesting and can be fun!

About the General Chemistry Laboratory II

Organizer: Rudolph W. Kluiber Rutgers University, Newark, NJ

217. Keynote Address: Is the Textbook Dead?

John C. Kotz, SUNY-Oneonta, Oneonta, NY

The speaker, a textbook author, has been expecting the gradual demise of chemistry textbooks for 25 years, but textbooks continue to dominate the curriculum. Is there evidence from our own students that they are as effective as we believe them to be? Do students use them and, if so, how are they used, particularly in introductory courses? What are the most and least effective aspects of textbooks? What improvements can be made? Are there effective, affordable alternatives to textbooks? Most importantly, what might the textbook become in the next decade? This talk will describe the use of textbooks and technology in an introductory, general chemistry course and will address the questions posed above.

218. Does the chemistry teaching laboratory have a future?

Melanie M. Cooper, Clemson University, Clemson, SC

The teaching laboratory has long been considered to be an integral and essential part of many chemistry courses. However, research studies of learning in the laboratory often indicate that traditional laboratory courses have very little effect on student achievement, and furthermore may inadvertently promote student misconceptions about the nature of scientific experimentation. In fact we often seem to be squandering the real opportunities that a well-designed laboratory course can offer. One thing is certain, with increasing pressure from legislatures and administrations to become more efficient with regard to both human resources and expenses we will need to be very certain what can and cannot be achieved in a teaching laboratory. Is it possible to take advantage of current research about student learning to design a meaningful and pedagogically sound laboratory experience for students, while satisfying the concerns of those who pay the bills? Can we show that a laboratory experience can result in higher student achievements and deeper learning? What should the chemistry teaching lab look like as we move forward?

219. Using Technology to Teach: Are Lab Instructors Really Needed?

Rudolph W. Kluiber, Rutgers University, Newark, NJ

Over the past 15 years we have developed software which allows the server, GenChem, to do most of the routine tasks in teaching a two semester, classical hands-on "cookbook" GenChem Laboratory. From creating a syllabus to evaluating final course grades, and in-between producing and grading individualized web-based PreLabs, providing 5-15 min downloadable videos plus web pages and tutorials in lieu of instructor talks, recording unknowns, evaluating each student's experimental work in real time, providing immediate one-time warnings on incorrect calculations and instant grading and long term record keeping. Our students work individually and the computer individualizes each experiment making it more difficult to mindlessly copy or cheat. Use of the computer has made the students more accountable and also provides an even treatment of students from person to person, section to section and also year to year! It also allows poorly done experiments to be repeated (with a small grade penalty). PlayChem, a series of short but significant experiments provides "extra-credit". Although our experiments have remained basically the same over the last decade, use of the computer, in particular, the individualized PreLabs (rated 4.0/5) and the videos (rated 4.5/5) are more highly rated than the previous prelabs and instructor talks (2-3/5). The multimedia approach, the accountability and our correlation of the lab with the lecture has rated the laboratory as being helpful in understanding the lecture (3.7/5) slightly more so than the lecture being helpful in the lab (3.6/5). However, GenChem has never received the "Teacher of the Year" award.

220. Million Dollar Data: Students constructing confidence in the laboratory

Stephen DeMeo, Hunter College of the City University of New York, New York, NY

The science laboratory is a highly managaged environment that often relies heavily on the transmition of knowledge by the teacher not the construction of concepts and processes by the student. Inquiry-based laboratory programs and activities are a direct challenge to this teacher centered pedagogy. One area that is in keeping with Inquiry and has had little attention in the literature is how students build confidence in their numerical and observational data. Using the Hunter college introductory chemistry lab program as an example, I will discuss how students can construct and use non-statistical tools to evaluate their data while in the laboratory. Million dollar data, as the title of this talk mentions, represents a level of confidence that students aspire to. Raising the bar means that students must analyze their data and explicitly think about how they can convincingly argue about the value of their lab work.

221. Undergraduate Research Center for Chemistry & Closely Allied Fields

Margaret Czerw[1], **Gregory F. Herzog**[2], John Krenos[2], Joseph A. Potenza[2], Paul Schueler[1] and Diane C. Trainor[3], (1)Raritan Valley Community College, North Branch, NJ, (2)Rutgers University, Piscataway, NJ, (3)Middlesex County College, Edison, NJ

We describe an NSF-supported, pilot program to develop an Undergraduate Research Center (URC) for students in chemistry and closely allied fields. By acquainting first-year students with the centrality of chemistry in science, we seek to influence their career decisions towards science in general and chemistry-related subjects in particular, and ultimately to strengthen the scientific workforce. In our URC, selected students from Middlesex County College, Raritan Valley Community College and Rutgers University engage in research experiences tailored to match their interests and knowledge. Activities take place in the context of a new 3-credit course. Students spend ~3 hours/week in a research laboratory supervised by a faculty mentor and either a graduate student or post-doctoral research associate. Participating faculty mentors come from several academic units: Marine and Coastal Sciences, Environmental Sciences, the School of Pharmacy at Rutgers, and at UMDNJ, the Graduate School of Biomedical Sciences. In the research laboratories, the students see first hand the practice of academic chemistry and get to know working scientists. The students also meet weekly as a group to discuss: chemistry as a discipline; open questions at the discipline's frontiers; and how work in the field is defined, structured, and supported. The URC has as corporate partners Enzon, Johnson & Johnson, Merck & Co., Novartis, Schering-Plough, and Wyeth, who share our goal of making chemistry and closely related sciences an attractive course of study for an increasing number of students. Over the course of the semester, the undergraduates visit three of these corporations.

222. A One Semester First Year Seminar: An Interdisciplinary Study of the SARS Virus

Julie B. Ealy, Penn State University, Fogelsville, PA

Students at Penn State University are all required to take a first year seminar. With an interest in chemistry, biology, and computers, I chose to develop a first year seminar on the severe acute respiratory syndrome (SARS) virus. Both science and non science students take the seminar. Reading and understanding primary literature, incorporation of molecular modeling using Spartan Pro, presentation of a drug, its side effects, and 3D structure, using ICM Pro for drug docking, and an end of semester poster presentation are some of the main aspects of the seminar. How do you ease nonscience majors into heavy duty science? How do you convince science majors that memorizing definitions does not contribute to sufficient understanding? What do students have to say about the seminar?

Exploring Routes for Becoming a HS/MS Teacher

Official: Anita J. Brandolini William Paterson University, Wayne, NJ

223. Exploring Routes for Becoming a HS/MS Teacher Panel Discussion

Anita J. Brandolini, William Paterson University, Wayne, NJ

Have you ever considered becoming a high-school or middle-school science teacher? Science educators are in high demand, and teaching young people can be a rewarding experience. Panel participants will include experts who can discuss licensing and certification requirements and the alternate-route option in New Jersey, and local teachers who will talk about the high- and middle-school classroom environment.

GPCR / Virtual Screening

Organizer: Robert Goodnow Hoffmann-La Roche, Nutley, NJ
Official: Dr. Shawn Erickson Hoffmann-La Roche, Nutley, NJ

224. Ligand Twisting and Counterion Switching in Rhodopsin Activation

Thomas P. Sakmar, The Rockerfeller University, New York, NY

My group uses techniques of molecular biology in combination with biophysical methods to study the molecular mechanism of G protein-mediated signal transduction. Over the past five years, about one-half of our effort has focused on rhodopsin, with much of the rest on chemokine receptors. Rhodopsin, the visual pigment of the vertebrate rod cell, comprises an opsin apoprotein and a retinylidene chromophore moiety. Photolyzed rhodopsin switches to its active state, which catalyzes the uptake of GTP by the heterotrimeric G protein, transducin. Rhodopsin is defined functionally as a G protein-coupled receptor (GPCR) since it couples to transducin during signal transduction. The crystal structure of bovine rhodopsin was the first report of a high-resolution structure of a GPCR. The structure provides an opportunity for the critical evaluation of a decade of structure-activity studies and forms the basis for exciting future work. The classical questions arising from visual physiology continue to inspire our research interests related to rhodopsin. We have made major advances in mapping the precise pathway of information flow through all of the specific amino acid residues involved in GPCR-mediated signaling. We recently proposed a mechanistic model to explain the molecular basis for how chromophore isomerization is linked to conformational changes in rhodopsin. Energy is stored in a twisted all-trans chromo-phore and then released by chromophore movements that are coupled to a counterion switching mechanism involving extracellular loop 2 and an active-site H-bond network.

225. Using Designed Peptide Panels for De-risking GPCR Projects

Waleed Danho, Hoffmann-La Roche, Nutley, NJ

The GPCR family of proteins has traditionally provided the pharmaceutical industry with a rich source of targets for drug discovery. The successful discovery of therapeutic compounds with activity at these targets is evidenced by the considerable number of marketed drugs. These discoveries have been facilitated by the fact that the endogenous ligands are either biogenic amines or peptide ligands with less than 10 amino acids in length. However discovery of small molecule agonists or antagonists molecules for GPCR targets that are characterized with endogenous peptide ligands of 10 or more amino acids has been considered difficult, if not risky. We developed a strategy for de-risking such projects by using a designed series of peptides which allow one to assess the probability of success or/ failure in rapid fashion. This strategy will be discussed, citing cases of obesity- related GPCR projects where the endogenous peptide ligands which include Melanin-concentrating hormone (MCH), Prolactin releasing peptide (PrRP), and NPW (NPW).

226. GPCR Ligands from Enzyme Targeted Libraries

Michael Ohlmeyer, Pharmacopeia, Cranbury, NJ

An encoded combinatorial library of benzimidazolyl pyrimidines targeted at iNOS was found to give hits against GPCR targets also. This talk describes the results of library screening vs. iNOS and Bradykinin B1. Optimization of the hits from Bradykinin B1 screen is described.

227. Discovery and Development of the First Centrally Active mGluR5 Positive Allosteric Modulators

Craig Lindsley, Merck & Co, Inc., West Point, PA

This talk will detail the discovery and SAR of 3 series of positive allosteric modulators of the metabotropic glutamate receptor subtype 5 (mGluR5) that potentiate the response to glutamate. I will highlight the application of a fragment library approach that identified a series of substituted N-(1,3-diphenyl-1H-pyrazol-5-yl)benzamides that led to the first centrally active positive allosteric modulator of mGluR5. An iterative analog library synthesis approach provided potentiators with excellent potency and selectivity for mGluR5 (vs mGluRs 1-4,7,8). demonstrated in vivo proof of concept in an animal behavior model where known antipsychotics are active, supporting the development of new antipsychotics based on the NMDA hypofunction model for schizophrenia.

228. A LMW CCR5 Antagonist in Combination with CsA Prolongs Graft Survival in Life Supporting Kidney TX Model in Cynomolgus Monkeys

Gerhard Thoma, Novartis Pharma AG, Basel, Switzerland

The chemokine receptor CCR5 plays an important role in inflammatory and autoimmune disorders as well as in transplant rejection by affecting the trafficking of effector T cells and monocytes to diseased tissues. Antagonists of CCR5 are believed to be of potential therapeutic value for the disorders mentioned above and HIV infection.

Here we report on the discovery and the SAR of a new series of highly potent and selective competitive CCR5 antagonists. One of them had IC50 values between 2 and 40 nM in in vitro assays, was about equipotent on human and cynomolgus CCR5 and acted as a competitive antagonist of MIP-1 binding to CCR5. It had an oral bioavailability of 43% in cynomolgus monkeys. The compound was tested in a model of life-supporting renal allograft rejection in cynomolgus monkeys as monotherapy or in combination with a non-therapeutic dose of cyclosporine (CsA) ineffective vs vehicle controls (MST=7 d; p=n.s.). It was not efficacious as monotherapy but when administered in combination with the non-effective dose of CsA graft survival was statistically significantly prolonged (MST=51.5 d; p< 0.05 vs. CsA). No PK inte! raction with CsA was observed demonstrating that the graft prolongation was compound related.

Inhibition of CCR5 may offer new therapeutic opportunities for transplant patients

Pharmaceutical Profiling II

Organizer: Edward H. Kerns Wyeth Research, Monmouth Junction, NJ
Presider: Edward H. Kerns Wyeth Research, Monmouth Junction, NJ

229. Preclinical Assessment of QT Liability and Proarrhythmic Risk

Paul Levesque, Bristol-Myers Squibb Co., Princeton, NJ

Regulatory Agency concern over the risk of life-threatening arrhythmias associated with QT interval prolonging drugs has led to recommendations for more thorough preclinical and clinical cardiovascular safety assessment. The long list of marketed drugs and compounds in development that have been withdrawn, have received unfavorable labeling or that have been subjected to regulatory approval delays, emphasizes the importance of investigating new chemical entities for this side effect before use in man. As a result of evolving regulatory guidelines and increased awareness of this issue, our understanding of the mechanisms underlying drug-induced prolongation of QT interval and our ability to detect QT interval prolongation and predict safety margins have improved significantly over the past several years. This talk will focus on in

vitro assays, but will also cover in vivo preclinical assays that are useful for predicting risk. Shortcomings of various models, remaining challenges and impact on drug discovery will be discussed.

230. Pharmaceutical Profiling: The Interface between Drug-like Property Prediction and Application for Project Impact

Li Di, Edward H. Kerns, Susan L. Petusky, Susan Q. Li and Hong Chen, Wyeth Research, Monmouth Junction, NJ

Medicinal chemists are very effective in optimizing potency. However, in many cases, very potent compounds failed in development, due to inadequate properties, such as: poor solubility, permeability, rapid metabolism and drug-drug interaction. One of the major reasons is that we tend to focus on potency optimization. This will limit us to a potency space that might not be optimal for drug-like properties. Nowadays, many of the pharmaceutical profiling assays have been implemented early in drug discovery, so that properties can be optimized in parallel with activity optimization. This presentation will discuss various pharmaceutical profiling assays and their applications. The assays can impact discovery projects by providing early alert on potential ADMET issues, developing structure-property relationships, predicting in vivo performance, prioritizing in vivo studies, guiding experimental design for biological assays and diagnosing in vitro/in vivo assay results. Examples and case studies will be discussed.

231. The Application of Pharmaceutical Profiling Data to Lead Identification and Optimization

John Ellingboe, Wyeth Research, Pearl River, NY

Good pharmaceutical properties, such as solubility and permeability, are key to successful drug development, and it is important to start focusing on these properties at the earliest stages of drug discovery. While detailed pharmacokinetic analyses are conducted during development, higher throughput pharmaceutical profiling assays are better suited to the larger numbers of compounds prepared in discovery. The identification of high quality leads provides the foundation for drug discovery. Leads are identified through a two-step process: - the full characterization of screening hits through biological and pharmaceutical profiling, - the optimization of the in vitro and pharmaceutical profiles of the hits to yield high quality leads.

232. The use of in vitro profiling in the optimization of IMPDH inhibitors

Murali Dhar, Bristol-Myers Squibb, Princeton, NJ

Inosine monophosphate dehydrogenase (IMPDH), a key enzyme in the de novo synthesis of guanosine nucleotides, catalyzes the irreversible NAD dependent oxidation of inosine-5'-monophospahte (IMP) to xanthosine-5'-monophosphate (XMP). Cellcept (MMF), a prodrug of mycophenolic acid (MPA) has clinical utility due to its inhibition of IMPDH, for the treatment of transplant rejection. This presentation will outline the use of in vitro profiling which in combination with structure activity relationships (SAR), led to the identification and optimization of a novel class of acridone based IMPDH inhibitors.

233. Strategies and techniques for providing in vivo PK and tissue penetration data for drug discovery

Timothy Olah, Bristol-Myers Squibb Co., Princeton, NJ

With the increased speed at which potential drug molecules are now synthesized and evaluated for pharmacological activity, a need exists to also provide fundamental data on their metabolic, pharmacokinetic, and toxicokinetic properties at earlier stages of drug discovery. The assessment of these properties is critical in determining whether or not a compound is selected for further evaluation and development as a viable drug candidate. Metabolic properties are related to the absorption, distribution, metabolism, excretion, and toxicity (ADMET) of a compound following administration. Factors that influence discovery teams' decisions are based on the review of the compound's ADMET characteristics in selected in vitro assays and in in vivo pharmacokinetic profiling following specific dosing regimens. Moreover, there has been an increased interest in more accurately determining the distribution of drugs and their metabolites into tissues and biological matrices in addition to blood, plasma, and urine. As bioanalytical procedures have improved through the continued development of key laboratory instruments such as multiplexed HPLC systems and mass spectrometers, so have tissue and biological sample preparation techniques. This has created the opportunity to extend bioanalysis to assess the exposure and toxicokinetic profiles within a variety of biological matrices by determining concentrations of drugs and metabolites within them. This presentation will detail bioanalytical strategies and techniques for providing in vivo pharmacokinetic and tissue penetration data for supporting drug discovery programs.

Bench Top To Pilot Plant II

Organizer: Ambarish Singh Bristol-Myers Squibb Company, New Brunswick, NJ
Organizer: Shankar Swaminathan Bristol Myers Squibb, New Brunswick, NJ

234. Case Study: The Approval of Somavert, a Bio-therapeutic Agent

Amit Banerjee, Pfizer Global Research and Development, Chesterfield, MO

Somavert (pegvisomant for injection) is a pegylated growth hormone receptor antagonist developed for the treatment of acromegaly. The regulatory approval of Somavert encountered many post-submission obstacles including; demonstrating comparability as a result of multiple process changes; characterization of a complex pegylated macromolecule; and technology transfer and validation at a contract manufacturing facility. This case study will discuss the successful resolution of these issues, and approval of Somavert.

235. Process Improvements in Synthesis of Therapeutic Oligonucleotides: From Grams to Kilograms

Yogesh S. Sanghvi, Rasayan Inc., Encinitas, CA

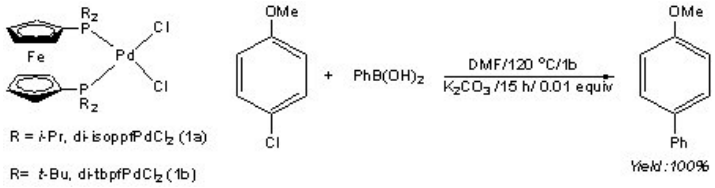
The increasing demand for synthetic oligonucleotides as therapeutics for antisense, aptamers, RNAi, CpG immunostimulators, microRNA, DNA decoys, ribozymes and spiegelmers have created an urgent need for process improvements that enable seamless scale-up from grams to kilograms. In recent years, a variety of process improvements have been created and successfully implemented for the assembly of oligonucleotides that are safe, scalable and cost-effective. This presentation will describe some of these accomplishments (listed below) and provide a progress report.

- Establish the supply-chain of synthetic nucleosides - Chemistry of reusable solid-supports and alternatives - Elimination of hazardous reactions and reagents - Recycling of reagents and reduction of solvent consumption - Cheaper chromatographic alternatives - Applications of Green Chemistry

236. Palladium Coupling Catalysts for Pharmaceutical Applications

Thomas Colacot, Johnson Matthey, West Deptford, NJ

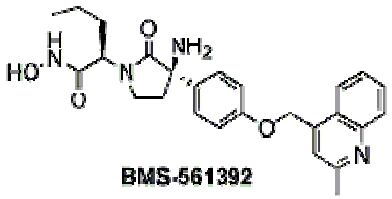
Cross-coupling reactions are among the most important chemical processes in fine chemical and pharmaceutical industries, as they represent the key steps in building complex molecules from simple precursors. Recently, there has been a burgeoning of interests in this area, mainly due to the interest in coupling challenging substrates. Recent studies carried out by Fu have shown that t-Bu3P, in conjunction with a Pd catalyst precursor, is a very good system for aryl chloride coupling chemistry. The work of Koie/Fu, Hartwig and Buchwald, Li, Guram, Beller and Reetz support similar concepts: the use of a bulky electron rich organophosphine to accomplish similar challenging transformations of aryl chlorides or related substrates. Although t-Bu3P is a very active ligand for challenging coupling reactions, this pyrophoric, low melting solid requires special, careful handling techniques. The use of air-stable, active catalysts is a preferred choice for many pharmaceutical and fine chemical companies. Our studies show the effective use of air-stable, Cp2Fe(PR2)2PdCl2 (R = i-Pr and t-Bu) in Suzuki coupling reactions. The di-tbpfPdCl2 catalyst was shown to be the more active catalyst for unactivated and sterically challenging aryl chlorides.



237. Development and Scale-Up of the TACE Inhibitor BMS-561392

Scott A. Savage, Bristol-Myers Squibb, New Brunswick, NJ

Retrosynthetic analysis of BMS-561392 identifies that the primary challenge is synthesis of the tetra-substituted amino acid stereogenic center. Two novel syntheses will be illustrated for the preparation of BMS-561392. Both syntheses developed rely on an efficient synthesis of a racemic tetra-substituted amino ester and subsequent resolution of the stereogenic center. One route utilizes an enzymatic hydrolysis to obtain the desired enantiomer. The second route utilizes a classical salt resolution which displays interesting solvent effects on enantioselectivity.



BMS-561392

238. The use of SMB as a chiral separation tool from bench to commercial production

Emile Farhan, Johnson Matthey Pharmaceutical Material, Devens, MA

Over the past decade, the use of Simulated Moving Bed chromatography, SMB, in the pharmaceutical industry has become more and more accepted, particularly as a chiral separation tool. The principals of SMB, pros and cons, equipments and advances in technology are illustrated in this presentation

239. Preparative supercritical fluid chromatography (SFC) at the kilogram scale

William R. Leonard Jr., Christopher Welch, Jennifer Albaneze-Walker, Mirlinda Biba, Jimmy DaSilva and Derek Henderson, Merck Research Laboratories, Rahway, NJ

Preparative chromatography is increasingly used to access kilogram quantities of developmental compounds to support preclinical pharmaceutical development. Historically, these separations have been performed using HPLC. However, supercritical fluid chromatography (SFC) is emerging as a powerful alternative technique, owing to the lower eluent viscosity, improved peak shape, and decreased solvent consumption and waste. A general approach to SFC from analytical screening methods to large-scale purifications will be discussed, and its considerable advantages illustrated with several case studies of kilogram scale purifications.

Analytical

Presider: Duxi Zhang Bristol-Meyers-Squibb, Princeton, NJ

240. Evaluation of a Rapid and Automated Intra Operative Parathyroid Hormone Assay

Michael A. Pesce, New York Presbyterian Hospital Columbia University Medical Center, New York, NY

Primary hyperparathyroidism is a common cause of hypercalcemia . In most cases, the recommended therapy is parathyroidectomy. Plasma Parathyroid hormone(PTH)levels are measured during the surgical procedure to confirm the removal of all hypersecreting parathyroid tissue. Intact parathyroid hormone is measured in plasma with a two-site immunochemiluminescent microtiter plate assay from Future Diagnostics Inc that uses two polyclonal antibodies against PTH. The day to day precision of the method was determined for 18 days using a normal and abnormal control. The means were 52 pg/ml (CV, 13.8%) and 602 pg/ml (CV, 10.1%). The linearity of the method is up to 2120 pg/ml. Our protocol is to measure PTH levels before and after manipulation of the gland and at 5 and 10 minutes after surgery. A successful parathyroidectomy procedure is a 50% or greater drop in PTH levels. The PTH levels measured in 20 patients who were undergoing parathyroidectemies showed that for 18 patients who had successful surgery, the PTH levels dropped by an average of 72%. For the two patients who had an unsuccessful procedure, the drop in PTH was < 25%. The PTH results correlated with the results of the surgery. At our Medical Center the analyzer is placed on a cart and the assay performed just outside the operating room. The entire procedure from centrifugation of the specimens to reporting of results to the surgeon takes < 15 minutes. In conclusion, the Future Diagnostic Assay is a rapid and accurate procedure for the assessment of patients undergoing parathyroidectomies.

241. Overcoming the LC Bottleneck in ADME Studies

Paren Patel, Nanostream, Pasadena, CA

Pharmaceutical research scientists look to high-throughput technologies to conduct ADME and drug metabolism and pharmacokinetics (DMPK) studies for large sample sets. Early determination of Log P, solubility and other physiochemical properties promises to limit downstream attrition of compounds due to poor ADME properties. However, HPLC presents a significant bottleneck for the analytical measurements critical to these studies. For DMPK and bioanalytical assays,

samples are typically prepared by liquid-liquid extraction, protein precipitation or solid phase extraction and are subsequently separated using HPLC before quantitative analysis using MS. Whereas high-throughput methods have emerged for extraction techniques, chromatography remains a significant bottleneck for DMPK studies.

Micro parallel liquid chromatography (mPLC) affords a high-throughput, low volume analytical platform to overcome the HPLC bottleneck. Physicochemical property profiling and DMPK assays, such as drug-drug interactions, and metabolic stability screening can be accelerated by incorporating a single analytical instrument with the capability to separate 24 samples in parallel microfluidic LC columns. A time-triggered fraction collector can be added for offline preparation of bioanalytical samples. By outputting fractions to micro well plates, the fraction collector offers a convenient interface to MS, thus allowing users to increase chromatographic throughput without employing large multiplexed or multi-pump LC systems. This presentation will include recent data for applications including solubility, Log D, glucuronidation, and pharmacokinetics using real-world samples.

242. Di-(2-Ethylhexyl)-Phthalate and its Metabolites Influence the Expression and Function of Fatty Acid Homeostasis Regulating Proteins in Rat Placental HRP-1 Cells

Yan Xu, Thomas J. Cook and Gregory T. Knipp, Rutgers, the State University of New Jersey, Piscataway, NJ

Di-(2-ethylhexyl)-phthalate (DEHP) is a widely used plasticizer and ubiquitous environmental contaminant. The potential health hazards, including teratogenecity, from exposure to DEHP may be related to the role of DEHP or its metabolites in the trans-activation of peroxisome proliferator-activated receptors (PPARs). Fetal essential fatty acid (EFA) homeostasis is controlled by directional transfer across the placenta through a highly regulated process, including PPAR activation. Using HRP-1 rat trophoblastic cells, the effects of DEHP and selected metabolites, mono-(2-ethylhexyl)-phthalate (MEHP) and 2-ethylhexanoic acid (EHA), on the mRNA and protein expression of the three known PPAR isoforms (α, β and γ), fatty acid transport protein 1 (FATP1), plasma membrane fatty acid binding protein (FABPpm) and the heart cytoplasmic fatty acid binding protein (HFABP) were investigated. This study also investigated the functional effects of exposure on the uptake and transport of six long chain fatty acids: arachidonic acid (AA), docosahexaenoic acid (DHA), linoleic acid (LA), α-linolenic acid (ALA), oleic acid (OA) and stearic acid (SA). In the presence of DEHP, MEHP and EHA, the expression of PPARα, PPARγ, FATP1, and HFABP were up-regulated in a dose- and time- dependent manner, while PPARβ and FABPpm demonstrated variable expression. The uptake rates of EFAs (AA, DHA, LA, ALA) increased significantly upon exposure, and the transport of AA (ω-6) and DHA (ω-3) were directionally induced. These results suggest that DEHP, MEHP and EHA can influence EFA transfer across HRP-1 cells, implying that these compounds may alter placental EFA homeostasis and potentially result in abnormal fetal development.

243. Investigation of the Dissociation of Double Stranded Oligodeoxynucleotides in an Ion Trap: Sequence, Length and Charge Level

Su PAN and Jeehiun K. Lee, Rutgers, The State University of New Jersey, Piscataway, NJ

A methodological study of the collision-induced dissociation of 28 double stranded oligodeoxynucleotides (ODNs) with various sequences, lengths and charge states has been implemented in an ion trap mass spectrometer. We define a new term “charge level” to express the amount of charge carried by an ODN as the ratio of the charge state to the total number of phosphate groups present in the ODN. The initial fragmentation pathway of double-stranded ODNs is either noncovalent dissociation and/or covalent cleavage. The major pathway for ODN duplexes with charge levels greater than 25% is noncovalent dissociation while the major pathway for ODNs with charge levels below 25% is covalent cleavage. For noncovalent dissociation, the half-wave collision energies (E_{50}) of the excitation RF voltage in the ion trap were measured to compare stabilities among ions with the same m/z ratios. Our studies establish the parameters that one should follow for examining gas phase duplex stability. Also, we have found that the E_{50}'s of duplex ions are consistent with their Tmax's in solution.

244. Trascient isotachophoretic (tITP) stacking of in-line generated reactions products in CE

Timothy G. Strein, Rachel Slotcavage, Diana Scheerbaum, Brandi Sanders, Phillip Mason and Derek Schildt, Bucknell University, Lewisburg, PA

First reported in 1992 by Boa and Regnier, electrophoretically mediated microanalysis (EMMA) is a capillary electrophoresis (CE) based technique that involves the in-capillary mixing of reactant ions in nanoliter volumes of solutions based on differences in electrophoretic mobilities of the reactants. Although relatively new, EMMA has become a widely accepted methodology in the bioanalytical laboratory. Most of the applications involve enzyme reactions where enzyme turnover can generate high amounts of product, overcoming the characteristically poor concentration sensitivity observed with CE methods. This work is aimed at designing a system for EMMA with small molecules in which the product of the in-line EMMA reaction is stacked. Stacking, the process of concentrating an analyte, is accomplished either through local field amplification or, more effectively, by transient isotachophoresis (tITP) at an ionic boundary within the capillary. We have been working with the clinically relevant small molecule chemistry of the Jaffe method for creatinine. This chemistry involves the reaction of creatinine with picrate, under alkaline conditions, to form an anionic product. This presentation will include our application of both field amplified stacking and tITP stacking of the in-line generated product, by altering the borate background buffer concentration, and by creating discontinuous ionic systems invoked by injecting a plug of a highly mobile anion. Dramatic increases in peak height, and thereby considerable lowering of the LOD for this

method is accomplished, making EMMA a reasonable choice for this small molecule chemistry with the concentrations of creatinine found in real samples.

245. Clean Chemistry for Trace Metals Analysis

Nimi Kocherlakota and Ralph H. Obenauf, Spex CertiPrep, Metuchen, NJ

The key issue in all chemical analysis is the integrity of the measurement. Present day instruments are capable of detecting metals at the ppb and ppt levels. Having an instrument of this type in the lab will not be of much help, if one does not use the reference materials that are specifically designed for trace metals analysis or identify and minimize contamination in the lab environment. The presentation will cover various issues including reference materials, sources of contamination and tips on how to prevent contamination.

246. Analyzing speciation of arsenic in iron rich groundwater and wastewater

Zhongqi Cheng[1], Yi He[2], Yan Zheng[3] and Alexander Van Geen[1], (1)Lamont Doherty Earth Observatory of Columbia University, Palisades, NY, (2)John Jay College, City University of New York, New York, NY, (3)Queens College, City University of New York, Flushing, NY

Groundwater contaminated by natural or anthropogenic arsenic often contains high level of iron, which in the air can be quickly oxidized and forms precipitation. The Fe-oxyhydroxides adsorb arsenate, arsenite, and organic As with different affinities, therefore will falsify the speciation data collected using liquid chromatography or field SPE cartridge separation methods. On the other hand, groundwater samples are usually acidified for preservation, therefore raising the pH is necessary prior to column separation because available methods only work at higher pH ranges, while this will also precipitate Fe that complicates As speciation analysis. Similarly, a lot of wastewater and sediment leachate also contain high Fe; while speciation data on leachate will be extremely useful considering limitation on the current detection limit (10 ppm) of surface analysis methods. We are investigating potential buffers that could stabilize Fe in groundwater and wastewater solutions, and the interference on the performance of column separation.

247. Quantitative Analysis of Lead (II) Carbonates Using Vibrational Spectroscopy

Christine A. Rapach and Gene S. Hall, Rutgers University, Piscataway, NJ

Basic lead (II) carbonate ($2PbCO_3 \bullet Pb(OH)_2$) powders purchased from a variety of chemical companies were analyzed using vibrational spectroscopy, both Raman and FT-IR. They were determined to contain various amounts of lead (II) carbonate ($PbCO_3$) in addition to the basic lead (II) carbonate. One sample in particular was strictly lead (II) carbonate. Quantitative analysis was performed using ATR-FT-IR spectroscopy. The amount of lead (II) carbonate in the samples was quantified using calibration curves constructed from the spectra of mixtures of the pure components. The content of lead (II) carbonate was determined by the absorbance of the band at 837 cm^{-1}. The amount of lead (II) carbonate in basic lead (II) carbonates may be indicative of the manufacture process. This may further allow for the distinction of basic lead (II) carbonates produced by different chemical companies. Future research includes quantifying the percentage of lead (II) carbonate in white lead house paints in order to distinguish between paint pigment manufacturers. Raman and ATR-FT-IR are complimentary techniques and offer excellent analytical methods to characterize lead-based architectural paints.

248. Concentrations of Phthalates in Plastic Toys as Determined by ATR-FTIR Spectroscopy

jeannine Matuza, Rutgers, The State University of New Jersey, Piscataway, NJ

Many plastics today contain non binding chemicals to alter their properties. Phthalate based plasticizers di(ethylhexyl) phthalate (DEHP)and diisononyl phthalate (DINP) are commonly used to make polyvinyl chloride (PVC) more flexible. The use of a nondestructive method, ATR-FT-IR, for quantitative as well as qualitative analysis of phthalate content is evaluated for plastics containing PVC. Thirty-five percent of the plastic samples analyzed were found to contain the phthatlates DEHP or DINP in concentrations from 2 - 70% w/w. The correlation coefficient of absorbance of a given band to the percent of phthalate present was 0.98. The high correlation value indicates a linear relationship between absorbance and concentration of the phthalate bands. The method illustrates the success of using a nondestructive method for quantitative analysis of phthalates in toys. In the future, the described method may be applied to determining authenticity or dating of the toy.

Assuring Water Purity

Presider: Sut Ahuja Ahuja Consulting, Calabash, NC
Official: Sut Ahuja Ahuja Consulting, Calabash, NC

249. Assuring Water Purity for Human Consumption

Sut Ahuja, Ahuja Consulting, Calabash, NC

Our drinking water comes from a number of sources such as rivers, lakes, wells, and natural springs. These sources are generally exposed to a variety of conditions that can contaminate the water. The contaminants can come from Mother Nature, even where the soil has not been influenced by any contaminants from human beings or from a whole host of the activities of people. A number of man-made contaminants such as insecticides, pesticides, herbicides, detergents,

gasoline additives, and even pharmaceuticals can affect our drinking water. Lately, our concern has included the treacherous activities of terrorists who threaten to poison our water supplies. The sources of nature's contamination are many, and the discussion will focus mainly on the massive impact of arsenic contamination on Bangladesh. Also, a number of countries in Asia, Europe, and South America, as well as Australia and the United States are affected by arsenic contamination for a variety of reasons. Right here in the US, a fairly large number of states are affected by arsenic contamination. Inorganic arsenic above 10 ppb can increase the risk of lung, skin, bladder, liver, kidney, and prostate cancer. The impact of such effects will be demonstrated on the basis of studies in Bangladesh, where 60 million people are at risk. Solutions offered by separation chemistry, which include monitoring by ultratrace analysis, will be discussed. It will be emphasized that vigilant monitoring of our water supplies by sophisticated techniques is needed to help us assure water purity.

250. Poison in the Well: The Crisis of Arsenic in Drinking Water in Bangladesh

Joe Graziano, Columbia University, New York, NY

In Bangladesh, a large number of people have been chronically exposed to high concentrations of naturally occurring arsenic (As) in drinking water, supplied by approximately 10 million tube wells. In addition many of the existing wells in Bangladesh also have manganese (Mn) concentrations which exceed the World Health Organization (WHO) standard of 500 ìg/l. Given the absence of a significant research base concerning the consequences of As or Mn in children, we sought to examine the possible associations between As exposure and intellectual function, taking into account possible effects of Mn. In 2000, we began a prospective study of the health effects of As in 12,000 adult residents of Araihazar, Bangladesh. The study site, a 25-square-km region located approximately 30 km east of Dhaka, was chosen because of its wide range of As concentrations in drinking water. Our survey of 6,000 contiguous wells in the region revealed that 75% exceed the WHO As standard of 10 ìg/L, while 53% exceed the Bangladesh standard of 50 ìg/L; water As concentrations ranged from <1 to 900 ìg/L. Roughly 80% exceeded the WHO Mn standard. We have recently completed two cross-sectional studies of roughly 400 children in this region. Our finding of a strong association between As and Mn exposure and intelligence is both important and tragic, and adds urgency to the need for effective remediation.

251. Leachability of Arsenic in Water Treatment Residuals

Xiaoguang Meng, Chuanyong Jing and Suqin Liu, Stevens Institute of Technology, Hoboken, NJ

Arsenic leachability in water treatment adsorbents was studied using batch leaching tests, surface complexation modeling and Extended X-ray Absorption Fine Structure (EXAFS) spectroscopy. Spent adsorbents were collected from five pilot-scale filters that were tested for removal of arsenic from groundwater in Southern New Jersey. The spent media included granular ferric hydroxide (GFH), granular ferric oxide (GFO), titanium dioxide (TiO2), activated alumina (AA) and modified activated alumina (MAA). The As leachability determined with the Toxicity Characteristic Leaching Procedure (TCLP) was below 180 µg L-1 for all spent media. The leachate As concentration in the California Waste Extraction Test (WET) was more than 10 times higher than that in the TCLP, and reached as high as 6650 µg L-1 in the spent GFH sample. The EXAFS results indicate that As forms inner sphere bidentate binuclear surface complexes on all five adsorbent surfaces. When the spent adsorbents were incubated in a closed system containing microbes and nutrients, the redox potential (Eh) was reduced to -400 mV in a few days. Analyses using x-ray absorption near edge structure (XANES) spectroscopy and solution speciation method revealed that reduction of arsenate [As(V)] to arsenite [As(III)] occurred in solutions and on solid surfaces.

252. Development and Deployment of an Arsenic Filter for Groundwater of Bangladesh

Abul Hussam, George Mason University, Fairfax, VA and A. K. M Munir, Sono Diagnostic Center Environment Initiative, Kushtia, Bangladesh

The presence of toxic level of arsenic in groundwater is causing a public health emergency in many parts of the world. In Bangladesh, thousands of people are suffering from arsenical keratosis and many people have died of cancer after prolonged drinking of such groundwater. To purify this water, we have developed an arsenic filter based on composite iron matrix (CIM) as the active material. Extensive field tests show the effluent arsenic concentrations were below 10 microgram/L (95% cases) even when the influent arsenic were 4000 microgram/L. The filtration process was monitored by measuring As (total), As(III), 23 other metals, 9 anions, pH, dissolved oxygen, conductivity, temperature and flow rate. The filter performance was verified in presence of dissolved iron, phosphate, sulfate, and silicate as the confounding factors. Experimental data and theoretical calculations show no breakthrough of arsenic, which is due to a zero order surface complexation reaction between arsenate and hydrous ferric oxide on CIM. A continuous decrease in As(total) below 10 microgram/L indicates a progressive increase of filter efficiency- unique to CIM based technology. These filters were thoroughly tested by an Environmental Technology Verification Arsenic Mitigation Program (ETVAM) and compared with other filter technologies. Approved by the government ETVAM for household use, Sono has deployed 15,000 filters throughout Bangladesh. These filters can last for at least five years with simple maintenance and producing no toxic waste. We estimate that about a billion liter of water has been consumed from these filters and continues to be used daily.

253. The Utilization of Common Paramater Monitoring as an on-Line Surveillence Tool for Water Security: Identifying Distribution System Incursions through the Use of Interpretive Algorithms

Dan Kroll and Karl King, Hach Homeland Security Technologies, Loveland, CO

The vulnerability of the drinking water distribution systems to accidental or deliberate contamination due to a backflow event is becoming a well-recognized possibility. The variety of potential threats and the innumerable access points make this a difficult scenario to defend against. This was clearly stated in a GAO report to Congress that listed the vulnerability of the distribution system to attack as the largest security risk to water supplies. A system designed to address the problem of distribution system monitoring is described here. The developed system employs an array of common analytical instrumentation, such as pH and chlorine monitors, coupled with advanced interpretive algorithms to provide detection/identification-response networks that are capable of enhancing system security. A variety of real world venues and testing protocols were used to verify the efficacy of the system. Data obtained from a Battelle/EPA ETV study and a cooperative research and development agreement (CRADA) between Hach HST the EPA Office of Research and Development addresses issues such as long-term deployment and ability to detect and characterize contaminants. Information obtained from test loop studies carried out by Hach HST, the US Army Corp of Engineers Research Lab, and the Edgewood Biological and Chemical Command as the result of a 3-way CRADA demonstrate data collected when the system is exposed to actual warfare a! gents and a series of data streams from real world beta sites demonstrate learning ability and deployment strategies. The system is shown to be a practical measure to help detect and characterize backflow events.

Biological Chemistry

254. Automation of Cell Culture to Support Cell-based Assays for Compound Profiling

Debra Burdick, Novartis Institute for Biomedical Research, Cambridge, MA

There is ever increasing pressure in the industry to provide profiling data early in the drug discovery process to try to minimize the loss of candidate compounds during development. This has lead to heavy demands on the support labs as the number of compounds tested quickly expands. For cell based assays one option to help increase throughput is to fully automate cell culture and plating. I will present our experiences in automating these processes and lessons learned.

255. A new factor required for Wnt-mediated cellular motility

Melissa Maglaqui, The College of Saint Elizabeth, Morristown, NJ and Raymond Habas, University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School

Wnt signaling plays important roles during embryonic development, including cell motility, cell proliferation, and cell fate determination. Wnt signaling has also been shown to play a causative role in human cancer formation. Understanding Wnt signaling will advance our knowledge of the role of this factor in development and tumor formation. One key aspect of Wnt signaling involves the non-canonical pathway, which regulates cellular motility. A crucial factor required for this process is the protein, Daam1, “Disheveled associated activator of morphogenesis”. How Daam1 affects cellular motility remains poorly defined. To identify effectors downstream of Daam1, a yeast two-hybrid screen was performed. This screen identified the protein MIM, “Missing in Metastasis”, as a Daam1 interactor. MIM was previously found absent in some cancers, but its biological functions remain unknown. The relationship of MIM and Daam1, and the effects of MIM on the cellular architecture were studied. Visualization by GFP fluorescence and detection of endogenous Daam1 using a Daam1 specific polyclonal antibody in NIH3T3 cells showed (1) colocalization of a transfected GFP-MIM construct with Daam1 and (2) a decrease in actin stress fibers in cells with high MIM expression. Immunoprecipitation studies were performed to detect an interaction between MIM and Daam1 using epitope-tagged constructs expressed in mammalian cells. These experiments revealed that HA-tagged Daam1 could be immunoprecipitated by Myc-tagged MIM and vice versa. These studies together provide evidence of an association between Daam1 and MIM and signify that MIM may be a key effector for Daam1 in cytoskeletal changes during development.

256. Investigation of polyamine analogs on the growth of MCF-7 breast cancer cell lines

Francis Charles Mayville Jr., Michelle Piel, Kristina Thornburg, Christopher Higgins and Peter Leonard, DeSales University, Center Valley, PA

In this study, we are synthesizing new polyamine analogs using 1,4-diaminobutane (putrescine) as the template. The new polyamine derivatives will contain two, three, or four carbon primers at the each amino end of the putrescine. It has been previously determined that the polyamine systems can bind to the minor grooves of DNA molecules and inhibit cell growth. In other previous work, the inhibition of cell growth has been studied using several synthesized polyamine derivatives, and it was found that these artificial systems had more inhibition ability then natural polyamines. In our study, the new polyamine systems will be compared with current polyamine analogs to determine their efficacy for inhibition of cell growth in MCF-7 breast cancer cell lines. The methods of analysis will include HPLC analysis of nuclear DNA and gross cell counting.

257. NMR studies of Liver Fatty Acid-Binding Protein in lipid membrane media

fouad Francis, Ruth Stark, Hsin Wang and Xiaomin Yang, College of Staten Island. City University of New York, Staten Island, NY

Liver Fatty Acid Binding Protein (LFABP) is a 14 kDa water-soluble protein that binds a variety of ligands and transports them across the cell membranes. Chemical shift perturbation has identified the ligands as binding, non-binding, or denaturing of the protein. While RDC measurements have led to a refinement of the tertiary structure of the apo form of the protein using C12E5 gel, the gel has proven unapplicable for the refinement of the holo form. Acidic bicelles have been used as a lipid membrane mimetic media. Two-dimensioinal solution-state NMR studies have yielded a preliminary identification of the regions on the tertiary structure that associate with both the holo- and the apo- forms of the protein.

258. Human Skin Odors

Michelle Gallagher[1], George Preti[1], Russell Bazemore[1], James J. Leyden[2], Arlene Foglia[2] and Andrew I. Spielman[3], (1)Monell Chemical Senses Center, Philadelphia, PA, (2)University of Pennsylvania, Philadelphia, PA, (3)NYU, New York, NY

Skin is the largest human organ. Human skin odors result, in part, from interactions of sebaceous and eccrine gland secretions with the resident cutaneous microflora; in vitro, these organisms generate small, volatile odor molecules when incubated with skin secretions. In the past, attention has been focused on skin secretions because of their importance as potential mosquito attractants, but these studies have generally employed a limited number of young volunteers. Recent studies also provide evidence that volatile cues from melanoma tissue, recognizable from healthy skin, can be detected by the canine olfactory system. Thus, identifying such volatile chemicals could greatly aid in the early detection of melanoma or other types of skin cancer. Our initial studies in this area have used Solid Phase Microextraction (SPME) and solvent extraction to examine skin volatiles from healthy males of different ethnicity and age. SPME-collected volatiles were analyzed by GC/MS and appear to be qualitatively similar for all individuals examined, although young males generally appeared to have less volatiles than some older males. Extracts contained high concentrations of C_8-C_{18} acids, and n-C_{12}, -C_{14} and -C_{16} alcohols. Our current studies focus on examining a larger population of normal, healthy subjects of different age, gender, and ethnicity in order to gain a better understanding of the normative odorant emission patterns. Expansion of this study across gender and ethnic groups is necessary to use skin volatiles as a medium for the diagnosis of skin carcinoma. Supported in part by grants from NIH (T 32 DC00014-26).

259. MHC-related Odorprints in Mice

George Preti[1], Alan Willse[2], Gary K Beauchamp[1], Kunio Yamazaki[1], Peter Yang[1] and Jon H. Wahl[2], (1)Monell Chemical Senses Center, Philadelphia, PA, (2)Pacific Northwest National Labs, Richland, WA

We describe the application of GC/MS to identify volatiles from urine samples obtained from two groups of inbred mice that differ only in the genes of the major histocompatibility complex (MHC): about 0.5% of the genome. Behavioral studies have shown that the MHC genes contribute to an individual's unique urinary odor. Our goal is to specify which components in urine are regulated by the MHC genes and contribute to mouse olfactory individuality. This is a difficult problem because complex mixtures from biological samples might comprise several hundred volatile compounds; the number and location of compounds we seek are unknown; and components overlap in complex chromatograms. Consequently, the statistical problems offer significant challenges. One of the few studies in this area (Singer et al., PNAS 94: 2210, 1997) showed that these mice differed in some volatile components but only a small number of easily identified peaks were examined and these were manually quantified. Our current research employs a novel statistical procedure to compare the GC/MS profiles between two MHC groups. Several dozen regions of significant differences were identified. This procedure enormously increases the analyst's ability to identify differential biomarker compounds in complex mixtures. Our results suggest that several dozen compounds are involved in MHC chemosignaling, including two mouse pheromones, 2,5-dimethylpyrazine and 2-sec-butyl-4,5-dihydrothiazole (Willse et al., Anal. Chem. 2005, in press). This work is sponsored by DARPA under ARO Contract DAAD 19-03-1-0109. Opinions, interpretations, conclusions, and recommendations are those of the authors and are not necessarily endorsed by the United States Government.

260. Characteristic Odor Components in Mouse Urine

Jae Kwak, Marcus Jackson, George Preti, Maryanne Curran, Kunio Yamazaki and Gary Beauchamp, Monell Chemical Senses Center, Philadelphia, PA

To the human nose, mice produce unique, strong and even annoying odors, which mainly derive from their urine. The volatile compounds of mouse urine have been studied, and large numbers of the volatiles have been identified. However, there is little published information regarding the identity of the compounds responsible for the unique odor of mouse urine. Lehman-McKeeman et al. (Toxicol. Appl. Pharmacol. 149: 32, 1998) identified 2-sec-butyl-4,5-dihydrothiazole as a characteristic odor compound that eminates from isolated mouse urinary proteins (MUPs). In addition, there is an indication that other compounds extracted from MUPs contribute to mouse urine odor (Novotny et al., Proc. R. Soc. Lond. B 266: 2017, 1999). We employed solid phase microextraction in conjunction with gas chromatography/olfactometry (GC/O) to investigate volatile compounds in whole mouse urine that contribute to it's unique odor character. We found three compounds responsible for the characteristic mouse urine odor. Two are previously identified 2-sec-butyl-4,5-dihydrothiazole and 2-isopropyl-4,5-dihydrothiazole. The third compound could not be identified since it was below GC/MS

detection limits. However, analysis of mouse urine volatiles by GC with flame photometric detection indicates that it is also a sulfur-containing compound. Consequently, 3 sulfur-containing compounds contribute to characteristic mouse urine odor. This work is sponsored by DARPA under ARO Contract No. DAAD19-03-1-0109. Opinions, interpretations, conclusions, and recommendations are those of the authors and are not necessarily endorsed by the United States Government.

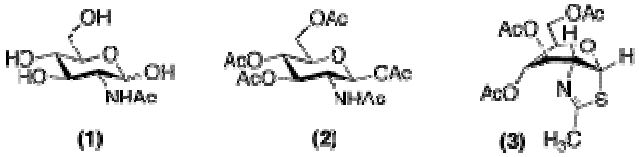
Carbohydrates

Organizer: Cecilia H. Marzabadi Seton Hall University, South Orange, NJ
Presider: Cecilia H. Marzabadi Seton Hall University, South Orange, NJ

261. Practical synthesis and crystal structure of GlcNAc-thiazoline

Richard A. Huhn, Thomas J. Emge and Spencer Knapp, Rutgers University, Piscataway, NJ

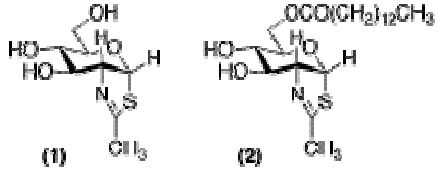
An improved route to the GlcNAc-thiazoline triacetate (3) is described, including the results of screening Lewis acids for acetylation of N-acetyl-D-glucosamine (1) and methods for thionation of pentatacetate (2). The crystal structure of the 2,4-dinitrobenzenesulfonate salt of (3) will also be presented.



262. Synthesis and crystal structure of GlcNAc-thiazoline-6-O-tetradecanoate

David Fash, Thomas J. Emge and Spencer Knapp, Rutgers University, Piscataway, NJ

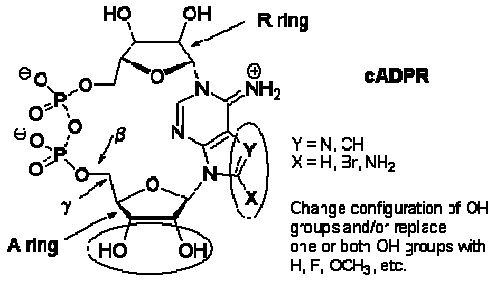
The conversion of GlcNAc-thiazoline (1) to the corresponding O-tetradecanoate derivative (2) is described, along with discussion of the crystal structure of (2) and its unique conformational and crystal packing characteristics.



263. Developing the Structure-Activity Relationships for cADPR: Conformational Analysis of cADPR Analog Agonists and Antagonists

Steven M. Graham, St. John's University, Queens, NY

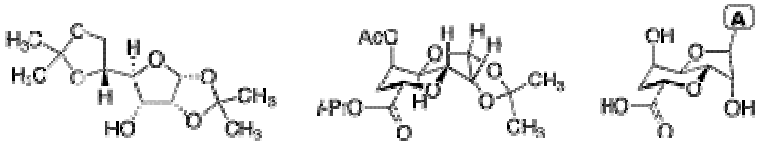
Cyclic adenosine diphosphate ribose (cADPR) is a putative second messenger that causes release of calcium from intracellular stores. It is well known that the conformation of the adenosine furanose ring is profoundly affected by the configuration and identity of electronegative substituents at the 2'- and 3'-positions. Changes at these positions have produced both cADPR agonists and antagonists, whereas only antagonists result from changes at the 8-position of the adenine ring. Replacement of the adenine N7 with CH leads to an analog that is resistant to spontaneous hydrolysis. We will present our recent work on the NMR solution structures of these analogs, with a discussion of how the conformations of the agonists and antagonists differ.



264. Short route to octosyl nucleosides

Vinay V. Thakur, Machender Madduru, Krishnan Malolanarasimhan and Spencer Knapp, Rutgers University, Piscataway, NJ

An efficient synthesis of octosyl nucleosides from diisopropylidene-D-allofuranose (1) features conversion of (1) to the bicylic ester (2), followed by N-glycosylation to give nucleosides such as (3), A = 9-adeninyl.

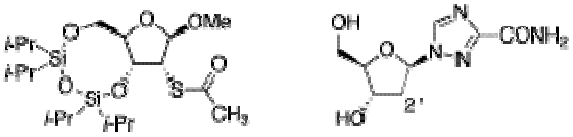


(1) (2) (3)

265. 2'-Deoxynucleosides through 2'-thio-S-acetyl participation

Srihari Pabbaraja and Spencer Knapp, Rutgers University, Piscataway, NJ

The synthesis of 2'-deoxynucleosides has been simplified through the use of the 2'-thio-S-acetyl participating group to direct N-glycosylation. Donor (1) reacts under Vorbruggen conditions to give a nucleoside that is desulfurized with Ra-Ni to give, for example, 2'-deoxyribavirin (2).



(1) (2)

266. Carbohydrate-fused heterocycles: Preparation and further transformations

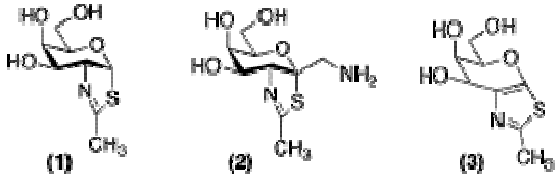
Cecilia H. Marzabadi and Michael De Castro, Seton Hall University, South Orange, NJ

A method for the preparation of C1 O-linked and C1 N-linked glycooxazolines in two steps from common precursor amides and glycals will be presented. The analogous preparation of thiooxazolines and ureaoxazolines will also be described. Methods to form other heterocycles such as lactams, oxazoles and oxazolidines from these precursors, as well as, the ring-opening reactions of the carbohydrate-fused oxazolines leading to the formation of N-chloroimines, oximes, hydroxylamines and amino glycosides will be discussed.

267. Synthesis of 1-C-elaborated GalNAc-thiazolines

Benjamin Amorelli and Spencer Knapp, Rutgers University, Piscataway, NJ

The GalNAc-thiazoline (1) is an effective inhibitor of N-acetylhexosaminidases such as SpHEX. To improve inhibition and to study bioconjugation, we have prepared 1-C-elaborated analogues such as (2). This synthesis along with a unique rearrangement leading to the thiazole (3) will be presented.



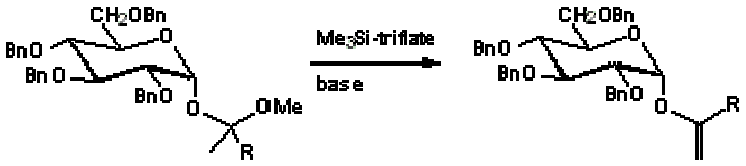
(1) (2) (3)

268. Vinyl glycosides and carbohydrate vinyl ethers: Synthesis and applications

Robert Giuliano, Kevin Hughes, Christopher Cummings and Tuan Nguyen, Villanova University, Villanova, PA

Vinyl glucopyranosides have been used as chiral auxiliaries in cycloaddition reactions, as precursors to branched glycals, as glycosyl donors, and in other applications. Vinyl glucopyranosides are most often synthesized by trans-vinylation reactions, by displacement reactions of glycosyl halides with bis(acylmethyl)mercury reagents, or by selenoxide or other elimination reactions. Recently, a mercury-free preparation of vinyl ethers has been reported, in which the vinyl group is introduced by the elimination of mixed acetals with trimethylsilyl trifluoromethanesulfonate in the presence of alkyl amines (Gassman method).[1,2] We have applied this reaction to the synthesis of protected vinyl a-D-glucopyranosides as well as to related carbohydrate vinyl ethers.[3] Hetero-Diels-Alder reactions of the vinyl ethers have been carried out as part of an approach to disaccharides that contain highly deoxygentated sugars. These reactions are

highly regioselective and give mainly endo cycloadducts. Cyclopropyl glycosides have also been prepared.



1. Gassman, P.; Burns, S. J.; Pfister, K. B. *J. Org.Chem.,***1993**, *58*, 1449, 2. Dujardins, G.; Rossignol, S.; Brown, E. *Tetrahderon.Lett.*, **1995**, *36*, 1653, 3. Edathil, J.; Nguyen, J.; Hughes, K.; Boyko, W. J.; Giuliano, R. M. *J. Carbohydr.Chem.* **2001**, *20*, 81.

Discovery to Commercialization

Organizer: Rhoda Kriesel Touchstone Marketing, Upper Montclair, NJ
Organizer: Ed Harris E. B. Harris & Assoc., Spring Valley, NY

269. Molding an Innovation to Market Needs: A Critical Key to a Start-up's Success!

Joe D'Antuono, ROW2 Techologies, Inc., Parsippany, NJ

Chemical Process Development has emerged as a vital step in the long path to drug commercialization. Not only must process chemists devise new, efficient, safe and scalable synthetic routes to a target compound, they must also meet tight deadlines, while identifying cost-effective ways to produce commercial quantities of a target molecule. Realizing that "route design" was still primarily an intellectual/intuitive process, and no technological tools had been developed to support this complex task, ROW2 Technologies developed intellectual property and an innovative software application to revolutionize the process chemistry world. ROW2 developed ChemSpire®, a software application with an underlying knowledge base of commercially-practiced chemistry and novel searches based on "synthetic analogy".

Dr. D'Antuono will outline the development process and critical learnings for launching a novel software technology. He will also describe how ROW2 has had to adapt to its customers' needs and emerged as a "software & solutions" company. Today, ROW2 markets products to process development, business development and sourcing professionals in the life sciences and chemical industries. Finally, Dr. D'Antuono will highlight the key issues faced in the commercialization process, and strategies taken to address those issues, which led ROW2 to develop a sustainable business model based on breakthrough technology

270. From a Eureka Moment to a Clinical Candidate: a Case Study of a PolymerDrug™

Karen Giroux, Polymerix Corporation, Piscataway, NJ

The effort involved in moving from the excitement of an initial discovery to the point of commercialization is often underestimated by those who make the initial invention. Dr. Kathryn Uhrich has made several innovative leaps forward in science, particularly in developing a new class of pharmacologically active biodegradable polymers, and it has been Polymerix Corporation's responsibility to find the right commercialization path for each. Some joys and pitfalls of developing an innovative platform technology in the post-web-bubble-post-9/11 investment environment will be described.

271. HydroGlobe - Commercializing an Innovative Water Purification Technology

John Schroeder, Graver Technologies llc, Hydroglobe Div, Glasgow, DE

HydroGlobe developed through a unique partnership between academia and the private sector. It was founded in 2001 by three professors from Stevens Institute of Technology in Hoboken, NJ, who had developed technology for the removal of heavy metals from water, and had done pioneering work in prototyping the technology to remove arsenic from water in such areas as Bangladesh. Stevens, under its Technogenesis program, initiated incubation of the company, whose purpose was to commercialize the technologies. The start up was also to allow continued involvement of the professors, students, and other Institute personnel as a learning experience in how a business is started and run.

Through a licensing arrangement, HydroGlobe's strong management team, which had high quality technical expertise, used their state of the art facilities for the commercialization process. After three years of product engineering, during with time HydroGlobe developed a series of water applications, HydroGlobe LLC was recently acquired by Graver Technologies, a leading player in the water treatment industry, who will move the technology through the next, expanded commercialization steps into a variety of markets.

272. Commercialization of Nanocomposite Barrier Coatings

Harris Goldberg, Inmat, Inc, Hillsborough, NJ

InMat®, Inc., headquartered in Hillsborough, New Jersey, is a leading company in the field of nanocomposite coatings that dramatically improve the barrier properties of polymers and elastomers. Founded in 1999, and selling commercially

since 2001, InMat develops, markets and manufactures nanocomposite coatings based on the Nanolok™ breakthrough technology.

InMat's proprietary and patented Nanolok™ technology platform has lead to commercial products that have been marketed under the brand name Air D-Fense™ and Nanolok™. These products enable significant advancements in industries where barrier technology is key, including flexible and rigid packaging, automotive,medical device components, protective apparel, and sports equipment.

InMat's product line has been developed with the use of funding from large corporations, the founders, Angel investors, state agencies, federal agencies, and venture capital. All development efforts were focused on the needs of customers in specific markets. How these needs were addressed became the cornerstone of InMat's strategy and business plan, enabling InMat™ to hold a leading position in nanocomposite barrier coatings

Engineered and Novel Biomaterials

Organizer: Kathryn E. Uhrich Rutgers University, Piscataway, NJ
Presider: Michael S. Yu The Johns Hopkins University, Baltimore, MD

273. Non-Covalent Modification of Collagen Scaffolds

Michael S. Yu, The Johns Hopkins University, Baltimore, MD

Collagen, either alone or in combination with other component is used in a variety of medical applications ranging from hemostatic materials and biocompatible coatings to drug delivery and tissue engineering. While there are manifest interests in modifying natural collagen to improve its biochemical and mechanical properties, chemical coupling reaction of the amino acid side chains has been the only method commonly practiced for such purpose. As an alternative to the conventional “chemical” modification method, we have developed a novel “physical” collagen modification technique that is based on collagen's native ability to associate into triple-helical molecular architecture. Here we present a finding that i) collagen mimetic peptides (CMPs) of sequence –(Pro-Hyp-Gly)x- exhibit strong affinity to both native and gelatinized type I collagen under controlled thermal conditions, ii) gold nanoparticles passivated with CMP can be used for locating CMP-collagen interactive sites, and iii) cell adhesion characteristics of natural collagen can be readily altered by applying poly(ethyleneglycol)-CMP conjugate to a prefabricated collagen film. In the long run, this approach can be developed into a more general collagen modification method that can provide novel solutions to complications after vascular and ocular surgery, and to add therapeutic activities to conventional collagen-based biomaterials and tissue engineering scaffolds.

274. Biomimetic Scaffolds for Vascular Tissue Engineering

Joyce Y. Wong, Boston University, Boston, MA

Cardiovascular disease is the leading cause of death in the Western world. The development of suitable small diameter (< 6 mm) blood vessels has been particularly challenging. Currently there are no clinically acceptable synthetic or tissue-engineered small diameter vascular grafts. Here we focus on the medial layer of the blood vessel which is primarily composed of vascular smooth muscle cells (VSMCs), type I collagen, and elastin. The components have a unique hierarchical structural organization, but the importance of this organization on cell response and tissue properties remain unclear. Control of cell response is critical because VSMCs can switch between a synthetic (proliferative, migratory) and a quiescent (contractile) phenotype. While synthetic VSMCs are required for cell expansion and infiltration throughout the scaffold, it is critical to switch them to the contractile phenotype to avoid uncontrolled growth and migration that can severely reduce vessel patency. Recently we have shown that substrate stiffness affects VSMC proliferation and migration rate and that substrates characterized by gradients in stiffness can be used to elicit directional migration. We also find that micropatterned substrates can be used to reverse VSMC phenotype, as assessed by cell morphology, protein expression and localization, extracellular matrix organization, and cell function. We also will discuss our findings in developing processable elastin scaffolds and their potential use as provisional scaffolds.

275. Electrospun Polymer Nanofibers and Nanospheres for Drug Delivery and Tissue Engineering Scaffolds

John F. Rabolt, University of Delaware, Newark, DE

The goal of many tissue engineering scaffolds is to closely mimic the extracellular matrix (ECM), which contains protein fibers that range in diameter from a few microns to the nanometer scale. In our studies, electrospinning has been used to create membranes of nanometer scale collagen, genetically engineered polyurethanes, PLGA and other biocompatible polymer fibers. The nature of the electrospinning process is such that a range of fiber diameters and surface morphologies can be produced depending on the choice of processing protocols (1,2). This talk will describe an electrospinning processing strategy to control the macroscopic shape, the polymer backbone orientation/conformation (3) and the surface topography/morphology of the micro- and nanofibers produced. The objective of these studies has been to optimize structure-processing-property relationships in the electrospun fibers for biological (tissue engineering, water filtration, drug delivery, etc.) and structural (high tenacity fibers and webs (4), membranes, etc.) applications. Raman spectroscopy, AFM, planar array infrared (PA-IR) spectroscopy, field emission scanning electron microscopy (FE-SEM) and confocal fluorescence microscopy have been used to investigate the structure of fibers over many different length scales and their interaction with cells.

1. S. Megelski, J. Stephens, D. B. Chase and J. F. Rabolt, Macromolecules 2002, 35, 8456; 2. C. Casper, J. Stephens, N. Tassi, D. B. Chase and J. Rabolt, Macromolecules 2004, 37, 573; 3. J. Stephens, D.B. Chase and J. F. Rabolt, Macromolecules 2004, 37, 877; 4. J. S. Stephens, J. F. Rabolt, S. Fahnestock and D. B. Chase, MRS Proceedings 2003, 774, 31.

276. Drug Delivery Vehicles Based on Poly(Oxyethylene Phosphonate)s

Kolio Troev, Bulgarian Academy of Sciences, Sofia, Bulgaria and **Ivan Gitsov**, SUNY College of Environmental Science and Forestry, Syracuse, NY

Conjugation with biocompatible or bioerodible polymers is one of the most widely used strategies to minimize drug toxicity and improve the efficiency of drug delivery. This talk will describe the synthesis, characterization and fundamental properties of organo-phosphorous polymers containing poly(ethylene glycol) segments and H-phosphonate moieties as promising drug delivery vehicles. The use of the Atherton-Todd reaction in the post-polymerization modification for the attachment of biologically active substances will be discussed. Results from the biomedical evaluation of poly(oxyethylene phosphate) conjugates with the radioprotective agent Cysteamine and the anti-HIV drug 3'-azido-2',3'-dideoxythimidine (AZT) will be presented.

277. Artificial Glycopolymers for the Inhibition of Bacterial Toxins

Brian D. Polizzotti and Kristi L. Kiick, University of Delaware and Delaware Biotechnology Institute, Newark, DE

Toxins and pathogens achieve highly efficient and selective binding through multivalent interactions between relevant oligosaccharides and multiple saccharide receptors on each toxin/pathogen subunit. The synthesis of polymers via protein engineering methods allows control over both the number and spacing of saccharides on a scaffold, which permits the structure-based design of polymers for inhibition of the multivalent binding event. In initial studies, we have synthesized a family of glycopolymers with a poly-L-glutamic acid backbone in which the type, density, and linker length of the pendant carbohydrate moiety was varied. The potential for these glycoproteins as high-affinity inhibitors of the cholera toxin has been indicated via competitive enzyme-linked immunosorbent assay and fluorescence titration experiments. Glutamic-acid functionalized helical protein polymers have also been modified with carbohydrates to permit more detailed characterization of bacterial toxin inhibition as a function of glycopolymer architecture. Investigations like these will aid in the deconvolution of the impact of multivalency, spacing, and backbone rigidity in a variety of biologically relevant binding events.

278. Glycosylation of Multifunctional Alanine-Rich Protein Polymers for Biological Applications

Ying Wang and Kristi L. Kiick, University of Delaware and Delaware Biotechnology Institute, Newark, DE

The development of routes for the production of well-defined glycopolymers is critical for the tailored design of materials that can mediate biological processes such as pathogenesis, inflammation, and the immune response. Accordingly, helical artificial proteins with sequences comprising primarily alanine and glutamine have been designed to contain glutamic acid residues at specific distances that are targeted to match the receptor spacing of certain toxins and lectins. These proteins are readily expressed and purified from E. coli and are highly helical under a variety of solution conditions. The helical artificial proteins are also competent for chemical modification with saccharides for inhibition of select bacterial toxins and lectins. In the investigations reported here, multivalent artificial glycoproteins bearing galactose moieties as pendant groups have been prepared via the coupling reaction of amine-functionalized galactose with the glutamic acid functional groups of the protein polymer. Glycosylation of proteins was confirmed via mass spectrometry, NMR spectroscopy, SDS-PAGE, and photometric methods. CD spectroscopy shows that the resulting glycosylated proteins maintain a highly helical structure, and competitive ELISA assays suggests the efficient binding of these glycoproteins to cholera toxin. These results demonstrate that the integration of biological and chemical approaches to the synthesis of well-defined polymeric structures offers significant opportunities in the purposeful design of polymers for applications in biology.

279. A Universal Synthetic Methodology to Prepare Peptide-Polymer Hybrids

Ying Mei, National Institute of Standard and Technology, Gaithersburg, MD

The hybrid biomaterials have received many attentions in recent years. The interests in including the peptides and protein in the biomaterials were driven by their ability to introduce the specific cell-material interaction. Moreover, the ability of the peptides to hierarchically self-organize into precisely defined nanostructure was proven to be critical in many biomedical and non biomedical applications. Traditionally, the hybrid materials were synthesized by the ring-opening polymerization of N-carboxyanhydride from a macroinitiator. By this method, the polypeptides are limited into one amino acid species. Alternatively, the hybrid materials were prepared from the coupling reaction of the polypeptides and a synthetic polymer. However, this method is associated with the low conversion or limited synthetic polymer species. Atom Transfer Radical Polymerization (ATRP) is one of the most dynamically developing areas in polymer science because ATRP allow the synthesis of various polymers with well-controlled molecular weight and molecular weight distribution with mild reaction condition. The ATRP of various monomers from the different surfaces were extensively studied for surface modification. Here, we prepared the GRGDS-poly(2-hydroxyethyl methacrylate), (HEMA) with relatively low polydispersity by

combination of solid state peptide synthesis and ATRP. The hybrid materials were characterized by proton NMR, solid state NMR and Gel Permission Chromatograph (GPC). The cell adhesion and spreading found from GRGDS-poly(HEMA) film compared with the negligible cell adhesion from poly(HEMA) film suggest the RGD functional groups in the hybrid materials were active in the promoting cell adhesion.

280. Protonation/deprotonation in natural (Bacillus subtilis spore) and synthetic (hydrogel) ionic reservoirs

Sergey V. Kazakov[1], Elizabeth M. Bonvouloir[2] and Korki Miller[1], (1)Pace University, Pleasantville, NY, (2)Pace University, New York, NY

Hydrogel is a synthetic ionic reservoir capable of accumulating and releasing ions. Its ability to swell or shrink reversibly is controlled by the charge on the network, counterions associated with the network charge, and difference in concentrations of mobile ions inside hydrogel and in the exterior solution. There is a hypothesis that behavior of bacterial spores and hydrogels can be analogous: a spore cortex, a peptidoglycan cross-linked polymer, has a negative net charge and a high content of mobile ions; a low degree of cross-linking allows the spore cortex to change the volume in response to varied water and ion content. The kinetics of establishing an equilibrium pH in the external suspensions of natural ionic reservoirs (Bacillus subtilis spores) and synthetic polymer networks (hydrogels) was studied experimentally by the time-resolved potentiometry. The methods of chemical kinetics were applied to estimate the rates of ion diffusion and binding to the ionizable groups inside hydrogel particles and spores. It was shown that the parameters of protonation/deprotonation kinetics are size-dependent in polymer network. In the case of spores, these parameters were found to be influenced by the spore germination effectors (extreme pH, temperature, and nutrients). The hydrogels of nanometer size (nanogels and nanofilms) are of great potential for the development of a new generation of actuators, biosensors, and environmentally responsive elements. The properties of bacterial spores are currently in the focus of scientific research which addresses the crucial principles of spore detection and identification, the mechanisms of germination and sporulation.

281. Preparation of heparinized polyethersulfone with anticoagulantion blood and it's membrance properties

Changjun Hou, Chongqing University/University of Illinois at Urbana-Champaign, chongqin/urbana, IL and Danqun Huo, Chongqing University, chongqin, China

A new heparinized polyethersulfone material with anticoagulantion blood property was synthesized and characterized in this article.On the basis of polyethersulfone by means of chemical amplification, polyethersulfone was sulfonated making use of chlorosulfonic acid. 2-Morpholinoethanesulfonic acid monohydrate and N-(3-Dimethylaminopropyl)-N'-ethylcarbodiimidhydrochlorid was served as dehydrator. two amines of 1,30-Hexanediamine served as space arms condensed respectively with sulfonic group of sulfonated polyethersulfone and sulfonic or carbonxyl group of heparin.we developed heparinized polyethersulfone anticoagulantion blood membrance. The materal was characterized by IR,TEM and fluorescence spectroscopy and it is demonstrated that sulfonic groups are distributed evenly on the material surface and heparin retains it's initial structure. Albumin absorption on material surface showed the biological activity of heparin. maximum stress of heparinized PES increases to 98.87% and maximum strain decrases to 82.23%.

282. The polymerization of actin: Structural changes from small angle neutron scattering

Alexander I. Norman[1], Robert Ivkov[2], Jeffrey G. Forbes[3] and Sandra C. Greer[1], (1)University of Maryland, College Park, MD, (2)Triton Biosystems Inc., Chelmsford, MA, (3)Laboratory of Muscle Biology, NIAMS, NIH, DHHS, Bethesda, MD

We present a new analysis of small angle neutron scattering data from rabbit muscle actin, in the course of the polymerization from G-actin to F-actin as a function of temperature. The data, from Ivkov et al. [R. Ivkov, J. G. Forbes, and S. C. Greer, J. Chem. Phys. 108, 5599 (1998)], were taken in D2O buffer, with Ca2+ as the divalent cation on the G-actin, in the presence of ATP, and with KCl as the initiating salt. The new analysis of the data provides dimensions of the G-actin monomer and of the growing actin oligomer in solution, as a function of temperature and salt concentration. The calculation of the pair distance distribution function, p(r), gives further information about the distribution of sizes and the polymer flexibility.

Gene Expression: Transcription

283. Structural studies of bacterial transcription

Seth A. Darst, The Rockefeller University, New York, NY

X-ray and cryo-electron microscopy studies of bacterial RNA polymerases, sigma factors, and associated factors will be presented.

284. Structure of bacterial RNA polymerase holoenzyme complexed with streptolydigin

Eddy Arnold[1], Steven Tuske[2], Stefan G. Sarafianos[1], Xinyue Wang[2], Brian Hudson[2], E. Sineva[2], Jayanta Mukhopadhay[1], Jens J. Birktoft[2], Oliver Leroy[2], Sajida Ismail[2], Arthur D. Clark Jr.[1],

Chhaya Dharia[1], Andrew Napoli[1], Oleg Laptenko[3], Jookyung Lee[3], Sergei Borukhov[3] and Richard H. Ebright[2], (1) Rutgers University, Piscataway, NJ, (2)Rutgers University, Piscataway, NJ, (3)UMDNJ, Stratford, NJ

RNA polymerase (RNAP) is the key enzyme of transcription. Bacterial RNAP core (subunits: ααββ'ω) binds a σ factor to form the RNAP holoenzyme (RNAPh)(ααββ'ωσ, MW~450 KDa), which is capable of specific promoter recognition and initiation of transcription. Streptolydigin (Stl) is an antibiotic that inhibits RNAP. Using saturation mutagenesis of the β and β' RNAP genes we have isolated and characterized Stl-resistant mutants with changes at a region proximal to the bridge helix and trigger loop . We have solved the 3.0 Å resolution crystal structure of T. thermophilus RNAPh complexed with Stl. Stl makes several contacts with resistance mutation sites on the bridge-helix and trigger-loop. The observed bridge-helix conformation is similar to that seen in eukaryotic RNAP II but different from that in structures of bacterial RNAP. It has been proposed that RNAP cycles between straight and bent bridge-helix conformations during RNAP translocation. We propose that Stl inhibits RNAP by blocking cycling between straight and bent bridge-helix conformations thereby blocking translocation. Authors represent the the following units. 1. Department of Chemistry and Chemical Biology, Rutgers University, Piscataway NJ 08854, USA 2. Center for Advanced Biotechnology and Medicine, Rutgers University, Piscataway NJ 08854, USA 3. Waksman Institute, Rutgers University, Piscataway NJ 08854, USA 4. Howard Hughes Medical Institute, Piscataway NJ 08854, USA 5. Department of Cell Biology, UMDNJ, Stratford NJ 08084, USA

285. Complexes of CAP in Transcription Activation

Catherine Lawson, Andrew A. Napoli, Brian Benoff, Helen M. Berman, Yon W. Ebright and Richard H. Ebright, Rutgers University, Piscataway, NJ

Global regulators control cellular behavior by turning on many genes at once in a coordinated way. The catabolite activator protein (CAP) is a global regulator of E. coli and is the most extensively studied member of a large, ubiquitous family of structurally related regulators in bacteria. Transcription activation by CAP is substantially simpler than most examples of transcription activation in bacteria and eukaryotes, which can involve complex arrangements of macromolecular components and/or DNA binding sites. Structural knowledge of CAP and RNA polymerase (RNAP) and their interactions with promoter DNA elements is quite advanced. In contrast, knowledge about about the interactions between CAP and RNAP on promoter DNA in the two simple classes of transcription activation is still based largely on biochemical and genetic data. We will present our progress towards obtaining high-resolution structures of sub-assemblies representing Class I and Class II CAP-RNAP-promoter DNA complexes.

286. Direct Observation of Abortive Initiation and Promoter Escape: Single-Molecule DNA Nanomanipulation

Andrei Revyakin[1], Chenyu Liu[1], Terence Strick[2] and **Richard H. Ebright**[1], (1)Howard Hughes Medical Institute, Rutgers University, Piscataway, NJ, (2)Institut Jacques Monod, Paris, France

DNA-footprinting results indicate that the upstream boundary of the DNA segment protected by RNA polymerase (RNAP) is identical in RNAP-promoter open complexes and in RNAP-promoter complexes engaged in abortive synthesis of RNA products up to 9-10 nt in length. To account for the ability of RNAP to synthesize RNA products up to 9-10 nt in length without apparent change in the upstream boundary of the protected region, three models have been proposed: (i) "inchworming" which invokes transient expansion of RNAP, (ii) "scrunching," which invokes transient compaction of DNA, and (iii) "transient excursions," which invokes transient cycles of forward and reverse RNAP translocation.

We have used DNA nanomanipulation to define the extent of promoter unwinding, at the single-molecule level, in RNAP-promoter open complexes and in RNAP-promoter complexes engaged in iterative abortive synthesis. The results show unequivocally that the extent of promoter unwinding increases during abortive synthesis, increasing by a factor of up to ~1.5-fold in a manner dependent on RNA-product length.

We further have used DNA nanomanipulation to monitor the extent of promoter unwinding, at the single-molecule level, in real time, during promoter escape. The results show unequivocally that the extent of promoter unwinding transiently increases during promoter escape, increasing by a factor of ~1.5 during promoter escape, then returning to the original level during elongation.

287. Single-molecule-spectroscopy analysis of transcription

Achillefs Kapanidis, University of Oxford, Oxford, United Kingdom

We are using single-molecule fluorescence spectroscopy to measure subunit stoichiometries and intramolecular distances within single transcription complexes. I will be presenting recent advances on the mechanism of abortive initiation and on the fate of sigma-70 factor in transcription elongation.

Inorganic and Organometallic Polymers II

Organizer: Frieder Jaekle Rutgers University, Newark, NJ
Presider: Greg Tew University of Massachusetts, Amherst, MA
Presider: Matthias Wagner J. W. Goethe-Universität, Frankfurt (Main), Germany

288. Photocontrolled Routes to Functional Metallopolymers

Ian Manners, University of Toronto, Toronto, ON, Canada

Polymers containing transition metals are attracting growing attention as a result of their interesting physical and chemical properties. In this talk the use of controlled ring-opening polymerization routes to these materials will be described. In particular a new photocontrolled method will be discussed which allows access to a variety of new materials. Self-assembly of the block copolymers accessible using these routes allows the formation functional nanometer-sized domains containing metals with applications as etch resists, redox-active materials, or in catalysis. This talk will also survey some recent research by ourselves and our collaborators in these areas.

289. Hydrosilylation Polymerizations of Metal-Containing Monomers with Dialkynes

John B. Sheridan, Rutgers University, Newark, NJ

Ferrocene-containing polymers with one and two ferrocenes per repeat unit have been prepared via hydrosilylation polymerization of various dialkynes and ferrocene-containing bis-enynes with 1,1'-bis(dimethylsilyl)ferrocene using Karstedt's catalyst (platinum-divinyltetramethyldisiloxane) or Rh(PPh3)3I. Titanium-based polymers were similarly prepared from the disilyl sandwich compound dimethylsilylcycloheptatrienyl(dimethylsilylcyclopentadienyl)titanium(II) and dialkynes.

290. Nanocluster Catalysis for Regioselective Synthesis of Multifunctional Hybrid Polysiloxanes

Bhanu P. S. Chauhan and Jitendra S. Rathore, Nanomaterials Laboratory of Center for Engineered Polymeric Materials, City University of New York at CSI, Staten Island, NY

Combining inorganic and organic functionalities to form well- defined hybrid polymer composites is a challenging task and catalytic routes to such macromolecules are highly desirable. Poly(methylhydro)siloxane (PMHS) is an excellent inorganic template due to it's availability in various molecular weight ranges and well-defined microstructures. Moreover, evenly distributed Si-H bonds in PMHS can be viewed as chemical handles on which organic groups can be catalytically attached to generate hybrid polymers not achievable by physical mixing of individual phases. Catalytic hydrosilylation i.e. the addition of Si-H bonds across the carbon-carbon multiple bonds can be employed as a tool to organically tailor the silicones. Although selective hydrosilylation of monomeric species is well-documented, selective hydrosilylation of polyhydrosiloxanes is a challenging task due to the side reactions such as redistribution of functional groups, self-dehydrocoupling and cross-linking reactions to name a few. Recently, our laboratory has been developing new strategies for the generation of catalytically active metal nanoclusters and successfully demonstrated their utility as potent catalysts for silaesterification and chemoselective hydrogenation reactions. Herein, we report the first example of “Pt”-nanocluster catalyzed regioselective organic modification of PMHS to generate hybrid polymers (Scheme 1). In addition, we also probe “Pt”- nanoclusters as catalysts of choice for polyhydrosilylation reactions with a unique combination of reactivity, stability, selectivity and recyclability.

291. Macromolecules for Supramolecular Polymer Science Containing Metal-ligands in the Side Chain

Greg Tew, University of Massachusetts, Amherst, MA

Polymeric materials have been used as essential components in the synthesis of supramolecular materials rarely, despite their many advantages. Success in this area will deliver multifunctional properties for the next generation of materials. Most importantly, they increase organizational length scales compared to small molecules, opening a range extending from the atomic (0.1 nm) to the mesoscopic (2,000 nm). We focus on metal-ligand interactions since these are discrete, well defined, geometrically constrained, and competitive under a variety of environmental conditions. In addition, the interaction strength is widely tunable based on the choice of metal ion and organic ligand. We were the first laboratory to demonstrate successfully the impact these groups have on solution viscosity. In addition, the synthesis of block copolymers in which metal ligands are confined to one or more segments had never been reported until our recent work. To prepared block copolymers and narrow polydispersity materials we use ‘living' or controlled radical polymerization techniques including atom transfer radical polymerization (ATRP) and reversible addition fragmentation chain transfer (RAFT). These novel architectures have allowed the discovery of new materials that emit yellow light or self-assemble into higher order structures based on the addition of metal ions.

292. Synthesis and Properties of Rodlike Ruthenium(II) Coordination Polymers

Matthias Rehahn, Oliver Schmelz and Steffen Kelch, Darmstadt University of Technology, Darmstadt, Germany

High-molecular-weight chain molecules whose backbones are held together by coordinative bonds are usually referred to as coordination polymers. Due to their large number of closely neighbored transition metal complexes, such multinuclear species show a number of unusual properties. Especially when rodlike in shape, they may find future application in fields like (opto-)electronics, for example. Ruthenium(II)-based coordination polymers might be of outstanding benefit here.

In order to make available adequate materials, we have tested various synthetic pathways. Specifically, we compared routes where the polymers grow via the formation of the organic ligands with competitive routes where the polymer chain formation occurs via the generation of the metal complexes. Throughout, flexible side-chains were attached in order to guarantee solubility of the resulting macromolecules despite of their rodlike shape.

The constitution of the obtained polymers was verified using NMR spectroscopy, and the degrees of polymerization obtained under optimum conditions were Pn > 30. This result was supported by viscosity experiments where the intrinsic viscosities not only prove the considerable chain length but additionally provide some information on the shape of the molecules in solution. Moreover, due to the charged complexes, these polymers show pronounced polyelectrolyte effects.

In addition to coordination polymers where the ruthenium is surrounded octahedrally by six nitrogen donor atoms, we broadened our synthetic concepts to coordination polymers which contain some carbon-ruthenium bonds in their transition metal complexes as well. The charge density of the polyelectrolytes thus obtained is lowered, and clearly changed spectroscopic and solution properties are observed.

Organometallic-based Catalysis

Organizer: Alan S. Goldman Rutgers University, Piscataway, NJ
Presider: Alan S. Goldman Rutgers University, Piscataway, NJ

293. A Synergy between Synthetic Organic and Organometallic Chemistry

John F. Hartwig, Yale University, New Haven, CT

Fundamental information on organometallic chemistry, including information from kinetic studies of stoichiometric reactions, can be a powerful guide for the selection and design of catalysts for new organic methods. This seminar will present case studies in cross coupling, C-H bond activation and functionalization, additions of N-H bonds to olefins, and enantioselective allylation of amines and alkoxides to show the relationship between these two fields.

294. Catalytic Asymmetric C-C and C-O Bond Forming Reactions

Patrick J. Walsh, University of Pennsylvania, Philadelphia, PA

Two highly enantio- and diastereoselective one-pot procedures for the synthesis of epoxy alcohols with up to three contiguous stereocenters will be presented. Route one involves asymmetric addition of an alkylzinc reagent to an enal followed by diastereoselective epoxidation or asymmetric vinylation of an aldehyde with divinylzinc reagents and subsequent diastereoselective epoxidation. The second route uses a catalyst we have developed for the asymmetric addition of alkyl groups to enones followed by epoxidation. The scope of the asymmetric addition of alkyl, vinyl, and aryl groups to ketones will be discussed.

295. Development of New Generation of Asymmetric Hydrogenation Catalysts

Xumu Zhang, Penn State University, University Park, PA

The aim of our research is to develop a highly active (10-100 times more turnovers than old generation of catalysts), highly enantioselective (>99%ee) new generation of hydrogenation catalysts with easier synthesis of chiral ligands, broad substrate scopes, high tolerance of substrate impurities. Examples with potential industrial applications will be given to illustrate the synthetic usages of new chiral ligands such as TangPhos, DuanPhos and Binapine. Our new chiral phosphines are electron-donating trialkyl phosphines with t-butyl groups and they are rigid. Discussions of these ligands discovered in 2000's will be given by comparing results with chiral phosphines invented in the 1980's (BINAP) and 1990's (DuPhos).

296. C-H Bond Functionalization in Complex Organic Synthesis

Dalibor Sames, Columbia University Columbia University Columbia University, New York, NY

The possibility of direct and selective introduction of a new functionality (or a new C-C bond) via C-H bond functionalization has long intrigued practitioners of organic preparative chemistry. The value of such methods is readily apparent as multi-step synthetic sequences, often needed for establishing a new group at a preset position, may substantially be truncated. As a consequence, the possession of such synthetic ability will inspire new strategies for the assembly of organic compounds. Although there is ample precedent for C-H bond activation by transition metals (C-H metallation) the next key challenges in this area include: (1) the ability to link the C-H bond activation with the subsequent C-C bond formation in an one-pot process; (2) achievement of high functional group tolerance of these new transition

metal systems. In this lecture, the impact of C-H bond functionalization on contemporary thought in organic synthesis will be discussed, followed by an overview of the synthetic program in Sames group. An update on new developments in the area of direct arylation of heteroarenes and direct cross-coupling of sp3 C-H bonds with haloarenes and alkenes will be given.

P450 Metabolism Enzymes

Presider: Donglu Zhang Bristol-Myers Squibb, Princeton, NJ
Presider: Leslie Romanyshyn Merck & Co., Rahway, NJ

297. P450 in drug discovery and development - Now and the future

Ronald E. White, Schering-Plough Research Institute, Kenilworth, NJ

As the major means of biotransformation of a majority of drugs, P450 enzymes are the subject of much attention in the process of designing and developing new clinical medicines. This effort falls into five major areas: inhibition, induction, substrate phenotyping, kinetics, and mechanism. Examples will be given of the purpose and practice of each type of activity. Our present state of knowledge of P450 is mature, and we employ standardized approaches to most P450-related questions. However, we still occasionally run into a surprise, showing that the field of P450 is not yet all wrapped up.

298. The Incorporation of Active and Reactive Metabolite Data into the Drug Discovery Process

Griffith Humphreys, Bristol Myers Squibb Pharmaceutical Research Institute, Princeton, NJ

Early knowledge of the metabolite profile of a clinical candidate compound, especially as it pertains to the generation of pharmacologically active or chemically reactive metabolites, can positively affect lead optimization efforts, candidate selection as well as early development plans. Information on the major metabolic soft-spots for a given chemotype is often used to attempt to alter clearance, however, extending metabolite identification to the determination of active metabolites can have a more dramatic impact on structure activity relationships. The reduction in formation of reactive intermediates is another area where early biotransformation information can be applied to the lead optimization process. This seminar will cover strategies, methodologies and examples of how early biotransformation information on active and reactive metabolites can impact the discovery and early development of drug candidates.

299. Human Extrahepatic Cytochrome P450 (CYP) Enzymes: Role in Xenobiotic Metabolism and Toxicity

Jun-Yan Hong, UMDNJ, Piscataway, NJ

Most of human CYP enzymes that are responsible for drug metabolism have the highest expression levels in the livers. However, certain human CYP enzymes are preferentially expressed in different non-hepatic tissues. Similar to the role of hepatic CYPs in the first-pass clearance of ingested xenobiotics, the extrahepatic CYPs in the portal-of-entry tissues for xenobiotics such as the respiratory tissue, may also contribute to the first-pass clearance of these xenobiotics. In addition, metabolic activation in situ of carcinogens or toxicants by extrahepatic CYPs, which generates highly reactive and unstable metabolites, has been recognized as a major mechanism for tissue-specific carcinogenic or toxic effects. In comparison with human hepatic CYPs, the function and regulation of human extrahepatic CYPs are generally much less known. This presentation will describe our recent research work on CYP2A13, which is predominantly expressed in human respiratory tissue, including substrate identification and structure-activity study (supported by NIH Grant RO1-ES10048).

300. Drug-Drug Interactions: P450 Inhibition and Induction

Michael W. Sinz, Bristol_Myers Squibb, Wallingford, CT

A dug intraction liability manifests itself as a significant safety concern, regulatory hurdle, and marketing challenge. The most common forms of metabolic drug interactions are inhibition and induction of drug metabolizing enzymes resulting in increased and decreased drug exposures. Unfortunately, the majority of drug interactions are not well represented in animals and require the use of human-based in vitro models or clinical studies to predict or determine the actual magnitude of the interaction. The tools and interpretations for reversible enzyme inhibition have matured over the years and reached a level of reasonable predictability. These tools are employed at the earliest stages of drug discovery and throughout the clinical development. A unique area of enzyme inhibition known as metabolism dependent inhibition is not yet as predictive as reversible inhibition, nonetheless evaluating the overall inhibitory nature of a new drug candidate in regards to reversible and metabolism dependent inhibition is crucial. Although our models and predictions have improved, the area of enzyme induction is still immature and only gross interpretations are possible at this time. The most difficult predictions of drug-drug interactions occur when a single drug simultaneously causes both enzyme induction and inhibition of the same enzyme. In these cases it is a competition between the potencies of inhibition and induction, as well as the overall ADME properties of the drug. Ultimately, when assessing any drug-drug interaction multiple factors such as the interaction potency, the dose or efficacious plasma levels, the therapeutic area, and the competitive landscape need to be considered.

Solid State and Materials Chemistry II

Organizer: Jing Li Rutgers,The State University of New Jersey, Piscataway, NJ
Organizer: Martha Greenblatt Rutgers, The State University of New Jersey, Piscataway, NJ
Presider: Jing Li Rutgers,The State University of New Jersey, Piscataway, NJ
Presider: Martha Greenblatt Rutgers, The State University of New Jersey, Piscataway, NJ

301. Abalone Nacre: A Perfect Marriage of Soft and Hard Materials

Nan Yao, Princeton University, Princeton, NJ

Nacre (mother-of-pearl) from mollusc shells is a biologically formed lamellar ceramic. The structure and growth of nacre has been the subject of study due to its remarkable mechanical properties produced by its deceptively simple microstructure makes its fracture toughness about 3000 times that of aragonite, its main component. More than 95 weight percent of nacre consist of tablets of aragonite, an orthorhombic form of calcium carbonate (CaCO3). These tablets lie in a matrix of biological macromolecules, which make up the remaining composition. The aragonite tablets are about 0.5 μm thick and roughly 10 μm across. Layers of the single-crystalline tablets are separated by thin (20 nm to 30 nm) organic layers containing nanometer-scale pores. In this talk we will discuss this brick-and-mortar microstructure, as a perfect model for soft and hard (bio-inorganic) nanocomposites, which gives nacre its exceedingly high fracture toughness and elastic modulus.

302. Solution processable semiconductive coordination networks based on large aromatic building blocks

Zhengtao Xu, Kunhao Li, Hanhui Xu and Jacqueline M. Ryan, The George Washington University, Washington, DC

We present our initial efforts to promote electronic communications across polycyclic aromatic molecules through intervening metal halides moieties. Such efforts stand as part of the larger scheme to overcome the limitation of the van der Waals barrier in molecular semiconductors. In particular, the polycyclic aromatic ligands of 2,3,6,7,10,11-hexakis(alkylthio)triphenylene (alkyl: methyl, ethyl and isopropyl; corresponding abbreviations for the molecules: HMTT, HETT and HiPTT) were interacted with bismuth(III) bromide and chloride to produce in high yields a series of semiconductive hybrid networks featuring flexible network dimensionalities and electronic properties, as well as promising solution processing properties. Enlarging the side group from methyl to ethyl and to isopropyl groups effectively reduces the dimensionality of the bismuth halide components (and consequently the dimensionality of the overall coordination framework). Solid-state optical absorption measurements indicate effective electronic interactions between the organic g-system and the bismuth trihalide component, and the electronic band gap decreases monotonically with increasing dimensionality of the coordination network. Compared with molecular semiconductors, these integrated hybrid networks feature stronger electronic communication across the organic molecules, and point to potentially higher charge carrier mobilities.

303. Graphite Nanofibers in Direct Methanol Fuel Cell Electrodes

Carol A. Bessel[1], Donna Omiatek[1], Susan Thai[1], Georgia C. Papaefthymiou[1], Arthur Viescas[1], Douglas A. Blom[2] and Lawrence F. Allard[2], (1)Villanova University, Villanova, PA, (2)Oak Ridge National Laboratory, Oak Ridge, TN

Some of the most easily prepared and least expensive highly crystalline carbon materials are graphite nanofibers (GNFs). These materials are produced catalytically by the decomposition of hydrogen and carbon monoxide and/or selected hydrocarbons on mono- or bimetallic surfaces. The choice of growth catalyst and conditions have enabled the GNF to be tailored to specific technological needs, such as their use as supports for platinum catalyst particles in direct methanol fuel cell (DMFC) anodes. In this presentation, we will discuss the synthesis of the GNF-growth catalysts as well as their resultant GNFs. These materials have been characterized by using HRTEM, SEM, TGA, and Mossbauer spectroscopy. While the commercial practicality of carbon-supported platinum electrocatalysts suffer from requirements of high percent weight loading as well as self-poisoning, we have found that 5 wt% Pt on platelet or ribbon-type GNF exhibit improved activities of 400% when compared with the industry standard, Vulcan carbon-supported platinum. Additionally, self poisoning studies indicate notable decreases with platelet or ribbon GNF compared to Vulcan carbon. The decreases in weight loading and self-poisoning may be attributable to various causes including: a more efficient mechanism for the removal or adsorbed species, increased electrical conductance, decreased impurities in the carbon support and/or a preferred crystallographic orientation of the platinum catalyst particles as a result of the highly ordered GNF morphology. Each of these will be discussed.

304. Hydrogen Storage on Metal Organic Frameworks

Jeffrey T. Culp, U.S. D.O.E. National Energy Technology Laboratory, Pittsburgh, PA

The President's Hydrogen Fuel Initiative seeks to develop practical and cost-effective hydrogen, fuel cell, and infrastructure technologies needed for a gradual future transition from gasoline to fuel cell vehicles. One major technological hurdle to this goal is the development of safe and efficient methods of hydrogen transport and on-board vehicle storage of hydrogen. On-board storage systems must be compact and reasonably light weight. Targets set for

achieving a typical vehicle range of 300 miles will require an on-board hydrogen storage ratio of approximately 6 weight percent or higher. Current technologies being pursued to meet this demand include compressed gas, liquified gas, carbon-based sorbents, metal-hydrides, and most recently, porous metal coordination polymers. While none of these technologies currently meet DOE cost and performance guidelines, porous metal coordination polymers have recently generated a great deal of interest. These ordered metal-organic crystalline materials, akin to the well-known zeolites, can be synthesized from a wide variety of transition metal and organic-linker building blocks to possess pores of different sizes and physical properties. Numerous examples of these materials have appeared in the scientific literature, but reports of their gas storage properties have been much less prevalent. The gas storage properties of several of these structures have been investigated in our laboratory by gravimetric and volumetric techniques at both low temperature and room temperature and up to pressures of 50 atm. The results for these studies will be presented along with discussions concerning the viability of these materials as hydrogen sorbents.

305. Preparation and characterization of zinc titanate nano-crystal powders via sonochemical synthesis

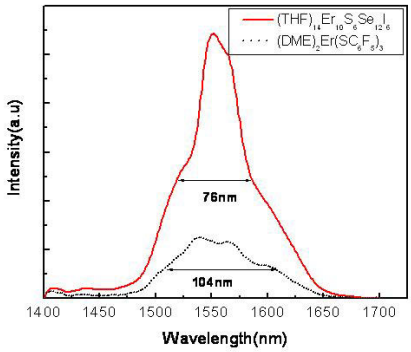
Feng Chen[1], Kirstan Bowser[1] and Tamara Bell[2], (1)Rider University, Lawrenceville, NJ, (2)George School, Newtown, PA

A novel sonochemical method to prepare nanocrystalline zinc titanate has been developed. The desired products were synthesized by the hydrolysis of titanium tetraisopropyl in the presence of water and ethanol and combining which with zinc acetate solution under high-intensity ultrasonic irradiation for 3-5 hours. The yielding powders were vacuum dried and then heated at various temperatures from 500 ∞C to 950 ∞C. All the products were characterized by powder X-ray diffraction (XRD). The dependence of the phase formation and the shape of the crystalline on heating temperatures were carefully studied. In this paper we will summarize our results and findings from this study.

306. Infrared Fluorescence Emission Characteristics of Chalcogenide-Bound Erbium Complexes and their Fluoropolymer Composites

Santanu Banerjee[1], Anna Kornienko[2], John G. Brennan[2], G.A. Kumar[2] and Richard E. Riman[2], (1)Rutgers,The State University Of New Jersey, Piscataway, NJ, (2)Rutgers,The State University Of New Jersey, PISCATAWAY, NJ

The synthesis, characterization and near infrared luminescence properties of new erbium ceramic cluster (THF)14Er10S6Se12I6 (Er10) and the molecular erbium thiolate (DME)2Er(SC6F5)3 (Er1) are described. The near infrared luminescence properties are studied by optical absorption, photoluminescence and vibrational spectroscopy. The recorded emission spectrum of the 4I13/2 □4I15/2 transition of Er3+ was centered at 1544 nm with a bandwidth of 76 and 104 nm for Er10 and Er1 respectively. The 1544 nm emission decay time for all reported similar Er-organometallic complexes are in the microsecond regime resulting low reported quantum efficiencies. The fluorescence decay times of 3 and 2.88 ms are obtained for Er10 and Er1 respectively, yield calculated quantum efficiencies of 78% and 75%. These values are the highest reported efficiencies for molecular compounds. These efficiencies and improved fluorescence spectral properties are attributed to the absence of direct Er coordination with fluorescence quenching vibrational groups such as C-H and O-H and direct coordination of Er to heavy anions like S, Se, and I which form weak bonds that facilitate a locally reduced phonon energy host environment for the erbium. Since these Er-compounds are surrounded by organic ligands, solubility in organic polymers and solvents is expected which will also minimize the light scattering and effect high transparency. We will report the near infrared optical properties of Er10 and Er1 doped into perfluorocyclobutyl (PFCB) polymer as the host because of its low attenuation in the infrared region compared to the well known PMMA system. These fluoropolymer composite materials emit strongly at 1544 nm



307. Optical Switching Properties of Dye Doped Organic/Inorganic Composite Films

Nathan Stevens and Daniel L. Akins, The City College of New York, New York, NY

Easily processable composite films consisting of a non-ionic surfactant, Pluronic P123, as the organic component, and silica as the inorganic component have been fabricated. These films served as the host matrices for various squarylium-

and xanthene-type organic dyes. Picosecond time-resolved luminescent studies revealed that the excited state lifetimes of the squarylium dyes increased when compared to those measured in solution. The xanthene dyes' lifetimes, on the other hand showed a moderate decrease upon being incorporated into the solid matrix. In the case of the squarylium dyes, addition of antimony doped tin oxide nanoparticles led to either an increase or decrease in the lifetimes, depending on the structure and charge of the dye. Also, substantial decreases in excited state lifetimes are observed with the addition of well known organic quenchers: methyl viologen, p-nitroaniline, or bromophenol blue. The high quenching efficiencies observed indicate that the dyes and the quenchers form complexes from both being sequestered within the micro-environment of the micelles formed by the surfactant. The excellent photostability and ultrafast ground state recovery of the intercalated dye complexes make these composite films ideally suited for use as the active component in an optical switching device.

Spectroscopy of Biomolecules, Inferfaces and Materials II

Organizer: Edward, W. Castner Rutgers University, Piscatway, NJ
Presider: Edward, W. Castner Rutgers University, Piscatway, NJ

308. Probing Photophysical Processes by Time-Resolved Linear Dichroism Spectroscopy

Dustin Levy and Bradley R. Arnold, University of Maryland Baltimore County, Baltimore, MD

Time-resolved linear dichroism (TRLD) spectroscopy is a powerful tool for studying the relationships between molecular structure, electronic configuration, and reactivity. In a TRLD experiment, the absorption of a beam of linearly polarized light is used to produce an oriented sample of excited states by a process known as photoselection. When this oriented sample is probed with a second beam of linearly polarized light, the difference between the absorbance measured parallel and perpendicular to the excitation beam is defined as the linear dichroism. The initial magnitude of the linear dichroism is related to the absolute angle between the excitation and probe transition moment vectors and the time decay of the linear dichroism is related to the rotational diffusion of the excited states. Detailed descriptions of photophysical processes are possible when these two types of information are analyzed simultaneously. Examples of this approach are presented for the charge separation dynamics of excited charge transfer complexes and the anisotropic rotational dynamics of polycyclic aromatic hydrocarbons.

309. Single molecule studies of protein conformational dynamics

David S. Talaga, Rutgers University, Piscataway, NJ

Recent developments in the Talaga lab regarding the single molecule measurement of conformational changes in proteins and protein aggregation are discussed with particular emphasis on the use of information theory and Hidden Markov models to analyze the single photon arrival time trajectories.

310. Ultrasensitive binding and transport studies of model membrane-active peptides at bilayer interfaces

Douglas S. English, Xiang Wang and Nikolai Sinkov, University Of Maryland, College Park, College Park, MD

The binding and diffusion of two model membrane-active peptides at a phospholipid bilayer interface were measured using single-molecule burst-counting methods and autocorrelation analysis. Hydrophobic considerations predict that both peptides should possess similar adsorption free energies. Significant differences in the adsorption and diffusion of the two model peptides are observed and are attributed to peptide-specific interactions with the bilayer. These studies illustrate the power and promise of single molecule methods to reveal details about binding and transport of peptides at cellular interfaces.

311. Fast Long-range Electron Injection at Molecule-Nanoparticle Interfaces

Piotr Piotrowiak, Rutgers University at Newark, Newark, NJ

Electron transfer processes in heterogeneous materials consisting of semiconductor nanoparticles and molecular components are being investigated. The goal of these efforts is to achieve a similar degree of control over electronic interactions at interfaces between molecules and nanoparticles as it is possible in purely molecular systems. Progress in three areas will be reported: (1)Sub-picosecond electron injection from 'molecular tripods' bearing light absorbing electron donors into the conduction band of TiO_2 was observed over distances in excess of 20 Å. The three-point attachment of the tripod to the metal oxide particles allows one to control the distance and orientation of the sensistizer with respect to the surface. The ultrafast injection rates demonstrate the feasibility of 'hot electron' injection over long distances. (2) Novel hybrid systems consisting of amphiphilic host-guest complexes (hemicarceplexes) bound to nanoparticles were prepared. The molecular container spontaneously and reversibly encapsulates a guest and binds it to the surface of a semiconductor nanoparticle. Photoexcitation of the guest results in electron tunneling across the molecular cage to the nanoparticle. (3) Time resolved confocal microscopy experiments revealed a broad range of residual emission lifetimes of surface modified TiO_2. The inhomogeneity of the emission depends on the substrate and on the treatment of the sample. Films prepared in the ‘Graetzel cell' fashion display the broadest range of lifetimes reaching hundreds of nanoseconds. In contrast, dilute nanoparticles that were extensively dialyzed prior to the measurement exhibit a much narrower range of lifetimes of only a few nanoseconds .

312. Conformational Dynamics in Triplet Repeat Models of DNA

Benjamin J. Lee, Maryan Barch, Jens Völker, Edward W. Castner Jr. and Kenneth J. Breslauer, Rutgers, The State University of New Jersey, Piscataway, NJ

Triplet repeat diseases contain repeated sequences of (CAG) and (CTG) above a critical threshold number. Using the adenine analogue, 2-aminopurine, we investigate triplet repeat diseases by studying the temperature dependent dynamics of these triplet repeat units in hairpin, duplex, and complimentary hairpin structures using ultrafast time-resolved fluorescence spectroscopy. 2-aminopurine is used because it minimally perturbs DNA structure and also absorbs at longer wavelengths than natural DNA bases. This allows direct probing of the inner loop environment of the DNA at 3 separate sites. We are correlating changes in dynamics with a change in base stacking resulting from conformational changes in DNA.

Career Enhancement for Chemical Technicians

Official: George J. O'Neill Consultant, Kingsport, TN

313. Today's Chemical Technician –How ACS Can Help Your Career!

George J. O'Neill, Consultant, Kingsport, TN

"We've come a long way, "exclaimed John Engelman, the Chair of ACS' Committee on Technician Affairs (CTA) in C&EN1. He was proudly referring to the 40-year history of CTA as well as the 10th anniversary of the Division of Chemical Technicians. John recalled that in the 1960's there was little awareness that chem techs would develop their own rewarding, scientific careers. Furthermore nobody in those days had any thoughts of how ACS could help support these careers. Today's presentation will offer modern profiles of chem techs and their careers by answering these questions, 1. Who are they, 2. What kind of work do they do, 3. Where do they work, 4. How much are they paid, 5. What is the job outlook in the Middle Atlantic states, 6. What can ACS do to help them?

1. Chemical and Engineering News, July 26, 2004, page 47.

Bench Top to Pilot Plant Posters

Organizer: Anita J. Brandolini William Paterson University, Wayne, NJ
Organizer: A. Singh Bristol-Myers Squibb Company, New Brunswick, NJ
Organizer: Shankar Swaminathan Bristol Myers Squibb, New Brunswick, NJ

314. Membrane Pervaporation Process for Diacetone Alcohol – Water Separations

Timothy Schurmann, Joshua MacMillan, Angela Zimarowski and C. Stewart Slater, Rowan University, Glassboro, NJ

Membrane pervaporation is a very effective technology for organic solvent–water separations in specialty chemical manufacture. It has the ability to perform solvent dehydrations and produce solvents of high purity without complex entrainer-based or azeotropic distillations. With the proper selection of membranes, pervaporation can be used in many applications from organic recovery from dilute aqueous process streams to final solvent purification. Pervaporation has been successfully utilized in the dehydration of diacetone alcohol (DAA)-water mixtures. Studies have been conducted to examine the effect of various operating parameters such as feed concentration, temperature, and permeate-side pressure on flux and selectivity. The use of a polyvinylalcohol membrane was quite selective for the parameters studied. At benchmark processing conditions of feed concentration of 90% DAA, 50ºC and 2 mmHg (abs) permeate-side pressure, water selectivity was 169.9 and total flux was 0.26 kg/m2-hr. Our studies examined feed concentrations over the range of 1%-50% w/w water in DAA. Feed temperature affected flux in an exponential manner; as temperature was increased, so too did the flux. Decreasing the permeate side pressure showed no significant effect on the quality of separation, but as pressure increased, flux decreased exponentially. A selection of Sulzer dehydration membranes were also compared over benchmark conditions. Data correlated well, and empirical models were developed. Scale-up calculations were performed to determine needed membrane area for a commercial dehydration. The model we developed predicts a membrane area of 85 m2 is needed to achieve a final product purity of 99% DAA from a feed of 90% DAA.

315. Nucleophilic displacement at suitably activated secondary benzylic alcohol by a sulfonamide-Development and scale-up for the preparation of an intermediate in the synthesis of a drug candidate in Alzheimer's disease

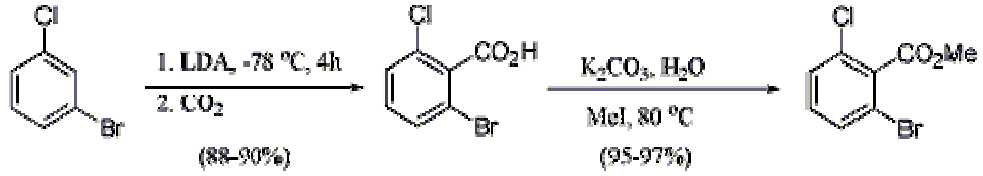
Ming Yang, M. Saindane, C. Nilsen, A. Staab, K. Gesenberg, K. Wong, T. Vu, Z. Shi, J. Fan, G. Crispino, Y. Pendri, Siva J. Prasad and A. Singh, Bristol-Myers Squibb Company, New Brunswick, NJ

The compound under investigation is an intermediate for an Alzheimer disease drug candidate. This poster presents the synthetic evolution from discovery chemistry to chemistry sucessfully scaled up in the pilot plant. The scale up issues and remedies are also addressed.

316. Process Development for Pilot Plant Synthesis of Methyl 2-Bromo-6-chlorobenzoate

Matthew R. Hickey, Shawn P. Allwein, Todd D. Nelson, Michael H. Kress, Osama S. Sudah, Mahmoud Kaba, Aaron J. Moment and Paul Fernandez, Merck Research Laboratories, Wayne, PA

Development of a scalable process for the synthesis of methyl 2-bromo-6-chlorobenzoate is described. Focus will be on the development of the process from screening of various routes to route selection and implementation on 50+ kg scale in a pilot plant. A critical cryogenic temperature requirement is essential to avoid exothermic decomposition via a benzyne type pathway. Other features of this route include an acid/base extractive workup, a single purification by crystallization, inexpensive and readily available starting materials, and scale independent isolated yields around 80% over both steps.



317. Implementation of HPLC Automation for the Analysis and Purification of Chiral Molecules

Craig K. Esser, Regina M Black and Derek Von Langen, Merck Research Laboratories, Rahway, NJ

An HPLC automation strategy was developed and implemented in a big pharma research department of 200+ medicinal chemists for the analysis and purification of chiral molecules. Discussions of why a decentralized, Open-Access HPLC strategy was chosen over a centralized, Expert-Only strategy will be presented, and why certain HPLC hardware and software was selected to implement this strategy. Finally, we will offer the reasons why we were successful with implementing our HPLC automation.

318. Photodegradant of Razaxaban: Structure Characterization Using 15N NMR Techniques

Qingmei Ye, Yande Huang, Liya Tang, Scott Miller, Charles Pathirana and VP Palaniswamy, Bristol-Myers Squibb, New Brunswick, NJ

Razaxaban is an oral Factor Xa inhibitor that is being developed for the treatment of thromboembolic disorders. When the API (Active Pharmaceutical Ingredient) was exposed to ICH photo-stability conditions, a degradant at ca. 1.5 A.P. was observed in the HPLC profile. Initial LC-MS and LC-MS-MS analyses suggested that the degradant was an isomer of razaxaban containing a structural modification at the “isoxazole” moiety of the molecule. In order to establish the exact structure, a pure sample of the degradant was isolated by preparative HPLC from an enriched sample of razaxaban, which had been exposed to high intensity UV light for 15 days. Comprehensive analysis of 1D and 2D NMR data, including 1H-15N HMQC and HMBC in comparison with the comparable data for the API and commercially available compounds, benzooxazol-2-ylamine and 1,2-benzisoxazol-3-amine, led to a novel structure assignment for the degradant. A plausible mechanistic pathway for the formation of the photodegradant is proposed.

319. Solvent swap tracking using an in-situ Foss Near-IR probe

Charles Van Kirk, Elias Mattas, Ehrlic Lo, Scott Savage and Shih-Ying Chang, Bristol-Myers Squibb, New Brunswick, NJ

The distillation process is found in nearly every API formation. Usually this process has been modified many times from the original discovery process due to cost considerations, equipment availability and solvent selection. For example, while using roto-evaporation to remove excessive solvent may be the optimal technique in the lab, such a technique is unreasonable to use at the pilot plant scale. In order to circumvent this obstacle, a solvent swap is used to replace the initial solvent with a solvent that the sample would be more stable in, thus increasing yield or improving upon the processability of the product.

Presented here is an alternative to the traditional off-line analysis techniques with an in-situ near-infrared (NIR) process analytical technology (PAT). The use of the NIR probe to monitor the changing concentration of the distillate can be used to correlate back to the amount present in the mother liquor. In order to provide quantitative assessment of the distillate, a chemometric model was developed based on a GC analyzed calibration set of samples. This model was then able to provide immediate process feedback and could accurately predict the concentration of the target solvent (RMSEP < 0.1 % by volume in the range of 0 to 50 % v/v). This PAT technique enabled the process to be continuously monitored during the solvent swap and enable for immediate process adjustment (e.g., increasing pressure/temperature) by providing real-time analysis during the distillation. As such, unnecessary handling and exposure of the operators to the batch were prevented.

320. Solvent and Temperature Mediated Pharmaceutical Polymorphic Transformation

Lifen Shen and Dimuthu Jayawickrama, Bristol Myes Squibb, New Brunswick, NJ

In the pharmaceutical industry, polymorphism control of an active pharmaceutical ingredient (API) is critical since polymorphs have different chemical and physical stability, solubility, morphology, and hygroscopicity. During the manufacturing process, it is often required to convert a less stable form to a more stable form.

This work describes the development of a polymorph transformation process to convert a monohydrate (A) to a neat form (B) of an API (X). Discussions will be focused on three aspect: (1) strategy for solvent selection, which was driven by thermodynamic boundary and practical considerations; (2) kinetics for the form transformation, in particular, its dependence on temperature and solvent composition; (3) Effect of solvent composition and temperature on particle size and morphology. In this work, an integrated crystallizer equipped with Lasentec, Raman, and temperature probes was used to allow real -time monitoring of the crystal size and form, which offers great advantage of quantitative characterization of the polymorph transformation process.

321. A Novel IGF-IR signaling inhibitor: A Challenge to Process Chemists

Joel S. Slade, Joginder Bajwa, Prasad Kapa, Hui Liu, John Calienni, James Vivelo, David Parker, Guang-Pei Chen and Edwin Villhauer, Novartis Pharmaceutical Corp., East Hanover, NJ

A new and efficient synthesis of an advanced intermediate in the preparation of a novel Insulin-like Growth Factor I Receptor (IGF-IR) signaling inhibitor is described. The new route eliminates the problematic steps found in the Discovery synthesis (length, high vacuum distillations, chromatography) and establishes the crucial 1,3-cis stereochemistry of the cyclobutane ring in the early steps. The synthesis involves 5 linear steps and provides the API starting material in an overall yield of 20% as opposed to the original approach which utilized 21 steps (including purifications) and provided the same compound in an overall yield of 8%. The challenges involved in the design and execution of this new strategy will be described.

322. Assessing Feasibility of Supercritical Reaction Processes Using Benchtop Laboratory Equipment

Kenneth J. James and Kenneth R. Krewson, Supercritical Fluid Technologies Inc., Newark, DE

The primary goal of laboratory supercritical fluid reaction unit testing is to assess technical feasibility of a potential supercritical fluid reaction application. Initial screening with a Phase Equilibrium analyzer should be carried out to determine the processing conditions in which the reagents and products of interest solubilize and/or precipitate from the supercritical fluid. Experimentation then moves to the use of a supercritical fluid reaction bench top laboratory unit. The Laboratory Unit typically has a 50ml to 4 liter reaction vessel fitted with the appropriate reagent addition modules, mixing, flow meters, and sensors. Product samples and data from the feasibility testing are used to assess product quality, and to research the following process variables: 1) Preparation and solubility of reagents 2) Reaction conditions (temperatures, pressures, use of Co-Solvents to enhance reagent or product solubility. 3) Collection conditions. The reaction product is analyzed to determine how changes in these parameters change yield, purity, and economics of the proposed process. This information can then be utilized to fine tune the reaction to maximize key parameters for a commercial scale supercritical fluid reaction process. Examples demonstrating the use of both and laboratory SFR unit and supercritical fluid phase equilibrium instrument will be shown.

Biological Chemistry Posters

Organizer: Anita J. Brandolini William Paterson University, Wayne, NJ
Presider: Wilma K. Olson Rutgers University, Piscataway, NJ

323. Purification and Characterization of Ricin from Castor seed

Srinivas V.S Chakravartula, New York Medical College, Valhalla, NY and Nagaraj Guttarla, Directorate of Oilseeds Research, Hyderabad, India

Ricin a toxic protein present in the castor seed belongs to a family of RIP-II (ribosome inactivating proteins)composed of two subunits or two polypeptide units (A&B chain)linked by a single disulfide bond.The A-chain forms the toxic moiety while the B chain binds to the galactose unit of cell receptors and thus termed as lectin(sugar binding protein).Recently there is increasing interest in the medicinal applications of ricin as immunotoxin which have been sucessfully applied in several human diseases.Present avaliable data suggests that ricin exists in several isoforms with a molecular weights ranging between 62,000 to 65,000 daltons and its subunits between 32,000 and 34,000 daltons.Our studies have shown a significant difference in the molecular weights of ricin and its subunits. The molecular weights of ricin and its subunits were 57,257, 29,000 and 28,000 daltons confirmed by SDS-PAGE and Mass spectrometry.Ricin when subjected for amino acid analysis revealed a total of 517 amino acid residues and its subunits composed of 269 and 242 amino acid residues . The total helical content of ricin based on circular dichrosim studies revealed 53.6% which is stabler than other existing isoforms of ricin. Thus our experiments have shown that there could be a variation in ricin structure and also its toxic properties which will be discussed.

324. Effects of phytoplankton and eelgrass uptake on bioavailability of toxic trace metals in marine environments

Peter R. Pascucci and Steven W. Sabean, Community College of Denver, Denver, CO

The bioavailability of metals in marine waters has been an issue of concern for environmental scientists for several years now. No longer are total (bulk) measured concentrations the only environmental factor considered in both risk assessment and fate/transport mechanisms. The actual trace and ultra-trace level concentrations of metals that are potentially metabolized by specific organisms are considered hazardous. This type of study may also have impacts on chemical elements or compounds that are considered nutrients to marine life.

The marine phytoplankton T. suecica, and Atlantic eelgrass species Z. marina were investigated for divalent Ni, Cd, Cu, Pb, and Zn ion uptake with comparisons for both live algal cells versus lysed cells. The lysed cells would be a quantitative indicator for bioavailable metals concentrations leaching into the marine water column, with possible effects on other organisms. The eelgrass was chosen due to its larger surface area than individual phytoplankton cells, which are more effectively utilized in aggregate.

In addition the effect of solubility versus water column temperature was investigated at the preliminary stage for the uptake of the aforementioned metal ions using the phytoplankton T. suecica. Stresses to precipitation equilibria of these metal ions due to temperature fluctuations may mean possible resuspension in the water column leading to a seasonal fluctuation in bioavailability of these metal ions. Another bioavailability dynamic to consider for future experimentation would be seasonal algal blooms, although this may not significantly affect marine plants such as Z. marina. Herbivore organisms that ingest algae must also be scrutinized.

325. FAD Synthetase is slightly promiscuous

David M. Yearsley[1], William S. McIntire[2] and Robert J. Stanley[1], (1)Temple University, Philadelphia, PA, (2)Department of Veterans Affairs Medical Center, San Francisco, CA

FAD Synthetase (FS) is a bifunctional enzyme in that it catalyzed both the phosphorylation of riboflavin to produce flavin mononucleotide (FMN) and the adenylylation of FMN to produce flavin adenine dinucleotide (FAD). In the latter reaction the adenosine moiety, along with one phosphate group, is taken from adenosine triphosphate (ATP) in a divalent cation dependent mechanism. It has been shown that FS does not except any other nucleotides - such as TTP, CTP, GTP or UTP – as substrates. However, no studies have been done to determine if the nucleotide binding site of FS will accept ATP analogs with an adenine moiety modification. Our early results suggest that FS may be promiscuous enough to accept 2-Aminopurine-2'-deoxyriboside-5'-triphosphate as a substrate instead of ATP.

326. Biochemical properties of Ricin in Immature Castor seed

Srinivas V.S Chakravartula, New York Medical College, Valhalla, NY and Nagaraj Guttarla, Directorate of Oilseeds Research, Hyderabad, India

Castor seed consists of two proteins ricin and RCA (ricinus communis agglutinin). The RCA protein is made up of with four subunits having a molecular weight of 1,20, 000 daltons and ricin 62,000 to 65,000 daltons.RCA is not toxic but agglutinates red blood cells of mammals while ricin is toxic(inhibits protein synthesis) but doest not agglutinate red blood cells.One common factor in most of the work reported in the literature involving ricin and RCA toxins is lack of information related to the biochemical properties , physilogical functions at different stages of seed germination and their mode of formation. Keeping these point in view we have studied the chemical properties in immature castor seed.Hemagglutination, SDS-PAGE and UV-spectrometry studies showed total absence of RCA protein in the immature seed.Interestingly, ricin extract on SDS-PAGE showed only one protein band with a molecular weight of 29,000dalton corresponiding to the molecualr weight of A chain of ricn that was seen in the normal seed.Our results have shown that at immature seed level only the toxic moiety of ricin (A chain) is being synthesized first and gradually the RCA and ricin which will be presented.

327. Spin-Labeling and Characterization of DNA Oligonucleotides

Joseph J. Schramm III, Christopher Tuohy, Heather Skiff and Dr. Donald J. Hirsh, The College of New Jersey, Ewing, NJ

Our goal is to examine spin-spin interactions between two sites with unpaired electrons using Electron Paramagnetic Resonance (EPR) spectroscopy at low temperatures. We propose the use of the DNA double helix as a “scaffold” to which paramagnetic groups are attached at varying bases and therefore varying distances. To determine the suitability of this system, a number of questions were addressed. 1) Could we attach a paramagnetic group to the DNA? 2) Could we accurately measure concentrations of the two single strands to ensure the formation of a 1:1 DNA duplex without excess of either strand? 3) Could we develop a buffered cryoprotectant solution that allowed DNA duplex formation and formed a good glass at low temperatures? 4) Finally, could we determine the conformation of the DNA duplex in the cryoprotectant solution? Knowledge of the conformation allows us to model the structure and estimate the distance between the sites. One of the DNA strands has been labeled at the 5'-end with a nitroxide group at over 90% yield, as measured by HPLC. Extinction coefficients of the single strands were determined analytically. A solution containing 55 % phosphate buffer, 30 % polyethylene glycol (6000), and 15 % ethylene glycol formed a good glass and depressed the melting temperature (T_m) for the DNA duplex only slightly, from ~60 °C in buffer to ~52 °C in cryoprotectant solution. A UV-melting curve

demonstrated 30% hyperchromicity in phosphate buffer and 29% hyperchromicity in cryoprotectant/buffer solution. Circular Dichroism spectra of this duplex are consistent with B-form DNA.

328. Sequence-dependent Cyclization of Short DNA Sequences

Luke F. Czapla and Wilma K. Olson, Rutgers University, Piscataway, NJ

A new non-canonical Monte Carlo sampling methodology is applied to approximate the conformational properties of DNA in a discrete elastic base-pair step model. This technique can be used to investigate arbitrary-length DNA with greatly enhanced sampling sizes (N=10^{16}) and elucidate sequence-dependent features which are expected to contribute greatly to the dynamics of DNA at short lengths. Electrostatic repulsion between base-pair steps is also considered. DNA is modeled as either intrinsically straight or with local sequence-dependent bending, twisting, and shearing, both with or without anisotropic bending and more deformable base-pair steps. These models are intended to fit data from cyclization experiments of short DNA sequences by Cloutier and Widom, which suggest possible faults in current theories of DNA elasticity, and to address the need for further modeling and sampling techniques.

329. Oxygen Binding and Cooperativity in a De Novo Designed Heme Protein

Ronald L. Koder, Christopher S. Moser, A. Joshua Wand and P. Leslie Dutton, The Johnson Foundation and the University of Pennsylvania, Philadelphia, PA

We have reported the de novo design of a 4 helix bundle protein with built in conformational gating that couples helical rotation to histidine ligation of heme (Huang, S. S., Koder, R. L., Lewis, M., Wand, A. J., Dutton, P. L. PNAS 101(15) pp 5536-41 2004). Here we exploit the molecular strain of this rotation to control tight, reversible binding of O2 to heme without rapid electron transfer, functions performed in nature by the transport and storage proteins hemoglobin and myoglobin. Surprisingly, this designed protein displays much better discrimination against the physiological toxin CO than native O2 carriers. While hemoglobin suppresses the 10,000 fold greater affinity of free heme for CO over O2 to a tolerable 100 fold greater affinity, the designed helical bundle protein rejects CO in favor of O2 by over an order of magnitude.

330. Comparison of Chondroitinase Digestion on Rat Spinal Cord Using Anion Exchange Chromatography

Rohini D'Souza, William J Dollard, Anthony O Caggiano, Gargi Roy, Yelena G Sheptovitsky, Sarah J Kasperbauer and Elliott Gruskin, Acorda Therapeutics, Hawthorne, NY

Chondroitinases are enzymes that degrade chondroitin sulfate proteoglycans (CSPG) and show promise for the treatment of spinal cord injury1 and related neurological disorders.

Anion exchange chromatography is commonly used to detect chondroitin disaccharides2. Recombinantly manufactured chondroitinases (ABCI, AC, and B) were tested on a series of substrates and on rat spinal cord for specificity and activity using an improved anion exchange HPLC method.

This method detects disaccharide CSPG cleavage products (&Deltadi-4S and &Deltadi-6S) with a quantification limit of 50ng. Measurements of liberated disaccharide revealed optimal enzyme concentrations, enzyme combinations, and substrate characteristics in rat spinal cord.

331. The Influence of Abasic Sites on the Self-Assembly of DNA Quadruplexes

Cosimo Antonacci and Richard D. Sheardy, Seton Hall University, South Orange, NJ

The self assembly of G-rich DNA sequences into quadruplex structures has been extensively noted in the literature and has been implicated in biologically relevant segments of the genome, such as telomeres. Quadruplexes are composed of G-quartets stabilized by four coplanar guanines in a Hoogstein base pairing motif forming a quartet pore capable of housing mono and, to a lesser extent, divalent cations. We are interested in observing the G rich sequences T_XG_4 and D_XG_4, where x=1,2 and 4 and D is a nucleotide without a base. The purpose is to examine the thermodynamic contributions of the T base versus no base and to identify the effect of 5' T elongation on quadruplex stability in 100 mM potassium phosphate buffer. We will present results from Circular Dichroism, Differential Scanning Calorimetry and UV-Vis studies.

332. The role of proline in the folding of alpha-conotoxins

H. Reyne Herold, Amy K. Croskey and Balazs Hargittai, Saint Francis University, Loretto, PA

Evaluation of the significance of disulfide bridges is an important part of understanding the concept of protein folding. Our group is involved in determining how slight changes in the sequence of small peptides influence their folding properties. Our present studies focus on the folding of a group of multiple disulfide bridge containing small peptides, alpha-conotoxins SI, SIA, GI, GII and MI. These thirteen-fourteen amino acid containing peptide amides have two disulfide bridges leading to three possible regioisomers. Most reduced forms of native conotoxins are able to fold to form the natural isomer. However, under certain conditions the oxidation of these peptides yields this native isomer in a mixture of the other two isomers. This poster describes our results on the affects of different amino acids in some key position in the sequence of alpha-conotoxins and compares oxidation results obtained under folding and denaturing conditions.

333. Electrostatic interaction between supramolecular host-guest assembly and zinc-substituted cytochrome c

Cynthia Pagba[1], Jane M. Vanderkooi[2], Kurt Deshayes[3], Eugene Piatnitski[4] and Piotr Piotrowiak[1], (1)Rutgers University at Newark, Newark, NJ, (2)University of Pennsylvania, Philadelphia, PA, (3)Genentech Incorporated, South San Francisco, CA, (4)Imclone Systems

The binding of supramolceular host-guest assembly to zinc-substituted cytochrome c is investigated by monitoring the electron transfer quenching of the long-lived triplet phosphorescence of the protein by selected metallocenes (namely; ferrocene, ruthenocene and nickelocene) encapsulated in a water-soluble octacarboxyhemicarcerand. The association between cytochrome c and hemicarcerand is evident in the observed spectral shifts exhibited by the protein in the presence of the empty cage. Both the emission and absorption spectra of the protein with the empty hemicarcerand are slightly blue-shifted. Moreover, enhanced phosphorescence intensity is obtained for protein with the empty cage. Introduction of metallocene into the cage, however, significantly reduces the emission intensity with corresponding decrease in the observed lifetimes of the protein. The quenching rates obtained vary with the pH of the medium, which is indicative of the electrostatic nature of the protein-cage interaction. As expected, the degree of phosphorescence quenching also depends on the metallocene used suggesting the role of their different redox potentials. These observed quenching rates are used to estimate the protein-hemicarcerand binding constants and to deduce the approximate binding site.

334. Biochemical characterization of the amino-terminus of the capsaicin receptor, TRPV1

Christopher Jones, Marta Jimenez, Barry Selinsky and Joseph Rucker, Villanova University, Villanova, PA

Pain is a mechanism used by multicellular organisms to avoid potentially harmful stimuli in the environment. The receptor TRPV1 is found on the cell surface of pain-sensing neurons and is activated by several different stimuli: noxious heat (>45°), low pH, and vanilloids such as capsaicin, the active ingredient in 'hot' chili peppers. We have expressed an amino-terminal fragment of TRPV1 in Escherichia coli as a GFP-fusion protein. The expressed protein requires the addition of chaotropic agents for solubilization. We are currently optimizing methods for re-folding the protein. The structural integrity of the fragment is being characterized using several biochemical and spectroscopic methods.

335. Incorporation of the capsaicin receptor, TRPV1, into retroviral particles

Panagiotis Maniatis and Joseph Rucker, Villanova University, Villanova, PA

Research on membrane receptors is often complicated by the need to study them in the context of live cells. The technique of retroviral pseudotyping can be used to isolate plasma membrane proteins from the cell. We show that the complex membrane receptor TRPV1 can be incorporated into retroviral pseudotypes. Incorporation of TRPV1 requires expression of receptor at 32°C, which suggests an effect of receptor activity on pseudotyping. The role of receptor activity on incorporation is currently being studied using both receptor mutagenesis and pharmacological methods.

336. Bromoindoles and Bromotryptophan: Origin and Application of Red-Shifted UV Spectra

Ann E. Shinnar[1], Sevan Ozcetinkaya[2] and Dina C. Merrer[2], (1)Lander College, New York, NY, (2)Barnard College, New York, NY

Among marine natural products, halogenation of indole rings is common, due to the enzymatic action of haloperoxidases. Recently, bromotryptophan has been found in peptides from lower marine vertebrates, but the biological effects of brominating tryptophan are not yet understood. In studying the biophysical properties of these compounds, we have observed that UV spectra of halogenated indoles and tryptophan in solution show a distinctive red-shift in their λ_{max} values for the band corresponding to their π- π* transition. Time-dependent density functional theory (TDDFT) calculations reveal an increasing trend in the energy of the HOMO-LUMO transitions: 5-< 6- < 7- < 4-bromoindole regioisomers. The energy differences, arising from the relative destabilization of the HOMOs, thus parallel the experimentally observed red-shifts. In solution, the largest red-shift is observed for the 5-regioisomer ($\Delta\lambda_{max}$ = 9 nm), followed by the 6-regioisomer ($\Delta\lambda_{max}$ = 6 nm). The red shift shows only a very slight dependence on % organic co-solvent, of less than 1 nm. These observations can be applied in a new method to identify the different regioisomers in solution, using the value of the UV red-shift to distinguish these brominated natural products.

337. Ab initio and Density Functional Calculations of the Nucleic Acid Bases in Free and Watson-Crick Hydrogen-bonded States

A. R. Srinivasan, Ph.D.[1], Ronald R. Sauers[1], Marcia O. Fenley[2], Alexander H. Boschitsch[3], Atsushi Matsumoto[4], Andrew V. Colasanti[1] and Wilma K. Olson[1], (1)Rutgers University, Piscataway, NJ, (2)Florida State University, Tallahassee, FL, (3)Continuum Dynamics, Inc., Ewing, NJ, (4)Quantum Bioinformatics Group, Kyoto 619-0215, Japan

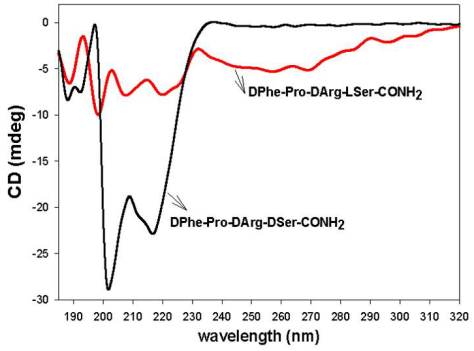
Ab initio and density functional theory molecular orbital calculations have been performed for the four heterocyclic nucleic bases — adenine, thymine, guanine, and cytosine — in free and Watson-Crick hydrogen-bonded states using the

Gaussian 98 suite of programs. Geometric optimizations and vibrational analyses were carried out by combinations of different methods and basis sets of increasing accuracy. The structures are optimized in stages of increasing computational intensity, starting with Hartree Fock self-consistent field calculations and successively followed by Becke-style three-parameter density functional theory (using the Lee-Yang-Parr correlation functional) and second-order Møller-Plesset perturbation theory. Preliminary computations reveal interesting features in the nucleic acid bases and hydrogen bonding complexes. Notably, the partial charges on the base-pair atoms differ significantly from those on the free bases. The differences occur primarily at the Watson-Crick hydrogen bonding sites and are more pronounced for G·C than A·T. Other atomic sites on the base pairs show significant accumulation of partial charge. The direction and magnitude of the dipole moments of the A·T and G·C complexes also differ significantly. In addition, the optimization of Watson-Crick interactions generates a propellering of base-pair planes of the same handedness found in high-resolution structures and heretofore attributed to stacking interactions between aromatic side groups. The low frequency normal modes of the energy-minimized base pairs also match sequence-dependent deformational tendencies observed in ensembles of crystal structures. (Supported by the U.S. Public Health Service research grant GM20861 to WKO and the National Science Foundation Advance Fellows Award 0137961 to MOF).

338. Structure-based design, structure-conformation and structure-activity relationships of DPhe(D/L-Tic)-Pro-DArg-P1'-CONH2 tetrapeptides with inhibitory activity for thrombin

Cristina C. Clement and Manfred Philipp, Lehman College, City University of New York (CUNY), NYC, NY

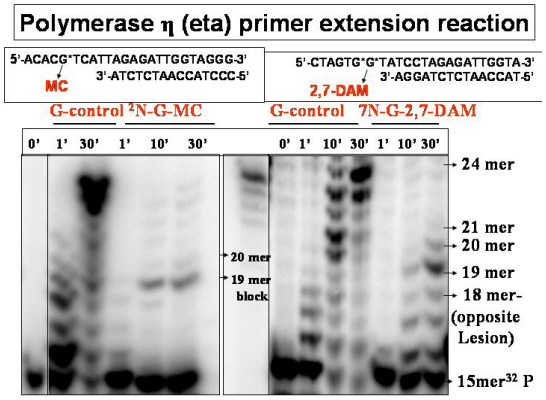
A structure-based design of tetrapeptides containing the sequence space D-Phe/X-(P3)-L-Pro(P2)-D-Arg (P1)-P1'-CONH2 was employed to discover potential inhibitors for thrombin (X= analogs of Phe, such as constrained analogs (L)/(D)-Tic [1,2,3,4-tetrahydro-isoquinoline-3-carboxylic acid]). The advanced MM3 force-field was used to minimize individual tetrapeptides. The backbone dihedral angles phi and psi were predicted to favor in most cases beta turns and beta hairpin conformation, very similar with the original peptide inhibitor from which they were designed-PPACK. Circular dichroism investigations shows that the D-Arg- in i+3 position followed by D-amino acids (polar and neutral like D-Thr, D-Gln, D-Ser and D-Ala) or L-Pro in i+4 position favors beta turn and beta hairpin structures in solution at low and neutral pH. SAR (structure-activity relationship) suggests that tetrapeptides which adopt beta turn or beta hairpin conformation in solution are more active toward inhibiting thrombin. The order of activity for the peptides containing analogs of Phe in the P3 position is (D)Phe>>(D)Tic>(L) Tic with conserved residues at P2=Pro and P1=DArg and variable L/D- amino-acids at P1'.



339. Different translesion bypass of guanine–N2 monoadducts of mitomycin C and guanine-N7 monoadducts of 2,7-diaminomitosene by eta, Klenow exo-, Klenow exo+ and T7 exo- DNA polymerases

Cristina C. Clement and Maria Tomasz, Hunter College, City University of New York (CUNY), NYC, NY

The guanine (G)-N2 DNA monoadduct of mitomycin C (MC), a cytotoxic anticancer drug, inhibits translesion bypass by DNA polymerases. The non-cytotoxic MC metabolite 2,7-diaminomitosene (2,7-DAM) forms a G-N7 DNA monoadduct in vitro and in vivo. We tested a potential correlation between the relative ease of bypass of this adduct and the lack of cytotoxicity of 2,7-DAM. In a 24 mer template/15 mer primer system the G-N7-2,7-DAM adduct was bypassed by all four polymerases, resulting in the production of a fully extended primer. The extension was at a slower rate as compared with the control, non-alkylated template. Klenow exo- has the highest efficiency of bypassing the lesion followed by T7 exo-, klenow exo+ with the lowest efficiency being observed for eta polymerase. In sharp contrast, the G-N2-MC monoadduct was not bypassed beyond the adduct position by none of the four polymerases.



Inorganic and Organometallic Posters

Organizer: Anita J. Brandolini William Paterson University, Wayne, NJ
Presider: Alan S. Goldman Rutgers University, Piscataway, NJ

340. Exploring the Chemistry of Aqueous Ionic Zinc for Various Applications

Sabrina G. Sobel, William F. Nirode, Tracy Concepcion and Allison Haigney, Hofstra University, Hempstead, NY

Zinc complexes have been used in various ways in both biological and industrial contexts. Industrially, complexation of ionic zinc by citric acid is a proposed process for leaching zinc from coal fly ash before disposal. Biologically, aqueous ionic zinc plus citric acid has been used to enhance availability of zinc ions in liquid fertilizers for plants. In addition, zinc ions are a recognized therapy for the common cold, bad breath, wound healing and burn treatment. One question that remains is; what form of zinc is best for each situation? From the chemical point of view, the most pertinent questions involve the solubility of the zinc complexes and the 'strength' of the zinc complexes, measured by the percent free zinc ions present in aqueous solution. An analysis of some zinc complexes has shown a remarkable difference in strength, from 0% free Zn(II) for zinc citrate (very strong complex) to 91% free zinc for zinc gluconate (very weak complex). An interesting result is the enhancement of percent of free zinc ions when glycine is added to zinc gluconate (93% free Zn(II)). In this research, we have investigated the enhanced solubility of poorly soluble zinc salts and increased free zinc ion concentration when weak ligands such as amino acids are added to zinc citrate and other zinc salts.

341. One-Pot Synthesis of Acyclic Epoxy Alcohols and Allylic Epoxy Alcohols

Ann Rowley Kelly, Alice E. Lurain and Patrick J. Walsh, University of Pennsylvania, Philadelphia, PA

Epoxy alcohols are extremely useful compounds in asymmetric organic synthesis and have been employed extensively in the assembly of natural products. In this report, we outline a highly enantio- and diastereoselective one-pot method for the efficient synthesis of synthetically useful acyclic epoxy alcohols and allylic epoxy alcohols. Our method takes advantage of a highly enantioselective C-C bond-forming reaction to set the initial chirality. The resulting allylic zinc alkoxide intermediate is then epoxidized in situ using either dioxygen or TBHP in the presence of titanium tetraalkoxide. Epoxy alcohols with up to three contiguous stereocenters are formed in one pot with excellent enantio- and diastereoselectivity. In cases where the zinc alkoxide intermediates contain two different allylic olefins, the more electron-rich double bond is chemoselectively epoxidized to afford an allylic epoxy alcohol. This method represents a highly efficient, stereoselective, and chemoselective approach to the synthesis of a wide range of useful epoxy alcohol and allylic epoxy alcohol products that were previously difficult to access.

342. In Vitro Studies on Solubilizing Tattoo Pigments

Lisa Sibley, Raymond Nocon, M Gerety and S. A. Katz, Rutgers University, Camden, NJ

As alternatives to "derm abrasion" and "laser abulation",

343. The Interactions of Simple Co(III) Complexes with DNA Oligomers

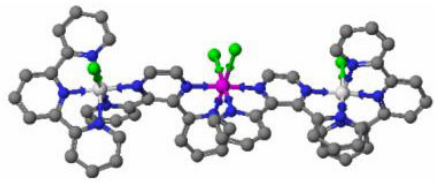
Jaime M. Ferreira and Richard D. Sheardy, Seton Hall University, South Orange, NJ

Simple Co(III) complexes can interact with DNA oligomers and polymers in a variety of fashions which are dependent upon the sequence of the DNA as well as the nature of the ligands present on the cobalt center. It is well known that $[Co(NH_3)_6]^{3+}$ can induce the B to Z transition for poly d(G-C) and poly d(G-5meC). Our lab has shown that replacement of one or two of the ammine ligands on $[Co(NH_3)_6]^{3+}$ with more labile ligands such as chloro and/or aquo can lead to irreversible binding of the cobalt center to the DNA, presumably at N7 of the guanine bases. This report investigates the effects of $[Co(NH_3)_6]^{3+}$, $[Co(NH_3)_5Cl]^{2+}$, *cis*-$[Co(NH_3)_4Cl_2]^{1+}$, $[Co(NH_3)_5(OH_2)]^{3+}$, and *cis*-$[Co(NH_3)_4(OH_2)_2]^{3+}$ on the thermodynamics associated with the duplex to single strand transition as well as any conformational transitions for two model oligonucleotides, $d(C\text{-}G)_4$ and $d(5meC\text{-}G)_4$. The DNA oligomers were incubated with the cobalt (III) complexes at various concentrations and the stabilities of the modified DNA duplexes determined by optical melting studies and Differential Scanning Calorimetry (DSC). The values of T_m, ΔH_{vH}, ΔH_{cal}, and Δn obtained allow us to compare DNA oligomer stability associated with various cobalt (III) complexes due to different ligand substituents. Any structural changes associated with the binding of the Co(III) complexes were determined by Circular Dichroism (CD) at each concentration. Isothermal Titration Calorimetry (ITC) was utilized to measure the enthalpy associated with the initial mode of binding. Together, the results will lend insight into the thermodynamics associated with the binding of simple Co(III) complexes with oligonucleotides.

344. Investigation of trimetallic light absorbing complexes that photocleave DNA

Matthew T. Mongelli, Mark Elvington, David Zigler, Jerita Dubash, Matthew Jeletic, Brenda S. J. Winkel and Karen J. Brewer, Virginia Tech, Blacksburg, VA

Trimetallic complexes of the form LA-BL-BAS-BL-LA that contain exterior light absorber units (LA) connected through a bridging ligand (BL) to a central bioactive site (BAS) have been synthesized and characterized. The complexes have traditionally used ruthenium (II) and osmium (II) subunits as the light absorber and rhodium (III) as the central electron acceptor to act as the bioactive site. The ability to access a low lying MMCT state gives these complexes the ability to photocleave DNA. Modification to these subunits can greatly changes the light absorbing properties of the complexes. An investigation of complexes currently used and modification of these complexes will be studied with respect to there light absorbing properties and ability to photocleave DNA will be examined.



$[\{(tpy)OsCl(dpp)\}RhCl_2\{(dpp)OsCl(tpy)\}]^{3+}$

345. The Effect of Spacer Chain Length in Phosphine-Imidazolium Compounds on the Catalytic Hydrogenation of Polymeric Materials

Richard J. Rosso, Nawras Harsouni, Christi Gandham, Aman Deep and Vicky Choda, St. John's University, Jamaica, NY

Hydrogenation of polymers is of great interest to the rubber industry as hydrogenation increases such factors as thermal stability and tensile strength. The current method for hydrogenation is a homogeneous system that involves a costly separation step; development of a biphasic system is cost effective as it removes the separation phase. Our focus is investigating ionic liquid/organic biphasic media as a possible alternative for these reactions. Specifically, we have synthesized imidazolium analogs of diphenylalkylphosphines with different carbon chain lengths between the phosphorus atom and the imidazolium group and have begin to study the effect spacer chain length has on the hydrogenation of polymeric materials. Both the extent of hydrogenation and the ratio of the internal 1,4-olefins to vinyl 1,2-olefins was monitored.

346. First Isolation, Characterization, and Binding Studies of a 1,2-Diborylated Ferrocene Dimer

Krishnan Venkatasubbaiah[1], Lev N. Zakharov[2], Scott Kassel[2], Arnold L. Rheingold[2] and Frieder Jäkle[1], (1)Rutgers university-Newark, Newark, NJ, (2)University of California at San Diego, La Jolla, CA

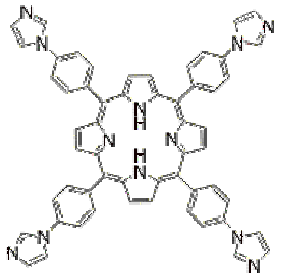
Bifunctional boron Lewis acids are known to be effective for olefin polymerization, chelation of Lewis bases and anions. Amoung the bifunctional Lewis acids studied to date, those which incorporate boron into a ring systems are highly intriguing. Especially 9,10-diboraanthracenes, 1,8-diboranaphthalene and 1,8-diboraanthracenes have been studied extensively. The ferrocene based bifunctional Lewis acids studied to date are mostly 1,1'-disubstituted. 1,2-Disubstituted ferrocenes on the other hand are very limited due to lack of suitable synthetic routes.

Recently we have shown that heteronuclear bidendate Lewis acids comprised of boron and tin, can be readily synthesized through a rearrangement reaction from 1,1'-bis(trimethylstannyl)ferrocene and boron halides. Here in we report the first example of a 1,2-diborylated ferrocene dimer and its redox behavior and binding properties.

347. Imidazolium porphyrins as precursors to porphyrin arrays

Virginia W. C. Seng, Rukya Ali, Xiulan Wang, Farah Charles-Pierre, Weici Fang and Alison G. Hyslop, St. John's University, Queens, NY

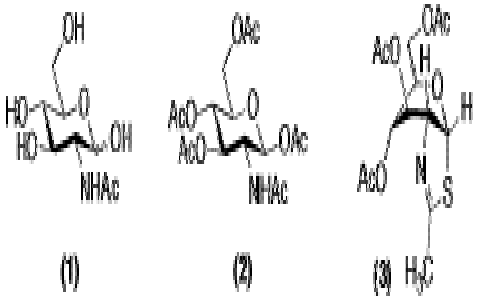
Porphyrin arrays are ubiquitous in nature and play key role in light harvesting processes in photosynthesis through absorbing light energy and transferring the energy to a reaction center. Our research interests lie in the formation of porphyrin arrays through novel binding modes to metal centers. We have recently synthesized and characterized a series of porphyrins with imidazole groups incorporated onto the porphyrin periphery and we have begun to investigate the binding of the imidazole to metal to form porphyrin arrays. The imidazole ring affords two binding sites, the unsubstituted nitrogen can act as a Lewis base to coordinate to a metal or by substituting both nitrogens, the N-heterocyclic carbene can be formed and this carbene used to bind to metals. We will describe the formation and the electronic properties of the compounds.



348. Phosphorous Substituted Porphryins, Synthesis and Characterization

Salome Bhagan and Alison G. Hyslop, St. John's University, Queens, NY

Porphyrin arrays are ubiquitous in nature and play key role in light harvesting processes in photosynthesis through absorbing light energy and transferring the energy to a reaction center. Our research interests lie in the formation of porphyrin arrays through novel binding modes to metal centers. We have recently synthesized and characterized a series of porphyrins with triphenylphosphine oxide groups incorporated onto the porphyrin periphery. These compounds were synthesized using Suzuki coupling methods to join the porphyrin to the triphenylphosphine moiety. We will describe the formation and the electronic properties of the compounds.



349. Organic polymer frameworks that become fully-conjugated upon metallation

Donald W. Carpenetti II and Alan Grubb, Marietta College, Marietta, OH

Recent efforts have focused on the preparation of an organic polymer framework that contains a cyclopentadienyl moiety. This polymer will be capable of reacting with a broad array of metal ions, yielding a fully conjugated organometallic polymer and allowing a comprehensive study of how the incorporation of different metals into the same organic framework effects the conductivity of the resultant material.

350. The Hexakis(thiocyanato)ferrate(III) Ion: a Coordination Chemistry Classic Reveals an Interesting Geometry Pattern for the Thiocyanate Ligands

Anthony W. Addison, Drexel University, Philadelphia, PA, Vitaly V. Pavlishchuk, Institute of Physical Chemistry, Kiev, Ukraine, Raymond J. Butcher, Howard University, Washington, DC, Laurence K. Thompson, Memorial University, St. John's, NF, Canada, Zoltan Homonnay, Eötvös Loránd University, 1117 Budapest, Hungary and Michael J. Prushan, LaSalle University, Philadelphia, PA

$(NMe_4)_3[Fe(NCS)_6]$ crystallizes from ethanol in the monoclinic space group C2/c. Two different types of complex ions are contained in the unit cell, though both possess exclusively N-coordination of the thiocyanates. In one ion, the thiocyanates are all essentially linearly bound, with an FeNC angle of 174±4°, while in the other, there are two cis-thiocyanates with notably small FeNC angle of 146.5°. The EPR and Mössbauer results show that all the irons(III) maintain the high-spin state down to 80 K, while the magnetic susceptibility confirms this to 2 K. Infrared and Mössbauer spectra provide evidence for an unusually "soft" lattice. Traditional criteria for interpretation of the infrared frequencies are not strictly applicable for this compound.

351. Effect of lanthanum and neodymium incorporation on oxygen storage capacity of ceria-zirconia mixed oxides

Donald W. Carpenetti II and Eric Seabright, Marietta College, Marietta, OH

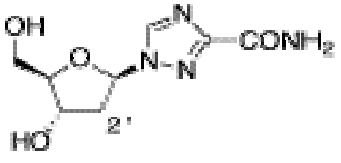
A series Ceria-zirconia mixed oxides with varying levels of lanthanum and neodymium incorporation were prepared by co-precipitation. The lower oxidation state of La(3+) and Nd(3+) compared to Ce(4+) and Zr(4+) should result in oxygen vacancies in the lattice of the solid solution. The effect of these vacanices and their concentration on the oxygen storage capacity and oxygen release temperatures of the materials will be discussed.

352. Synthesis and Characterization of Mixed Ligand Rhodium(III) Complexes

Stephanie R. Ovalles and Elise G. Megehee, St. John's University, Jamaica, NY

Rhodium polypyridyl complexes are of interest because they exhibit visible to near infrared emission upon excitation with visible or ultraviolet light and as such are candidates for photochemical or electrochemical reaction catalysts, as models of photosynthetic reaction center, as energy and electron transfer agents, as emissive DNA labels, and photochemical DNA cleavage agents. While some of the rhodium complexes are known, their published syntheses are difficult and require extensive purification. We have developed a new, general synthetic methods that allow easy preparation of pure complexes in high yields. We have demonstrated that $[Rh(NN)_2(OTf)_2]OTf$ {where NN = 2,2'-bipyridine and 4,4'-dimethyl-2,2'-bipyridine, and OTf = trifluoromethansulfonate} are versatile precursors to a wide variety of mixed ligand complexes in high yields. We will discuss the synthesis of these compounds and their characterization by ^{1}H and ^{13}C NMR, cyclic voltammetry, absorbance and emission spectroscopies.

(1)



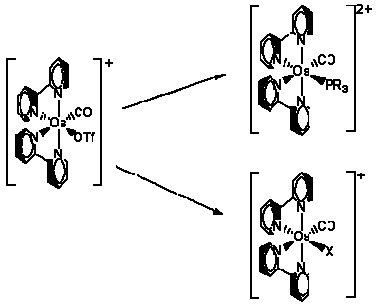
(2)

353. Synthesis and Characterization of Luminescent Osmium (II) Halide and Phosphine Complexes

Pantea Menhaji and Elise G. Megehee, St. John's University, Jamaica, NY

Osmium metal complexes are of interest absorb visible or ultraviolet light and emit light at a lower frequency as such are possible models of photosynthetic reaction center, possible energy and electron transfer agents, and possible photochemical or electrochemical reaction catalysts. We have utilized the versatile *cis*-$[Os(bpy)_2(CO)(OTf)]OTf$ precursor, where bpy = 2,2'-bipyridine and OTf is trifluoromethansulfonate, to synthesis new luminescent osmium complexes. Our research has focused on studying the effect of electron donating and electron withdrawing groups on the electronic properties of the *cis*-$[Os(bpy)_2(CO)$ moiety. We have synthesized fifteen complexes (thirteen new and two known), eleven

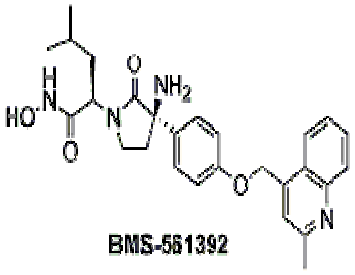
of the form *cis*-$[Os(bpy)_2(CO)(PR_3)](PF_6)_2$ where PR_3 are various substituted triphenylphosphines and four of the form *cis*-$[Os(bpy)_2(CO)(X)](PF_6)$ where X = F, Cl, Br, and I. We will discuss the synthesis and characterization of these complexes by ^{1}H-NMR, ^{13}C-NMR, electrochemistry, UV-vis and emission spectroscopies.



354. Synthesis and Characterization of New Luminescent Osmium(II) Polypyridyl Complexes

Irma N. Tertulien and Elise G. Megehee, St. John's University, Jamaica, NY

Osmium metal complexes exhibit visible luminescence upon excitation with visible or ultraviolet light. These compounds are of interest as possible models of the photosynthetic reaction center, as energy and electron transfer agents, and as photochemical or electrochemical reaction catalysts. As part of an ongoing study to explore the electronic properties of the bis-(polypyridyl)-carbonyl-osmium(II) moiety, we have synthesized *cis*-$[Os(NN)_2CO(py)]^{2+}$ and *cis*-$[Os(NN)_2CO(pyPor)]^{2+}$ where NN= 2,2'-bipyridine, 1,10-phenanthroline, and assorted substituted diimines; py = pyridine, and pyPor = 5-pyridyl-10,15,20-triphenylporphyrin. By investigating a series of polypyridyl ligands containing various electron donating and electron withdrawing groups, we can determine the effect of these groups on the electronic properties and on the balance between electron and energy transfer. We will discuss details of these syntheses as well as characterization of these complexes by ^{1}H NMR, ^{13}C NMR, electrochemistry, and absorption and emission spectroscopy.



355. Characterization of biologically active bis-(hinokitiolato)copper(II) complexes

S. Y. Kim[1], C. A. Heyer[1], M. Berardini[1], D. M. Ho[2] and G.M. Arvanitis[1], (1)The College of New Jersey, Ewing, NJ, (2)Princeton University, Princeton, NJ

Bis-(hinokitiolato)copper(II) [hinokitiol = 3-isopropyl-7-oxocyclohepta-1,3,5-trienol] is a biologically active complex with reported antibacterial, antiviral, and antifungal properties. The mechanism of its activity remains unknown, along with what form or forms of this extensively polymorphic complex are responsible for biochemical interactions. Our structural studies suggest that the ability of this compound to hydrogen bond is a prevalent feature which may lead to greater understanding of its interaction with biological molecules. We have begun to examine the DNA binding capabilities of this complex and of *bis*-(tropolonato)copper(II). Characterization of these and other derivatives (complexes with urea and guanidinium chloride) by spectroscopic methods and thermal analysis will also be discussed.

356. Copper(II) Complexes of Tetradentate Thioether-Oxime Ligands

Michael J. Prushan, LaSalle University, Philadelphia, PA, **Anthony W. Addison**, Drexel University, Philadelphia, PA, Raymond J. Butcher, Howard University, Washington, DC and Laurence K. Thompson, Memorial University, St. John's, NF, Canada

$[Cu(DtdoH)]_2(ClO_4)_2$ and $[Cu(DtudH)]_2(ClO_4)_2{\cdot}2CH_3OH$ are the first representatives of copper(II) thioether oximes which exhibit the classical out-of-plane oximate oxygen-metal dimer structure. $[Cu(DtdoH)]_2(ClO_4)_2$ reacted with excess $BF_3{\cdot}OEt_2$ to yield $[Cu(Thyclops)]ClO_4$, a BF_2^+-macrocyclized di-oxime. $[Cu(DtdoH)]_2(ClO_4)_2$ and $[Cu(Thyclops)]ClO_4$ were structurally characterized by single-crystal x-ray diffraction. The geometry about each copper(II) in $[Cu(DtdoH)]_2(ClO_4)_2$ is a distorted square pyramid (τ = 0.14). The geometry of $[Cu(Thyclops)]ClO_4$ reveals an almost perfect square pyramid (τ = 0.027) of N_2S_2O donors. ESR spectra show a typical axial pattern, except for the powder spectrum of $[Cu(DtudH)]_2(ClO_4)_2{\cdot}2CH_3OH$ which displays a small rhombic distortion. Variable-temperature magnetic susceptibility measurements indicate very weak ferromagnetic interactions in $[Cu(DtdoH)]_2(ClO_4)_2$(J = +0.52 cm-1) and very weak antiferromagnetic interactions in

$[Cu(DtudH)]_2(ClO_4)_2 \cdot 2CH_3OH$ (J = -0.59 cm-1). Electrochemical measurements reveal that the mixed thioether-oxime coordination environment tends to stabilize Cu(II), as all electrochemical reductions were quasi-reversible or irreversible. $[Cu(Thyclops)]ClO_4$is more oxidizing than $[Cu(DtdoH)]_2(ClO_4)_2$ by 0.14V.

357. Dehydrogenation of aliphatic polymers (polyolefins) catalyzed by pincer-ligated iridium complexes

Amlan Ray and Alan S. Goldman, Rutgers University, Piscataway, NJ

The introduction of double bonds into saturated polyolefins has great potential value with respect to polymer functionalization, and the resulting modification of chemical and physical properties. In an extension of our studies of alkane dehydrogenation we find that pincer-ligated iridium complexes are capable of dehydrogenating poly(1Ðhexene) and polyethylene to give the corresponding polyunsaturated polymers with up to 22% and 10% dehydrogenation, respectively, per monomer unit. [*p*-MeO-$C_6H_2(CH_2P^iPr)_2$]IrH_2 is found to be significantly more effective for this purpose than other derivative investigated. Kinetics of dehydrogenation and subsequent isomerization steps have been investigated.

Medicinal Chemistry Posters

Organizer: Anita J. Brandolini William Paterson University, Wayne, NJ
Organizer: Robert Goodnow Jr. Hoffmann-La Roche, Nutley, NJ

358. Synthesis of 3-beta-acyloyloxy-4,6-pregnadiene-6,20-dione derivatives as antiandrogens

Elena Ramirez[1], Eugene Bratoeff[1], Marisa Cabeza[2], Victor Perez[1], David Valdez[1], Alejandro Orozco[1] and Alejandra Munguia[1], (1)National University of Mexico City, Mexico City D.F., Mexico, (2)Metropolitan University of Mexico City-Xochimilco, Mexico City D.F., Mexico

Antiandrogens offer a potentially useful treatment for androgen-mediated diseases such as benign prostatic hyperplasia, prostate cancer and acne. Dihydrotestosterone has been implicated as a causative factor in the progression of these diseases. In this study we report the synthesis and antiandrogenic effect of four new 3-acyloyloxy-4,6-pregnadiene-6,20-dione derivatives (A-D). Upon treatment with m-chloroperbenzoic acid the 16-dehydropregnenolone acetate afforded the 5,6-epoxy derivative, which was oxidized with chromic anhydride to the 5-hydroxy-6-oxo derivative. In the following step, the 5-hydroxy-6-oxo compound was treated with pyridine and thionyl chloride, this reaction afforded the product of elimination, which was hydrolyzed with sodium hydroxide in methanol to the free alcohol. Esterification with the corresponding carboxilic acid and dicyclohexylcarbodiimide afforded the desired esters A-D. These compounds were evaluated, in vivo as well as in vitro experiments, by their binding affinity for the cognate receptor. In vivo experiment, the antiandrogenic effect of the steroids was demonstrated by the decrease of the weight of the prostate gland. The overall data of this study showed very clearly that these compounds A-D are good antiandrogenic agents. In the receptor-ligand binding study (in vitro experiment), compounds A (3-beta-p-bromobenzoyloxy-4,6-pregnadien-6,20-dione) and B (3-beta-p-fluorobenzoyloxy-4,6-pregnadien-6,20-dione) showed a higher binding affinity as compared to the standard dihydrotestosterone. In view of the fact that both compounds exhibited a very high antiandrogenic activity in vivo as well as in vitro experiments, in the future these compounds will be evaluated more thoroughly to determine if they could be considered as potential drugs for the treatment of prostate cancer.

359. Bicyclic Hydantoins as Androgen Receptor Antagonists

Weifang Shan, Aaron Balog, Mark Salvati, Donna Wei, Greg Vite, Jack Hunt, Leslie Leith, Arvind Mathur, Ricardo Attar, Jieping Geng, Cheryl Rizzo, Marco Gottardis, Robert Weinmann, Stanley Krystek and John Tokarski, Bristol-Myers Squibb Company, Princeton, NJ

Prostate Cancer is the second leading cause of cancer death in the Western male population. The front line treatment for advanced prostate cancer involves use of androgen receptor antagonists. Unfortunately, these therapies are only palliative and most tumors will eventually evolve into a currently untreatable hormone refractory form. In an effort to address this unmet medical need, we have recently identified a series of [2.2.1] bicyclic hydantoins as androgen receptor antagonists. The design, solution and solid-phase synthesis, and structure-activity relationships of these compounds will be presented.

360. Reduced FAK Phosphorylation and Migration Observed in Murine Melanoma Cells after Transfection with a Kinase-defective PKC alpha

Yaw Amo-Mensah[1], Regina Sullivan[1] and Susan A. Rotenberg[2], (1)Queensborough Community College, Bayside, NY, (2)Queens College, Flushing, NY

Protein Kinase C is a monomeric serine/ threonine kinase that has been implicated in the metastatic potential of murine melanoma cells (B16F10). An isoform profile of B16F10 revealed PKC alpha as the most abundantly expressed conventional isoform. B16F10 cell lines were stably transfected to overexpress a kinase-defective PKC alpha. Since migration is a phenotype that is highly related to metastasis, migration assays were performed with B16F10 cells. These results showed reduced rates of migration when cells were plated on fibronectin, a protein abundant in the extracellular

martix. Furthermore, these transfectants show reduced phosphorylation on tyrosine-397 of focal adhesion kinase (FAK) that is due to an autocatalylic event critical to the formation of focal adhesions. These results implicate PKC alpha activity and FAK autophosphorylation in signaling pathways that promote migration of murine melanoma cells. Yaw Amo-Mensah is a participant in the QCC-NIH Bridges to the Baccalaureate Program. (grant R25GM65096-03)

361. Analysis and Interpretation of DNA to Metallated and Nonmetallated Tetrapyridino Porphyrazines

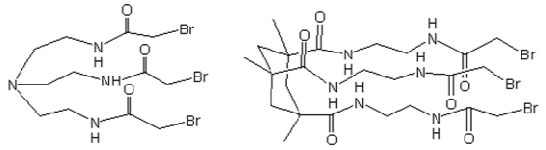
Melanie Bozza and Richard D. Sheardy, Seton Hall University, South Orange, NJ

Previous studies, done by the Sheardy research group shows that the tetracationic tetraethanol tetrapyridino porphyrazinium iodide has an positive effect on inhibitting two enzymes in the Human Immuno Deficiency Virus (HIV). We are investigating the interaction specificity of a series of the metallated and nonmetallated tetracationic tetraethanol tetrapyridino porphyrazinium iodide with synthetic (CG)2ATAT(CG)2 and T4G4. The metallated porphrazines are (Mn2+, Cu2+, Co2+, Mg2+ and Zn2+ = M), M-tetraethanol tetrapyridino porohyrazinium iodide. Preliminary experiments include thermal denaturation studies and spectroscopic studies to employ to investigate the secondary structure and stability of the synthetic oligonucleotide via UV/Vis thermal melts, Differential Scanning Calorimetry (DSC), and Circular Dichroism (CD) absorption studies. Once the initial characterization is completed, investigation of the DNA-tetracationic porphyrazine via Visible and CD absorption studies are conducted in the 400-850nm range, as well as UV studies in the 220-320nm range. Together the Visible, UV and CD studies provide evidence that all the porphyrazines are electrostatically binding along the phosphate backbone of both the duplex and quadruplex DNA with a higher binding affinity to the quadruplex DNA.

362. Template-Assembled Peptide Models of the N-Peptide Helix Bundle from HIV-1 Gp41

Weiming Xu and John W. Taylor, Rutgers University, Piscataway, NJ

The proposed post-fusion structure of HIV-1 envelope glycoprotein, gp41, includes a helical trimer of N-peptides with three copies of helical C-peptide folded onto it. Two template molecules have been synthesized, TREN-Br (**1**) and KTA-Br (**2**), and then three copies of peptide N29 (gp41 553-581) with a N-terminal Cys were connected to each template, giving the N-peptide three-helix model structures **1-3N29** and **2-3N29**, respectively. Compared with N-peptide alone, the template-assembled structures were much more helical (about 97% helical by CD analysis). At pH=7.40, thermal denaturation was irreversible. However, urea denaturation was reversible and indicated that **2-3N29** was more stable than **1-3N29**. At pH=2.50, these structures underwent reversible thermal denaturation, with T_m values of 81°C for **1-3N29** and 77°C for **2-3N29**. Analysis of these melting curves indicated that the folding of both structures was strongly enthalpy-driven. Meanwhile, detailed data showed that **1-3N29** had a less unfavorable folding entropy than **2-3N29**, but a less favorable folding enthalpy. Studies of the binding of C-peptide to these template- assembled helix bundles are underway.



1. TREN-Br

2. KTA-Br

363. Discovey Of PPARα/δ/γ Pan-agonists: Ligand Conformational Constraint and Selectivity

Daniel J. Miller, Hiroo Koyama, Joel P. Berger, Karen L. MacNaul, Thomas W. Doebber, Margaret Wu, David E. Moller and Soumya P. Sahoo, Merck Research Laboratories, Rahway, NJ

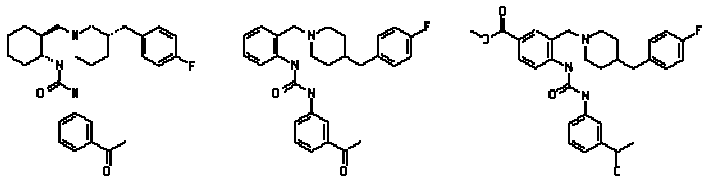
Type 2 diabetes mellitus (Type 2 DM) is a chronic disease characterized by insulin resistance in the liver and in peripheral tissues accompanied by a defect in pancreatic □-cells. In the clinic, type 2 DM is frequently associated with other features of metabolic syndrome such as obesity, dyslipidemia, and hypertension. These findings clearly indicate the unmet clinical needs of lipid profile management among diabetics. Because of these epidemiological findings, the focus of interest in PPAR agonists as therapeutic agents has shifted from selective PPAR□ agonists to PPAR□/□ dual agonists. Treatment of hyperglycemia by PPAR□ activation and improvement of an undesired lipid profile by PPAR□ activation are expected to offer comprehensive treatment for type 2 DM and associated metabolic abnormalities.

Three PPAR isoforms have been identified: PPAR□, PPAR□ and PPAR□. Unlike PPAR□ and PPAR□, PPAR□ has not been well characterized. However, researchers at GSK have reported beneficial effects of PPAR□ activation in non-human primates. Given the new interest in PPAR□ activation and recent interest in PPAR□/□ dual agonists, our goal was to optimize the phenylacetic acid class PPAR agonists towards PPAR□, -□, and -□ pan-agonism with improved potency and efficacy. We focused our attention on the relationship between the activity and the conformational restrictions given to the carboxylic acid group, a key functionality that triggers conformational changes of the receptor upon binding. Thus, the phenylacetic acid moiety was replaced by various fused benzo carbocyclic- and benzo heterocyclic-carboxylic acids and the results of the SAR studies will be presented.

364. Discovery and Structure-Activity Relationship of Potent CC Chemokine Receptor-3 (CCR3) Antagonists

Qing Shi, Patricia K. Welch, Eric A. Wedman, Soo S. Ko and George V. De Lucca, Bristol-Myers Squibb Pharmaceutical Research Institute, Lawrenceville, NJ

We previously disclosed DPC-168 **I** as a potent CCR3 antagonist with 2.0 nM binding IC50 and 34 pM chemotaxis IC50, which entered phase I human trails. Previous SAR studies on the phenyl linker series showed that a polar substituent could improve the binding potency, for example **II** and **III**. Accordingly we examined a number of substituents on the cyclohexyl ring of I, including basic amines, non-basic amides and sulfonamides. Our SAR studies indicated that compounds with these substituents could maintain the CCR3 binding and chemotaxis potency of **I**. The SAR of these compounds and their syntheses will be described in detail.



I

DPC-168
CCR3 Binding
IC50: 2 nM

II

CCR3 Binding
IC50: 125 nM

III

CCR3 Binding
IC50: 42 nM

365. Synthesis and Lipid Lowering Effects of Acyl-Carnitines

Kyle C. Pillitteri, Rider University, Mercerville, NJ

Acyl-carnitine will be studied for its lipid-lowering effects. Carnitines transport activated long-chain fatty acids across the mitochondrial membrane to the matrix for B-oxidation. So far, preliminary results have been obtained. Evidence has shown that there are significant lipid-lowering effects for total cholesterol for octanoyl-carnitine (38% reduction), acetyl-carnitine (26% reduction), and carnitine (37% reduction). On the other hand, triglyceride-lowering properties are inconclusive so far. A series of carnitine esters of fatty acids with varying chain lengths, unsaturated fats, and aromatics, such as benzoic acid, phenylacetic acid, and nicotine acid will be synthesized and evaluated for their lipid-lowering properties. The specific reaction that is being accomplished is the production of acyl carnitine from carnitine-HCl and an acid chloride (yield=70-90%). This reaction is run in triflouroaceitic acid (TFA) and is held at 50-60 degrees C, under nitrogen. The crude precipitant is purified by recrystalization from acetone and ether. The reaction is seen below. L-carnitine-HCl+acid chloride (TFA,50-60°C,N_2) --->acyl carnitine-HCl On CF-1 male mice, various carnitine compounds will be injected I.P. at 12mg/kg/day for two weeks with Lipitor and a diet as the controls. The new high fat diet induces hyperlipidemia. After seven days of dosing, the serum will be pulled from the mice and analyzed for triglycerides and total cholesterol. On day fourteen, the serum of the mice will be analyzed, but LDL and HDL will also be determined. Finally, triglyceride, total cholesterol, and protein will be determined from the tissue samples of the small intestine, liver, aorta, and feces.

366. Investigation of the effect that different drying methods have on the mechanism of theophylline release from microcrystalline cellulose beads

Francis Charles Mayville Jr., Kristin Kurek and Kathryn Smith, DeSales University, Center Valley, PA

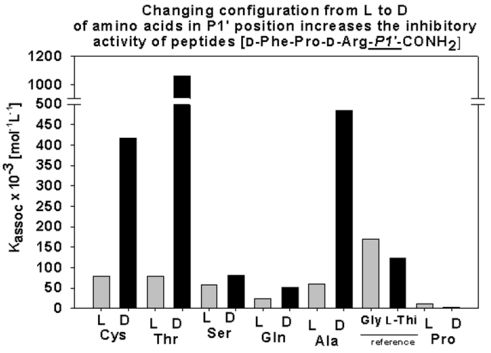
Samples of microcrystalline cellulose, MCC, and 10% theophylline were granulated, extruded and marumerized into wet sustained release beads. These wet beads were then exposed to several different drying methods including: freeze-drying, convection oven drying, and exposure to four different humidity conditions. The rate of theophylline release from the MCC bead systems was measured by dissolution methods using distilled water and 0.1 molar hydrochloric acid as the solvent systems. The control for this experiment was the convection oven dried beads. The results observed, based on these dissolution studies, suggest that the rate of theophylline release from each MCC dried bead system, either increases, decreases or follows the same release rate as the control sample. Which further suggests that the rate of release of theophylline from each MCC sample depends on the drying method used to dry the wet bead systems.

367. Switching the configuration from L to D of P1'substituents is increasing inhibitory activity for thrombin of peptides D-Phe-Pro-D-Arg-P1'-CONH2

Cristina C. Clement and Manfred Philipp, Lehman College, City University of New York (CUNY), NYC, NY

A structure-activity relationship (SAR) for reversible inhibitory activity toward thrombin of tetrapetides from series DPhe-Pro-DArg-P1'-CONH2 is reported. The P1' position was varied with D and L amino acids. The significant differences between the Kis of different tetrapeptides (varying from 2 to 500 fold) suggest that the interaction between the amino acid at P1' position and the S1' pocket in thrombin is very specific and requires hydrophobic and polar amino-acids in P1'-

ligand. There is a significant change in the affinity for interaction with thrombin as the configuration for the same amino-acid in P1' position is changing from L to D. Specifically, a switch from L-Thr into D-Thr in P1' was correlated with a 15 fold increase in the inhibitory activity. Similarly, a switch from L-Ala to D-Ala in P1' was increasing the affinity 8 fold. These differences in the binding affinities upon switching from L into D for amino-acids in P1' were confirmed both kinetically and through isothermal titration calorimetry (ITC).



368. Influence of Miswak on the Binding of Polyphenols to Protein Pellicle

DIna M. Alhelawe Sr., J.F.K. Memorial High School, Ocean Twp., NJ

Chewing sticks, known as miswak, are roots, or branches of specific types of plants that are used for dental cleaning, are used around the world. The most common source of the miswak is from the Salvadora persica tree and the Azadirichta indica tree found in the Middle East, and the Indian subcontinent, respectively. Miswak is known to be composed of many abrasives and components that are found in many whitening products. The aim of this study was to measure the effectiveness of the miswak in preventing extrinsic tooth staining caused by the adsorbtion and binding of polyphenols found in such products as red wine, and black tea in comparison to a well-known whitening toothpaste. Hydroxyapatite discs were exposed to saliva to form a protein pellicle mimicking a tooth's enamel. The discs were divided and exposed to the dentrifices, and then exposed to the polyphenolic mixture composed of red wine and tea. Distilled water was used as a control. A shade guide helped determine the differences in stain color according to the chroma (saturation of color), and value (brightness) of the discs. Statistically, there was a significant difference between the miswak group and the control ($p<0.05$). However, there was no significant difference between the whitening toothpaste, and the miswak group. In conclusion, due to the abrasives and components found in the miswak stick, it can be used to prevent harsh extrinsic staining on teeth.

369. Synthesis of 3-Substituted Cyclopent[a]pyrrolo[3,4-c]carbazole-5,7-dione Analogs as Potent Cell Permeable Inhibitors of PARP-1

Allison L. Zulli, James L. Diebold, Ron Bihovsky, Edward R. Bacon, Jean Husten, Mark Ator and Robert L. Hudkins, Cephalon, Inc., West Chester, PA

Poly (ADP-ribose) polymerase 1 (PARP-1) is a nuclear enzyme that catalyses the synthesis of poly(ADP-ribose) chains from NAD+ as part of the DNA repair process. Inhibitors of PARP have therapeutic utility in oncology through potentiation of the anti-tumor activity of radiation or DNA damaging chemotherapeutic agents. We have identified pyrrolocarbazole 1 (IC50 = 36 nM) as a potent PARP inhibitor from screening our internal library; although with poor cellular permeability and low water solubility. This paper will present the SAR for a series of 3-substituted ether, carbamate and aminomethyl derivatives with the goal of improving the enzyme potency, cell permeability, and solubility.

370. Developing novel inhibitors of the enoyl reductase from Mycobacterium tuberculosis (InhA): SAR studies of triclosan congeners

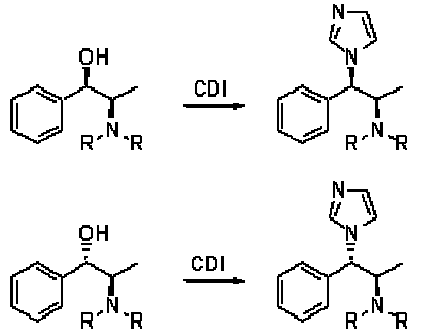
Todd J. Sullivan[1], Polina Novichenok[1], James J. Truglio[1], Francis Johnson[1], Richard A. Slayden[2] and Peter J. Tonge[1], (1) Stony Brook University, Stony Brook, NY, (2)Colorado State University,, Fort Collins, CO

InhA, the enoyl reductase enzyme from Mycobacterium tuberculosis (MTB), catalyzes the last step in the fatty acid biosynthesis pathway (FAS II). Frontline anti-tuberculosis drugs such as isoniazid (INH) target this enzyme. Drug resistance to INH results primarily from mutations in KatG, the enzyme that activates INH. Consequently, InhA inhibitors that do not require activation by KatG are attractive candidates for drug discovery. One such inhibitor is our lead compound for SAR studies triclosan, a common antibacterial additive in personal care products. Triclosan is a ìM inhibitor of InhA and a pM inhibitor of the enoyl reductase from E. coli (FabI). Using structural and mechanistic data, we have developed a series of aliphatic-substituted triclosan analogs with a nM affinity for InhA and with sub-ìM MIC99 values for H37Rv MTB. These compounds are currently being evaluated in an animal model of tuberculosis. Second generation analogues are now being developed to investigate and address compound bioavailability and cell membrane permeability.

371. Regio- and Stereospecific Syntheses of Syn- and Anti-1,2-Imidazolylpropylamines from the Reaction of 1,1'-Carbonyldiimidazole with Syn- and Anti-1,2-Aminoalcohols

Mark J. Mulvihill, Anthony I. Nigro, Cara Cesario, Vanessa Smith, Patricia Beck and **Kathryn M. Stolz**, OSI Pharmaceuticals, Farmingdale, NY

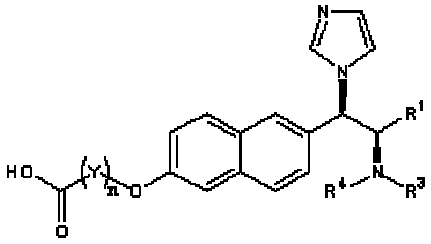
The regio- and stereospecific conversion of *syn*- and *anti*-1,2-aminoalcohols to their respective *syn*- and *anti*-1,2-imidazolylpropylamines via treatment with 1,1'-carbonyldiimidazole is described. The rationale behind the regio- and stereospecific nature as well as the generality of the reaction is discussed.



372. Potent and Selective 2,6-Disubstituted Naphthalenes as Retinoic Acid Metabolic Blocking Agents (RAMBAs)

Mark J. Mulvihill[1], Julie L. C. Kan[1], Andrew Cooke[2], Patricia Beck[1], Shripad Bhagwat[1], Mark Bittner[2], Cara Cesario[1], Carrie Ecker[1], David M. Keane[1], Anthony I. Nigro[1], Christy Nillson[2], Suzanne Russo[1], Vanessa Smith[1], Mary Srebernak[2], Feng-Lei Sun[1], Michael Vrkljan[2], Shannon L. Winski[2], Arlindo L. Castelhano[1], David Emerson[2] and Neil W. Gibson[1], (1)OSI Pharmaceuticals, Farmingdale, NY, (2)OSI Pharmaceuticals, Boulder, CO

A series of [2-imidazol-1-yl-2-(6-alkoxy-naphthalen-2-yl)-1-methyl-ethyl]-dimethyl-amines were designed and synthesized as CYP26 inhibitors, serving as retinoic acid metabolic blocking agents (RAMBA's). Optimized compounds possessed excellent pharmacokinetic and physiochemical properties and were highly CYP26 selective versus other cytochrome P450 enzymes, inhibiting both T47D and AT6.1 cell growth *in vitro* in combination with atRA and also increasing the half-life of atRA *in vivo* in mice.



Pharmaceutical Profiling Posters

Organizer: Anita J. Brandolini William Paterson University, Wayne, NJ
Organizer: Edward Kerns Wyeth Research, Princeton, NJ

373. Applications of Microsomal Stability Assays in Drug Discovery

Susan Q. Li[1], li Di[2] and Edward H. Kerns[1], (1)Wyeth Research, Monmouth Junction, NJ, (2)Wyeth Research, Princeton, NJ

Metabolic stability plays an important role in the success of drug candidates. An integrated high throughput microsomal stability assay was implemented using LC/MS/MS in our laboratory. We have applied this system to the routine metabolic screening of Wyeth compounds. In support of medicinal chemistry effort, we utilized this system to screen metabolic stability using different animal species (rat, mouse, human) and determine the potential difference in metabolic rate due to chirality. The system is also modified for cytochrome P450 phenotyping to identify which human CYP450 enzyme(s) is involved in the metabolic transformation of some compounds.

374. Comparison of PAMPA Methodology using Iso-pH and Multiple-pH Gradient Methods: Applications in Drug Discovery Research

Susan L. Petusky, Li Di and Edward Kerns, Wyeth Research, Monmouth Junction, NJ

This method utilized the PSR4p instrument from pIon, Inc. Permeability is determined by passive diffusion of a substance through an artificial membrane coated with lipid. Experiments were performed to determine the permeability of compounds at pH 7.4 in both acceptor and donor compartments. The same compounds were then tested using conditions in which the acceptor compartment was held at pH 7.4, while the pH of the donor well was varied as 5.0, 6.2, and 7.4. The sample set consisted of acidic, basic and neutral compounds.

Both methods produced good interday and intraday precision. The iso-pH method produced some false negative results for weak acids as a result of the compounds being charged at pH 7.4. The multiple-pH gradient method showed the pH dependence of permeability measurements.

Each method has a place in the drug discovery setting. For early screening in the very high throughput mode, the iso-pH measurement offers a good first estimation of compound permeability by passive diffusion in a timely manner. For lead series and later discovery compounds a multiple-pH approach can give a broader understanding of the compound permeability at different pH that mimic their passage through the intestinal tract.

375. Pharmacetical Profiling and Medicinal Chemistry Collaboration for Project Impact

Edward Kerns[1], Li Di[1] and Guy Carter[2], (1)Wyeth Research, Princeton, NJ, (2)Wyeth Research, Pearl River, NY

Profiling of drug discovery leads for their pharmaceutical properties (physicochemical and metabolic) provides great advantages for medicinal chemistry: HTS hit selection can include considerations of “lead-like” properties. Compound property liabilities can be quickly identified. Physicochemical and metabolic data relate directly to structural features, allowing medicinal chemists to make specific structural modifications to “tune” series properties. Project risk can be reduced by focusing on the most favorable compounds. Biological activity assays can be best planned and interpreted by knowing factors such as the solubility and permeability of compounds. Complex biological process (e.g., bioavailability) can be diagnosed using data from fundamental properties. Access to rapid property assays allows activity data and property data to be produced in parallel, so that a comprehensive data package is available in evaluating compound performance and planning structure re-design. All of these opportunities allow property profiling to be an integrated function within medicinal chemistry, for the enhancement of drug discovery.

376. Strategies and Techniques of Major Metabolite Profiling for Structure Optimization in Drug Discovery

Mei-Yi Zhang, Teresa Kleintop, Natasha Kagan and Edward Kerns, Wyeth Research, Princeton, NJ

Oral bio-availability is an important ADME property, if low, which may lead to failure of a drug candidate in development. High throughput *in vitro* metabolic stability screening assays have been widely used to identify such high clearance compounds in drug discovery. Early identification of the major metabolic pathways provides additional information to address the metabolism related liabilities. This poster describes the strategies and techniques for major metabolite profiling. Using our approach, the major metabolic pathways were identified at the physiologically relevant drug exposure concentrations. The metabolism-structure relationships were studied by profiling series analogues in parallel. The exact structure of major metabolites was determined using MS/MS and NMR with isolated metabolites. The study provides important information for discovery chemists to block metabolically labile spots on the molecules and design metabolically more stable compounds.

Solid State and Materials Chemistry Posters

Organizer: Anita J. Brandolini William Paterson University, Wayne, NJ
Organizer: Jing Li Rutgers,The State University of New Jersey, Piscataway, NJ
Organizer: Martha Greenblatt Rutgers, The State University of New Jersey, Piscataway, NJ

377. Sorption Properties of Pure Silica ITQ-13

Aleksandra Biedron[1], Miguel Camblor[2], David Olson[1] and Jing Li[1], (1)Rutgers,The State University of New Jersey, Piscataway, NJ, (2)Institute of Materials Science of Madrid (CSIC), Campus Cantoblanco, Madrid, Spain

The synthesis and structure of the pure silica zeolite ITQ-13 was recently reported by Biox et al and Corma et al. ITQ-13 has a three-dimensional, 9-ring [100], 10-ring [010] and 10-ring [001] channel structure and has similarities to the pore system of ZSM-5. As the ring sizes are 5-9% smaller than those of ZSM-5, the diffusion coefficients (D's) are expected to be lower. However, the thin platelet morphology of the material studied resulted in very rapid adsorption rates preventing accurate measurement of D; no comparison of the D's for these two zeolites could be made. The adsorption properties of propane, n-butane, n-hexane, 2,2-dimethylbutane, benzene, toluene, p-xylene and o-xylene have been measured and will

be presented. Of particular interest are the observations of a two-step para-xylene TPD and the more limited capacity and apparent preferred orientation of ortho-xylene. The latter was indicated by computer simulation of the adsorption process. No aromatics adsorb in the 9-ring channel regions.

378. Structural modifications of extended metal-organic frameworks

Ren Zhang and Jing Li, Rutgers,The State University of New Jersey, Piscataway, NJ

The synthesis of microporous materials has been an area of intense research interests due to their various structural chemistry and applications in catalysis, separation, and gas sorption. Recently the microprous metal organic frameworks (MMOFs) have attracted much attention as candidates for gas storage materials, because the MMOFs may be modified to bind gas molecules much more strongly than graphitic carbon, but not as strongly as real chemical bonds. Our group has published some MMOF structures such as $[Cu_2(hfipbb)_4](H_2hfipbb)_2$ which can adsorb up to 1 wt% of hydrogen gas at 48 atm. To improve hydrogen uptake, we have carried out rational synthesis to aim at modified structures with higher pore volume. In this presentation we discuss our results concerning use of a number of selected ligands.

379. Gas sorption studies of 3D supermicroporous metal organic frameworks

Jeongyong Lee and Jing Li, Rutgers,The State University of New Jersey, Piscataway, NJ

Metal organic frameworks (MOFs) represent a very important class of materials with potential for applications in various areas. Recently, unique and interesting properties are being discovered in microporous metal organic frameworks (MMOFs), a subset of MOFs. As MMOFs have very small pores, selection of adsorbate gas becomes an important issue. Argon and carbon dioxide have been selected as adsorbates to characterize the pore structure of 3D supermicroporous metal organic frameworks which have pore sizes between 7 and 20Å in diameter. High-resolution low-pressure sorption studies have been carried out to measure pore properties of $[Co_3(bpdc)_3bpy]$ 4DMF H_2O (bpdc = biphenyldicarboxylate, bpy = 4,4′-bipyridine, DMF = N,N-dimethylformamide) and $[Cu-(hfipbb)(H_2hfipbb)_{0.5}]$ ($H_2hfipbb$ = 4,4-(hexafluoroisopropylidene)- bis(benzoic acid) and several other related compounds, and the results are validated in terms of isosteric heat of adsorption, Qst. We have also studied hydrogen adsorption-desorption properties on these materials and the results will be discussed.

380. Versatile Metal-Organic Frameworks Synthesized Using Several

Long Pan, Brett Parker, Xiaoying Huang, David Olson and Jing Li, Rutgers,The State University of New Jersey, Piscataway, NJ

More than ten metal-organic frameworks have been synthesized using transition metals such as copper(II), zinc(II) and cadmium(II) and 5-tert-butyl isophthalic acid (H_2tbip), via hydrothermal and/or diffusion methods. Sorption experiment have been conducted on the 3D zinc framework material in which adjacent 1D channels are associated with closely spaced benzene rings (3.25-3.55Å) with strong - interactions. This material has a hydrophobic, microporous framework exhibiting a unique sorption behavior for methanol. The possibility of utilizing this material for gas phase separation of methanol from water, and for the separation of methanol from dimethylether will be exploited.

381. Synthesis and characterization of ZnO-L (L= ethylenediamine, aniline) materials

Min Wu, Hyun-Kyung Rhee, Xiaoying Huang and Jing Li, Rutgers,The State University of New Jersey, Piscataway, NJ

Zinc oxide is II-VI semiconductor with a band gap of 3.4 eV at room temperature. Compared with other semiconductor materials, ZnO has higher exciton binding energy (60 meV), more radiative recombination efficiency for spontaneous emission as well as a lower threshold voltage for laser emission. Research on epitaxial growth of ZnO nanoparticles has recently made remarkable progress. Therefore, it is clear that ZnO is a strong candidate for optoelectronic applications in the short wavelength range (green, blue, UV). In an effort to tune the structural and optical properties of ZnO, we have explored synthesis of ZnO hybrid materials using selected organic ligands. Here we report new ZnO-L (L = ethylenediamine, aniline) materials prepared by low temperature solvothermal reactions. UV-Vis spectra show a strong blue shift in their optical band edges with respect to ZnO, with estimated band gaps in the range of 4.5-5.0eV. The structures and selected properties of these hybrid compounds will be discussed.

382. Modification of extended metal-organic structures

Text Not Available

383. Synthesis of Microporous Materials containing Light Metals by Hydrothermal/Solvothermal Routes

Sanhita Pramanik, Long Pan and Jing Li, Rutgers,The State University of New Jersey, Piscataway, NJ

Porous metal coordination structures may be useful in renewable energy applications, such as hydrogen storage. Hydrogen gas is one of the best fuels because the byproduct of it is water, which is environmentally very safe and clean. The hydrogen storage materials are needed in fuel cell powered vehicles. Much effort has been made to develop suitable candidates for storage purposes but none of them is able to meet the current DOE target. Our recent work focuses on the

synthesis of a new type of storage materials, namely microporous metal organic frameworks (MMOFs) containing light metals such as alkaline earth metals and study their hydrogen absorption properties.

384. New Routes of II-VI Semiconductors and Hybrid Thin Film Fabrication

Wooseok Ki and Jing Li, Rutgers,The State University of New Jersey, Piscataway, NJ

Recently, thin-film semiconductors based on organic and inorganic hybrid materials have been developed by cost-effective solution-based deposition methods. These systems exhibit a number of improved properties, including high mobility and band gap tunability. In this study, we formulate the hybrid II-VI semiconductor thin films by solution based deposition involving ultrasonic irradiation and analyzed their electrical and optical properties, such as photoluminescence and conductivity. While II-VI semiconductors possess very high mobility, they have been restricted due to their poor solubility so that it is difficult to apply solution processing techniques. In order to overcome this limitation, we introduce new routes for enhancing the solubility of II-VI metal chalcogenide. For mobility measurement, solution processed thin films were fabricated by spin coating technique

385. (M_2Q_2)*L* and Mn doped (M_2Q_2)*L* (M = Zn, Cd, Q = S, Se, *L* = *n*-propylamine, *n*-butylamine, *n*-hexylamine): A class of promising multifunctional inorganic-organic hybrid II-VI

Xiaoying Huang and Jing Li, Rutgers,The State University of New Jersey, Piscataway, NJ

A novel class of Inorganic-organic hybrid II-VI nanocomposites with formula (M_2Q_2)*L* (M = Zn, Cd; Q = S, Se; *L* = *n*-propylamine, *n*-butylamine, *n*-hexylamine) have been synthesized solvothermally and characterized by PXRD, UV-vis and TGA. The crystal structures of these hybrid materials are composed of double-layered [M_2Q_2] slabs intercalated with monoamine molecules. Due to the strong quantum confinement effect (QCE), they exhibit a relatively large blue shift in their absorption edge, comparing to their parent binary II-VI semiconductors MQ. The photoluminescence (PL) studies revealed some interesting phenomena. The substitution of Zn by Mn in (Zn_2Q_2)*L* resulted typical dilute magnetic semiconductors (*DMS*) $(Zn_{1-x}Mn_xQ)_2L$ (*x* = 0.025, 0.05, 0.10, 0.15), which showed some interesting magnetic properties and Mn^{2+}-related emissions at their PL spectra. The introduction of Mn^{2+} to hybrid inorganic-organic semiconductors provides a promising route to generate multifunctional materials that combine the advantageous features of inorganic, organic and magnetic functionalities in a single structure.

386. Crystal Engineering with the Uranyl Cation: Use of Multiple Ligands as a Route to Novel Structures

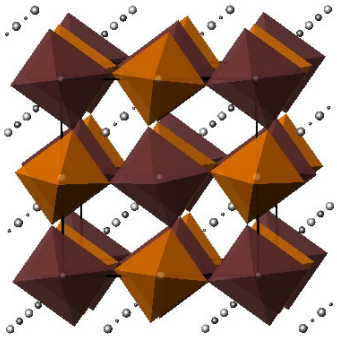
Lauren A. Borkowski and Christopher L. Cahill, The George Washington University, Washington, DC

The uranyl cation (UO_2^{2+}) is an attractive metal center that can be utilized for the construction of metal-organic framework and coordination polymer materials. This linear moiety coordinates readily to an assortment of functional groups including pyridyl and carboxylic acid species through equatorial positions typically resulting in three geometries: square, pentagonal and hexagonal bipyramids. The interaction between the UO_2^{2+} moiety and flexible dicarboxylates has been well established in the literature as well as by our group, yet the addition of a second type of ligand has not been well explored. With this in mind a new family of structures has been obtained by reacting uranium oxynitrate with flexible, aliphatic carboxylates and rigid bipyridyl ligands. The rigid species (4,4'-dipyridyl or 1,2-bis(4-pyridyl)ethane) interacts with the UO_2^{2+} moiety in one or more of three ways: 1) as a ligand directly coordinated to the uranium center, 2) as a charge balancing counter ion, or 3) as a structure directing or “templating” agent. Presented herein will be the synthesis and structural systematics of five novel uranium containing structures: **1** ($UO_2(C_6H_8O_4)(C_{10}H_8N_2)$); **2** $((UO_2)_2(C_5H_6O_4)_3\cdot(C_{10}H_{10}N_2)(H_2O)_2)$; **3** $((UO_2)_2(C_7H_{10}O_4)_2(C_7H_{11}O_4)_2\cdot(C_{10}H_8N_2)(C_{10}H_{10}N_2)(H_2O)_2)$; **4** $((UO_2)_4(O)_2(C_8H_{12}O_4)_2(C_{12}H_{12}N_2)_2)$ and **5** $((UO_2)_4Cu(O)_2(C_6H_8O_4)_3(C_{10}H_8N_2)_2\cdot(C_{10}H_8N_2))$.

387. SrFe1/4Re3/4O3: A metallic ferromagnetic double perovskite with an uncommon octahedral tilt as revealed by high-resolution synchrotron powder X-ray diffraction

Louis W. Whaley[1], Martha Greenblatt[1], Mark C. Croft[2] and Kandalam V. Ramanujachary[3], (1)Rutgers, The State University of New Jersey, Piscataway, NJ, (2)Rutgers University, Piscataway, NJ, (3)Rowan University, Glassboro, NJ

Structural, magnetic and transport characterization of a metallic, ferromagnetic double perovskite with 3d—5d orbital interactions, nominally $SrFe_{1/4}Re_{3/4}O_3$, has been performed. Synchrotron x-ray powder diffraction (SPXD) reveals an orthorhombic structure with an uncommon $a^+b^+c^+$ Glazer octahedral tilt system (*Pnnn*, a = 7.87422(4); b = 7.87726(6); c = 7.89795(4)Å; χ^2 = 3.12$_5$%; R_{wp} = 8.06%; R_p = 6.47%; 35 variables), with a slight symmetry lowering distortion (*P2nn*,a = 7.87722(6) Å; b = 7.87433(4)Å; c = 7.89800(4)Å; χ^2 = 2.90; R_{wp} = 7.42; R_p = 6.10; 45 variables). Fe-K-edge and Re L3-edge XANES data support Fe(III) and mixed valent Re(IV/VI). Temperature-dependent magnetic susceptibility reveals ordering near 150 º K and a hysteretic field-dependent magnetization indicates "ferromagnetism" (or ferrimagnetism but with a small, nearly vanishing contribution from the rhenium moment). Ordering of the B-site and the nearly linear B(Fe/Re)-O-B'(Re) bond angles (~170 º) apparently enhance magnetic exchange and (metallic) charge transport near room temperature ($\rho_{RT} \approx$ 2.5 mΩ-cm). A shallow resistivity minimum at 40 º K ($\rho_{40K} \approx$ 1.9 mΩ-cm) resembling a metal-semiconductor transition is attributed to weak localization.



388. Synthesis of $SrLaFeO_3H_x$

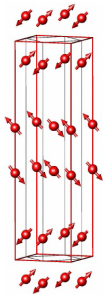
Sibel Dikmen, Viktor V. Poltavets and Martha Greenblatt, Rutgers, The State University of New Jersey, Piscataway, NJ

The covalent interaction between the O2- anion and d orbitals of the transition metal cation leads remarkable electronic properties. Developing synthetic routes to materials in which other anions partially replace oxide could open up the possibility of preparing completely new families of electronically active transition metal compounds. The hydride anion, H-, with 1s2 electronic configuration ,engages strong covalent bonding with transition metal centers and would be as effective as O2- ion for the transmission of exchange interactions among transition metal cations in an oxide hydride, if the synthetic difficulties to prepare such a phase could be overcome. H-, unlike O2-, is a powerful reducing agent and would be expected to transform the transition metal component of a transition metal oxide synthesis into the metal. Low-temperature topotactic route to the insertion of H- anions directly into an extended transition metal oxide array has been studied. The synthesis of SrLaFeO3Hx has been tried with a reaction shown; SrLaFeO4 + CaH2 SrLaFeO3Hx + CaO. PXD and magnetic sussectibility data is shown.

389. $Sr_3Fe_{1.225}Mo_{0.775}O_7$, a Unique n = 2 Ruddlesden-Popper Phase with a Metal-Insulator Transition

Louis W. Whaley[1], Martha Greenblatt[1], Mark C. Croft[2], Kandalam V. Ramanujachary[3], Maxim Lobanov[1] and Denis Sheptyakov[4], (1)Rutgers, The State University of New Jersey, Piscataway, NJ, (2)Rutgers University, Piscataway, NJ, (3)Rowan University, Glassboro, NJ, (4)Paul Scherrer Institute, CH-5232 Villigen PSI, Switzerland

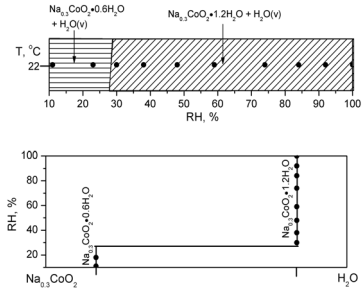
In a systematic search for an oxygen-stoichiometric $Sr_3(FeMo)O_7$, in a range of iron to molybdenum ratios greater than 1:1 that typically give phase mixtures, we have found (at a ratio of approximately 5:3:: iron:molybdenum), an n = 2 Ruddlesden-Popper (RP) phase $Sr_3Fe_{1.225}Mo_{0.775}O_7$. Synchrotron powder X-ray diffraction and neutron powder diffraction results support the n = 2 RP structure in the sample of highest purity fired at the 1275 ° C and quenched in liquid nitrogen (1275Q). In samples prepared at 1245 ° C (1245A) and 1260 ° C (1260A, 1260Q) possible partially ordered B-site n = 2 RP phases are detected. The magnetic structure derived from powder neutron diffraction patterns at various temperatures from 9 ° K to 490 ° K of 1275Q, displays an asynchronous decrease of the in-plane (μ_{xy}) component of the Fe/Mo moment, with respect to the out of plane moment (μ_z), upon increasing temperature from 9 ° K up to the AFM ordering temperature, ~150 ° K. All the samples are semiconducting between 125 ° K and 275 ° K. For example, a sample heated to 1260 ° C 45 minutes and annealed at 700 ° C, undergoes a transition centered near 75 ° K. A maximum in magnetoresistance in this sample (~14 %) is observed from 125 ° K down to 50 ° K at 5 Tesla, which coincides with the semiconductor-metal transition.



390. Isothermal section of the $Na_{0.3}CoO_2$ - H_2O system phase diagram at 22°C from 11 to 100% relative humidity

Viktor V. Poltavets and Martha Greenblatt, Rutgers, The State University of New Jersey, Piscataway, NJ

An isothermal section of the $Na_{0.3}CoO_2$ - H_2O system phase diagram at 22°C from 11 to 100% relative humidity is presented. Superconducting $Na_{0.3}CoO_2$•$1.3H_2O$ phase is stable at relative humidity higher than 30%, while single phase region of the $Na_{0.3}CoO_2$•$0.6H_2O$ hydrate is at lower partial water pressure. Cell parameters and temperature of superconducting transition of $Na_{0.3}CoO_2$•$1.3H_2O$ do not depend on relative humidity. Both hydrates have a constant water contents over the studied water vapor pressure range. Slow rate of the superconducting phase formation at relative humidity lower than 40% was found. Conditions for hydrate water contents optimization are proposed.



Figure

Isothermal sections of the $Na_{0.3}CoO_2$ - H_2O system phase diagram at 22°C from 11 to 100% relative humidity

a) RH - temperature coordinates.

b) composition - RH coordinates (H2O(v) is not shown on the diagram for simplicity)

Spectroscopy of Biomolecules Posters

Organizer: Edward W. Castner Jr. Rutgers, The State University of New Jersey, Piscataway, NJ
Organizer: Anita J. Brandolini William Paterson University, Wayne, NJ

391. Time-Resolved UV Resonance Raman Studies of Polyriboadenylic Acid and DNA

Alison P. Williams, Princeton University, Princeton, NJ and Ishita Mukerji, Wesleyan University, Middletown, CT

Time-resolved UV resonance Raman spectroscopy is a powerful method for monitoring structural changes in real time. The technique permits the exploration of transient intermediates on a time scale inaccessible to NMR studies and at a level of sensitivity not possible via electronic spectroscopy. To date, studies have explored protein dynamics, yet nucleic acid structural features have yet to be investigated by this method.

In this study, we report the results of time-resolved UV resonance Raman spectroscopic studies of base stacking in polyriboadenylic acid in the nanosecond to microsecond timescale. Preliminary results show that the kinetics of the associated conformational changes can be resolved; specifically, backbone conformational changes can be separated from those associated with the bases. We also explore conformational changes that occur in DNA.

392. Resonance Raman investigation of the structural/functional role of the unusual adduct in Mycobacterium tuberculosis catalase-peroxidase KatG

Sofia M. Kapetanaki[1], Xiangbo Zhao[2], Richard S. Magliozzo[2] and Johannes P. M. Schelvis[1], (1)New York University, New York, NY, (2)Brooklyn College and the Graduate Center of the City University of New York, New York, NY

Mycobacterium tuberculosis (Mtb) KatG is a catalase-peroxidase that is believed to activate the antituberculosis drug, isoniazid (INH). The X-ray crystal structure of Mtb. KatG has revealed an unusual three-amino acid adduct involving the covalently linked distal side tryptophan (W107), tyrosine (Y229), and methionine (M255) residues. Previous studies have shown that KatG(Y229F) has a decreased catalase activity and forms Compound II without detectable accumulation of Compound I, in contrast to the WT enzyme. In order to understand the functional/structural role of this adduct, the local environment of KatG(Y229F) is investigated by resonance Raman spectroscopy, using the exogenous ligands CO and NO. Moreover, the catalytic mechanism of KatG(Y229) is studied. The implications of these findings for the structural/functional role of the adduct and the catalytic mechanism of WT KatG are discussed.

393. Time-resolved Resonance Raman Spectroscopy of Tryptophans and Flavins

Ullas Gurudas and Johannes P.M. Schelvis, New York University, New York, NY

Photolyase is a flavoenzyme that repairs DNA-specific damage induced by ultraviolet light. The photoreactivation mechanism of photolyase is unique in the repair of the *cis,syn* cyclobutane pyrimidine dimer (CPD) by a light-driven, electron-transfer catalyzed monomerization. A second electron transfer process can occur in the photoreduction of the neutral radical form of the flavin cofactor to its catalytically active reduced form. The pathway of this electron transfer is debated in the literature, and electron-hopping through a chain of tryptophans has been proposed. Both electron transfer processes are initiated from a flavin excited, which plays an important role in the light-driven process of DNA photolyase and other blue-light photoreceptors, and tryptophan radical intermediates have recently been recognized as important electron transfer intermediates. Time-resolved resonance Raman (TR^3) spectroscopy is an excellent tool to characterize these species and may provide new exciting information about their roles in blue-light photoreception and electron transfer. We will present the first TR^3 spectrum of a neutral Trp radical intermediate in a protein and preliminary results on a flavin excited state.

394. Probing the Interaction Between Proteins and Some Small Molecules Using Fluorescence Spectroscopy

Rosa Patricia Rosales, Queensborough Community College, Bayside, NY and Ruel Desamero, York College, Jamaica, NY

The overall objective of the study is to understand the interplay between protein structure and mechanism, for some biologically important macromolecules. As a model system the enzyme dihydropteridine reductase (DHPR) was studied. DHPR catalyses the NADH-mediated reduction of quinonoid dihydrobiopterin to give tetrahydrobiopterin, which functions as an essential cofactor in the biosynthetic reactions that convert phenylalanine to tyrosine, tyrosine to dihydroxyphenylalanine, and tryptophan to dihydroxytrptophan. In this study the fluorescence signature of tyrosine, tryptophan, NADH, NAD+, some pteridines and the enzyme dihydropteridine reductase (DHPR) was determined. The presence of DHPR quenches the fluorescence of the cofactor, NADH, and the inhibitors folic acid, methotrexate and trimethoprim. One intriguing result was that for one inhibitor, 6,7-dimethyl 5,6,7,8 tetrahydropterin, the presence DHPR results in an enhancement of fluorescence. We also measured the fluorescence spectra of the ternary complexes involving DHPR/NADH/inhibitor. It is clear from our results that small molecules interact with DHPR and it appears that the inhibitors interact with DHPR even in the absence of the cofactor, NADH. We also conclude that fluorescence spectroscopy is an effective tool to study DHPR and we will extend this work to do fluorescence based transient measurements. Rosa Rosales is a participant in the QCC-NIH Bridges to the Baccalaureate Program (grant 1 R25 GM65096-03).

395. Ultrafast Electron Injection in Dye Sensitizer / Semiconductor Systems

Piotr Piotrowiak[1], **Mykhaylo Myahkostupov**[2], Dong Wang[2], Qian Wei[2] and Elena Galoppini[2], (1)Rutgers University at Newark, Newark, NJ, (2)Rutgers-Newark, Newark, NJ

Ultrafast electron injection processes for a serties of Ru-based dyes bound to the TiO2 nanoparticles have been studied. The Ru-based chromophores with spacers of different length (up to 24 Å) have been synthesized in order to study the effect of separation between the chromophore-bearing group and the semiconductor surface onto the rate of electron injection. Also, the effect of spacer conjugation on the rate of electron injection has been investigated by interrupting the spacer conjugation with bicyclooctane unit. Furthermore, sensitizers with different number of binding groups (bipods and tripods) were synthesized to study the effect of binding geometry to the semiconductor surface. It was found that electron injection is mostly complete within a sub-picosecond timescale. This behavior suggests that spacers work as molecular wires. The kinetics of electron injection turns out to be mostly biexponential that can be caused by the competition between the “hot” electron injection on one side and vibrational cooling and intersystem crossing on the other hand. The resolution of these competing processes is now being thoroughly studied and will be reported as well.

396. Formulating a Mechanism of Amyloid Growth using Single Molecule Spectroscopy

Jason T. Giurleo, Troy C. Messina, Hiyun Kim, Jongjin Jung and David Talaga, Rutgers University, Piscataway, NJ

We are investigating the mechanism for the initial stages of protein self-assembly leading to amyloid growth using single molecule spectroscopy (SMS). B-lactoglobulin (b-LG) has been shown to form amyloid under denaturing conditions and has been chosen as a model protein for this study. Initial bulk experiments have been performed utilizing dynamic light scattering along with steady state and time-resolved fluorescence of conformationally sensitive fluorophores, and a preliminary mechanism of amyloid growth has been formulated. However, SMS has the potential to directly identify critical intermediates that could only be hypothesized by bulk experiments. A single molecule imaging experiment utilizing incubated samples of mono-labeled TMR-(b-LG) has been designed to count number of precursor monomers per aggregate species by counting the number of photobleaching steps required to extinguish a single particle's fluorescence. The time evolution of the particle number distribution is fit to a kinetic model representing a mechanism of amyloid growth.

397. Ultrafast Folding of Trp-cage Mutants

Michelle R. DeRitter, Xi Yang, Jeffrey Saven and Feng Gai, University of Pennsylvania, Philadelphia, PA

Owing to its small size and simple structure, the mini-protein Trp-cage is an excellent model system for protein folding studies. Herein, we investigated the thermal stability and folding kinetics of a series of Trp-cage mutants, designed based on a statistic computational method, by static infrared (IR) and circular dichroism (CD) spectroscopies and IR temperature jump (T-jump) method. Our results support a folding mechanism wherein the formation of the salt-bridge between Arg-16 and Asp-9 is not rate-limiting, in disagreement with a recent theoretical study. Moreover, we found that mutant P12W exhibits not only an enhanced thermal stability but also a faster folding rate, indicating that the hydrophobic interaction plays an important role in the stabilization of both the native and transition states. In addition, our results highlight the usefulness of the stabilizing Trp-Trp interaction in protein design.

398. Trans/Cis Proline Isomerization in Different Solvents Studied by Fluorescence Quenching due to Intramolecular Electron Transfer

Youssef Issa, David S. Talaga, Edward W. Castner and Stephan S. Isied, Rutgers University, Piscataway, NJ

The factors that control the slow ($t_{1/2}$ ~ seconds) trans- to cis- proline isomerization in peptides and proteins continue to attract significant attention because of the involvement of proline residues in a diverse number of protein conformational processes. The Polyproline II (trans) structure is favored in high polarity solvents where as the Polyproline I (cis) structure is favored in solvents of low polarity. We report here on a series of donor acceptor proline peptides with one and two amino acid residues derivatized with the fluorophore, tetramethylrhodamine (TMR) at the N-terminus and dimethyl-1,4-phenelenediamine (DMPD), at the C-terminus. This series of molecules is soluble in solvents ranging from hexane to water. A sensitive method to evaluate the amount of trans/cis conformers in this series at low concentrations is using Time Correlated Single Photon Counting (TSCPC) by monitoring intramolecular electron transfer from the DMPD (electron donor) to the ^{1}S state of TMR (electron acceptor) . The fluorescence quenching of TMR in these derivatives was monitored over a broad range of solvent polarity. It was observed that the lifetimes of both the MonoPro and the Dipro residues decreases with decreasing solvent polarity with lifetimes for DiPro ranging between 2.0 ns (water) to 0.08 ns (hexane). The decrease in lifetimes follow the increasing amounts of the cis proline conformation at lower solvent polarity, where the electron donor and acceptor are in close proximity. Analysis of these lifetimes in terms of solvent effects on driving force, reorganization energy, and proline conformations will be discussed. .

399. A Stark Spectroscopic Study of Semiquinone FAD in DNA Photolyase

Goutham Kodali, M. Salim Siddiqui and Robert J. Stanley, Temple University, Philadelphia, PA

DNA photolyase is a light-driven flavoprotein that repairs cyclobutylpyrimidine dimers (CPD) in UV-damaged DNA via an ultrafast photoinduced electron transfer reaction from the fully-reduced anionic flavin adenine dinucleotide ($FADH^-$) cofactor to the CPD. Previously we have demonstrated the possibility that the electric dipole moment of the CPD induces an electrochromic shift in the absorption spectrum of the oxidized FAD cofactor in DNA photolyase. These results would indicate that the substrate electric field plays a critical role in the electron transfer process. A similar electrochromic shift has been reported by the Schelvis group (NYU) for semiquinone DNA photolyase upon CPD binding. In an effort to provide further insight into this result, we have explored the electronic structure of the ground and excited electronic states of the semiquinone FAD in DNA photolyase using Stark spectroscopy.

400. Solvent Transport inside Surface Modified Silica Nanotubes

Charles Luckett, Karthik Jayaraman, Kenji Okamoto, Sang Jun Son, Sang Bok Lee and Douglas English, University of Maryland CollegePark, CollegePark, MD

Owing to the enormous interest in using nanotubes for applications including biosensors, drug delivery, tiny reaction chambers and transport vessels, research was initiated towards understanding the transport properties of nanotubes. An improved sol-gel template synthesis was established to prepare silica nanotubes with varying diameters and with different surface chemistries. Hydrophobically modified nanotube interior surfaces were labeled with adsorbed dyes and the diffusion of the dye molecules inside the individual tubes was investigated using fluorescence recovery after photo bleaching (FRAP) experiments. We have observed that the wetting probability of these hydrophobic nanotubes is a function of solvent composition and nanotube diameter. Silica nanotubes with positively charged interior have been synthesized and transport of single biomolecules through these nanotubes will be understood. Results from these experiments are important for enhancing our understanding of solvent behavior in confined environments and for discovering ways to better use tubes as tiny reaction chambers or transport vessels.

401. Single Molecule Measurement of Fast Folding Proteins Using Fluorescence Resonance Energy Transfer Confocal Microscopy

Jongjin Jung, Hiyun Kim, Troy C. Messina, Jason T. Giurleo and David S. Talaga, Rutgers University, Piscataway, NJ

We are studying the folding dynamics of a l85 repressor, the truncated N-terminal domain of l repressor, using single molecule measurements. The l85 repressor with double mutants (Gly46 ® Ala, Gly48 ® Ala) was reported to fold with a lifetime of less than 20ms (RE. Burton et al J.Mol.Biol 1996 263 311- 322) without intermediate states. The mutant protein, G46A/G48A, has been labeled with a fluorescent donor (Alexa488) and acceptor (Cy7) at its N and C termini. Using a Fluorescence Resonance Energy Transfer (FRET) measurement, we can investigate the dynamics of fast-folding proteins in two different environments, i) one in which a protein is confined but freely rotating in agarose gel, ii) the other in which a protein is fixated on glass surface through nitrilotriacetic acid (NTA) - chelated Nikel. In addition to the end-to-end distance distributions by the different urea concentrations, the instantaneous events during folding in a microsecond time scale and the fast-folding dynamics will be elucidated to explore the folding landscape and the memory effects of the G46A/G48A by applying novel single molecule spectroscopy analysis tool, Hidden Markov Model (HMM).

Eminent Scientist Lecture

402. What's New In The New World Of Astrochemistry

Yorke Rhodes, New York University, New York, NY

If the physical world that we know and the universe are described by the same Physics, i.e., if Physics is universal, is chemistry also universal? Do the rules that we know continue beyond earth? Before 1960 that question was not often raised. No one thought much of chemistry off-earth. Yes, there was known to be water, CO and CO2 in the space around earth and even around other planets, even in the spectra of some stars. Such spectra were used to measure properties of some stars, but one didn't think of those molecules as chemistry.

The myriad of chemicals known on earth did not lead people to search off earth. But since the '60's what discoveries have been made! There are now known some 130 different molecules off-earth, out of the solar system, interstellar, intergalactic. Practically everywhere one looks in the heavens there are many molecules. Is the chemistry similar to what we know here on Earth? Three quarters of the now-discovered molecules are what we would call organic – some are similar to earth chemistry, some are exotic, all follow rules of structure and energy that we know, but many are very different and have unusual structures that we don't find in our temperate surroundings. A subtitle could be: "Recent Advances in the Chemistry of Natural Products". Come learn about unusual structures. What molecules exist? How did they form? Where do they occur? What mechanisms exist for molecule formation? What are some possible reactions? Let's see what we can predict.

Age-related macular degeneration (AMD)

403. Age-related Macular Degeneration (AMD)

Koji Nakanishi, Columbia University, New York, NY

A2E, a pyridinium pigment with two retinoid side chains, is an ocular pigment involved in AMD, the leading cause of blindness of person over age 55 in USA and Europe and for which no remedy exists. In addition to A2E several other A2E analogs have been characterized from the eye. Photooxidation of A2E with blue light (430 nm) gives rise to an unprecedented nona-oxo. In addition to this nona-oxo A2E , blue light irradiation gives rise to a complex mixture of oxidation products, some of which may damage the cell. The (S) and (R) isomers of all-trans retinal dimer have also been isolated from human eyes. The genesis, interrelations of these pigments and preparation of antibodies will be discussed. The constituents of bilberry that have beneficial effects on AMD will also be presented.

Enterprise 2015: Chemistry at the Crossroads of Science

Presider: William F. Carroll Jr. Occidental Chemical Corporation, Dallas, TX

404. A Future Outlook for the Chemistry Enterprise: A Pharmaceutical Industry Perspective

Magid Abou-Gharbia, Wyeth Research, Princeton, NJ

The Pharmaceutical Industry is currently facing major challenges: greater complexity in producing NCEs (New Chemical Entities), intensified regulatory requirements, more patent expiration of top products, propagation of generic competition, increased cost of technology, drop in share value, and diminished confidence from both the public sector and Wall Street. These challenges and the pressure to reduce cycle time without compromising innovation result in substantially increased cost of Drug Discovery and Development. Many of these challenges are addressed through resourcefulness, process refinement and optimization, and enabling technologies including combinatorial chemistry, HTS, and structure-based design. To implement these and other technologies, there is a staggering requirement for more chemists, and not diminished need for capacity as originally perceived. Outsourcing, collaborations, and alliance partnerships can present a

company with added flexibility and the chance to “stretch” the value of research dollars. The speaker will highlight these issues and provide his own assessment of the future outlook for chemistry.

405. Changing Face of Chemistry and Implications for ACS

Madeleine Jacobs, American Chemical Society, Washngton, DC

Stars, Branched, Graft and Dendritic Polymers

Organizer: Kathryn E. Uhrich Rutgers University, Piscataway, NJ
Presider: Kristi L. Kiick University of Delaware and Delaware Biotechnology Institute, Newark, DE

406. Potential Synergies of Tailored Branching and Intermolecular Interactions: From Gene Transfer Agents to Elastomers and Fibers

Timothy E. Long, Matthew McKee, John Layman, Serkan Unal, Afia Karikari and Casey Elkins, Virginia Tech, Blacksburg, VA

Branched macromolecules offer the versatility of enhanced reactivity and processibility due to a more compact, globular structure. Both solution and melt rheological studies were used to define the influence of both branching and the introduction of intermolecular interactions. Self-complementary hydrogen bonding was introduced to sub-micron fiber surfaces using electrospinning operations. In addition, branched topologies also permitted the incorporation of higher levels of therapuetic reagents due to the lower solution viscosity. Highly branched elastomers were also prepared when a well defined concentration of urea groups were located at the periphery of the branched macromolecule. This presentation will highlight recent synthetic efforts with a focus on the advantages of branched architecture in diverse, high performance, applications.

407. Assembly of Polysaccharide-Derivatized Star Polymers for Protein Delivery Applications

Kristi L. Kiick, University of Delaware, Newark, DE

Protein-polysaccharide interactions play important roles in a myriad of physiological and pathological processes. Materials in which assembly, mechanical response, and biological properties are controlled by these interactions may therefore be responsive to the biological environment and find use in a variety of biomedical applications. Despite this potential utility, polysaccharide-peptide interactions have only recently been demonstrated as useful in the assembly of noncovalently associated networks. We report here the use of functionalized poly(ethylene glycol) star copolymers in the noncovalent assembly of hydrogels via interaction of a heparin-modified star polymer with a variety of heparin-binding proteins and peptides. The rheological properties of the hydrogels have been measured via optical probe microrheology and bulk rheology methods and can be controlled by choice of specific peptide-saccharide interactions. The release of therapeutically important proteins from these heparinized hydrogels has also been demonstrated via immunochemical and cellular assays and is correlated with the erosion of the networks. The ability to manipulate the properties of the hydrogels will provide novel materials for use in controlled drug delivery and other biomedical applications.

408. Preparation of Biocompatible and Biodegradable Nanobrushes from Cellulose and Hydroxyapatite Nanocrystals

Ivan Gitsov, SUNY College of Environmental Science and Forestry, Syracuse, NY, Anne Kathrine Overgaard, Technical University of Denmark, Kgs. Lyngby, Denmark and Bhushan Hole, Syracuse University, Syracuse, NY

The main goal of this study was the preparation of biocompatible and biodegradable nanobrushes as composite ingredients and reactive precursors for reinforced hydrogels. The nanobrushes were formed from cellulose and hydroxyapatite nanoparticles via ring-opening polymerization of dl-lactide and stannous octoate as the catalyst. The effect of the polymerization conditions (time, monomer feed ratio, temperature and solvent) on the yield, grafting density and polymer chain length of the hybrid particles was investigated by FT-IR spectroscopy, NMR and chromatographic techniques. It was found that the yields of the polymer hybrids varied from 11 % to 64 % for the cellulose and from 12 % to 87 % for the hydroxyapatite depending on the reaction conditions. The formation of long or relatively short poly(lactide) chains was also affected by the polymerization conditions as revealed by FT-IR analyses and differential scanning calorimetry. The thermal properties of the nanobrushes were investigated by thermal gravimetric analysis, as well.

409. Dendrimers for Dual Imaging Modalities: Combining Magnetic Resonance and Optical Fluorescent Imaging

Vladimir S. Talanov[1], Hisataka Kobayashi[1], Marcelino Bernardo[1], Moinuddin Hassan[2], Amir H. Gandjbakhche[2], Peter L. Choyke[1] and Martin W. Brechbiel[1], (1)National Cancer Institute, NIH, Bethesda, MD, (2)National Institute of Child Health and Human Development, NIH, Bethesda, MD

The advantages of using dendrimeric chelated Gd-containing contrasting agents to enhance magnetic resonance imaging (MRI) by increasing molar relaxivity have already been well documented. We now describe dendrimeric materials conjugated with chelated Gd(III) and also with fluorescent labels for dual imaging modalities, i.e., MRI and optical fluorescent imaging.

PAMAM dendrimers were first modified with the bifunctional 1B4M-DTPA chelate. Thereafter, Gd(III) was introduced and that intermediate product was labeled with near-infrared (NIR) fluorescent cyanine dye Cy5.5 via covalent attachment to primary amines of the dendrimer. Optical studies and preliminary evaluation of the materials *in vivo* will be presented.

410. Fluorescence Probing of Drug Delivery Polymers

Karen Steege, Jinzhong Wang, Kathryn E. Uhrich and Edward W. Castner, Jr., Rutgers, The State University of New Jersey, Piscataway, NJ

Amphiphilic Scorpion-like Macromolecules (AScMs) and Amphiphilic Star-like Macromolecules (ASMs) are amphiphilic polymeric materials designed for drug delivery applications by the Uhrich group at Rutgers. AScMs are comprised of a hydrophobic part with alkyl chains pendant to a central linear sugar moiety and a poly(ethylene glycol) tail. The AScMs aggregate to form micelles at very low concentrations below 1 μM. ASMs are synthesized by coupling 3, 4 or more AScMs arms to a central core in a star arrangement. These molecules encapsulate hydrophobic drug molecules in their cores via their amphiphilic nature without the necessity of aggregation to form micelles. Local solvation and microviscosity of solvatochromic probe molecules are investigated by ultrafast time-resolved fluorescence spectroscopy. By selecting probe chromophores with different hydrophobicity, different regions of the AScM and ASM are characterized, in analogy to our recent work on probing A-B-A triblock copolymers (Grant, et al., Langmuir 2005, 21(5), 1745). By measuring and comparing emission spectra, excited-state lifetimes, and rotational anisotropies for three coumarins in ASM and AScM micellar solutions, polymer solvation dynamics and microviscosities relevant to drug delivery can be better understood.

411. Conjugation of folic acid on Amphiphilic Scorpion like Macromolecules for targeting drug delivery

Jinzhong Wang, Li Tao and Kathryn Uhrich, Rutgers, The State University of New Jersey, Piscataway, NJ

Amphiphilic Scorpion-like Macromolecules (AscMs) are amphiphilic polymeric materials designed for drug delivery applications by forming micelles in aqueous solution in our group. They are comprised of a hydrophobic part with 4 alkyl chains pendant to a central linear sugar (mucic acid) moiety and a poly (ethylene glycol) tail. The new AscM we synthesized is similar but has a primary amine group at the end of poly (ethylene glycol) tail for conjugations. For synthetic part, the four-hydroxyl groups on mucic acid are acylated by lauroyl chloride. This di-acid is selectively mono-activated by N-hydroxyl succinimide and coupled to one end of poly (ethylene glycol) bis-amine. The AScMs aggregate to form micelles at very low concentrations below 1 μM. the micelle size is about 15nm, small enough to avoid rapid clearance by reticuloendothelial system (RES). Drug loading of the control AScMs with an anti-cancer drug ellipticine is as high as 30% weight percent and efficiency can reach up to 94 percent. Folic acid activated by N-hydroxyl succinimide is conjugated with the amine group on the poly (ethylene glycol) tail. The conjugation process is followed by HPLC and GPC spectroscopy. The in vitro study using A 2780 cancer cell line with ellipticin is under way.

412. Phosphorescence Probes of Mobility and Site Heterogeneity in Amorphous Biomaterials

Richard D. Ludescher, Linda Pravinata, Sonali Shirke, Thomas Nack, Kasi Sundaresan, Rashmi Tiwari, Yumin You and Kristine Lukasik, Rutgers University, New Brunswick, NJ

The mobility of amorphous biomaterials, primarily carbohydrates and proteins, modulate the stability and shelf-life of foods, feeds, and pharmaceuticals, and the viability of spores, seeds, and even whole organisms during anhydrobiosis. We have developed phosphorescence methods to monitor the molecular mobility and dynamic site heterogeneity of amorphous solid biomaterials using steady-state and time-resolved emission and intensity from xanthene and indole chromophores. Measurements of peak frequency and linewidth monitor the rate and extent of solvent relaxation in the local amorphous environment around the probes. Measurements of intensity decay kinetics, analyzed using stretched exponential decay models in which the lifetime and the stretching exponent are the physically relevant fitting parameters, provide information about the rate and distribution of non-radiative quenching due to collisional interactions between the probe and the local matrix environment. And finally, systematic variations in the decay kinetics with emission wavelength provide a sensitive and novel indicator of the extent of dynamic site heterogeneity within the amorphous solid matrixes. The specific ways in which these chromophores respond to molecular mobility within amorphous solid sugars, sugar alcohols, and globular proteins as a function of temperature over the range from about -30 to 150C will be reviewed and correlated with rates of oxygen diffusion monitored by the extent of oxygen quenching of the probe phosphorescence.

These studies provide insight into how luminescence can be used to monitor molecular mobility in amorphous solids and how this mobility controls the rate of an important degradative process (oxidation).

413. Amphiphilic Graft Copolymers for Interfacial Assembly, Encapsulation, and Controlled Release

Kurt Breitenkamp, Bryan Parrish, Rebecca Breitemkamp and **Todd Emrick**, University of Massachusetts Amherst, Amherst, MA

Conventional polymer materials, such as polyolefins and aliphatic polyesters, can be tailored with organic and polymeric functionality to broaden greatly their potential range of biomaterials applications. For example, amphiphilicity provide an oil-water interfacial activity to polymer materials, allowing an encapsulation of one phase in a matrix of the other phase. When the polymers used in such assemblies contain reactive functionality, cross-linking chemistries can then convert interfacial assemblies into capsular materials. Tailoring cross-linking chemistry and polymer functionality leads to new systems for controlled release in, for example, targeted drug delivery applications.

Spectroscopy of Biomolecules, Interfaces and Materials III

Organizer: Edward W. Castner Jr. Rutgers, The State University of New Jersey, Piscataway, NJ
Presider: Edward W. Castner Jr. Rutgers, The State University of New Jersey, Piscataway, NJ

414. Solvation Dynamics of Excess Electrons in Ionic Liquids

James F. Wishart[1], Alison M. Funston[1], Tomasz Szreder[1], Edward W. Castner Jr.[2], Hideaki Shirota[2] and Tania Fadeeva[2], (1)Brookhaven National Laboratory, Upton, NY, (2)Rutgers, The State University of New Jersey, Piscataway, NJ

Ionic liquids (ILs) have potentially important applications in nuclear fuel and waste processing, energy production, improving the efficiency and safety of industrial chemical processes, and pollution prevention. They have dramatically different properties compared to conventional molecular solvents. We have been studying how these properties influence physical processes that determine the stability and lifetimes of reactive intermediates and thereby affect the course of chemical reactions and product distribution. Measurements of excess electron solvation processes by picosecond NIR pulse-probe radiolysis at BNL's Laser-Electron Accelerator Facility (1), and of excited-state emission dynamics (Stokes shift and polarization anisotropy decay) of solvatochromic coumarin-153, show that the reorganization dynamics of ionic liquids occur on much longer timescales (nanoseconds) than in conventional polar solvents (picoseconds). This phenomenon profoundly influences the reactivity and energetics of radiolytically-generated excess electrons. Scavenging of the excess electron before it becomes fully solvated is a significant facet of the overall radiation sensitivity of ionic liquids, possibly due to less competition from slower electron solvation processes.

(1) J. F. Wishart, A. R. Cook, J. R. Miller Rev. Sci. Inst. 75, 4359-4366 (2004). DOIs for further information on fast ionic liquid radiolysis: 10.1021/jp027792z, 10.1021/jp035265p, 10.1016/j.radphyschem.2004.09.005

415. Dynamic Probing of Microviscosity and Solvation in Ionic Liquids

Tania Fadeeva[1], Alison M. Funston[2], James F. Wishart[2] and Edward W. Castner Jr.[1], (1)Rutgers, The State University of New Jersey, Piscataway, NJ, (2)Brookhaven National Laboratory, Upton, NY

Temperature dependent dynamics in several ionic liquids are investigated by time resolved fluorescence. Polarization anisotropy provides detailed information on microviscosity, while emission shifts are a means to characterize solvent reorganization dynamics. Possible origins for the observed non-exponential relaxation and non-Arrhenius temperature dependence will be discussed.

416. Dynamics in Ionic Liquids: Silyl vs. Alkyl Cation Side Groups

Hideaki Shirota, Rutgers, The State University of New Jersey, Piscataway, NJ

The ultrafast dynamics of novel ionic liquids designed for lower room temperature viscosities will be discussed. In particular, the focus will be on optical Kerr effect studies of the inter- and intra-molecular vibrations, and the diffusive relaxation. Lower viscosity liquids are obtain by substituting one silicon atom for the central carbon of a neopentyl side group on the imidazolium cation. The interplay between ultrafast dynamics, measured viscosities, and electronic structure of the molecular ions will be discussed.

417. Thz-TDS and fs-Raman Probes of Intermolecular Interactions

William T. Lotshaw[1], Dale McMorrow[1] and Matthew C. Beard[2], (1)Naval Research Lab, Washington, DC, (2)National Renewable Energy Lab, Golden, CO

Far infrared spectroscopy has experienced a revolution in capability with the development of source and detector technology based upon femtosecond near IR solid-state lasers. The benchmarking and analysis of new high precision spectra in the 30 micron-10 millimeter wavelength range can be significantly streamlined by examining their

correspondence to femtosecond coherent Raman spectra in the same frequency range (0-300 cm-1). We will discuss the potential to exploit the complementarity of these probes in studies of intermolecular coordinates and interactions in liquids and glasses.

Analytical Posters

Organizer: Anita J. Brandolini William Paterson University, Wayne, NJ

418. Isotope Effects in the Chromatographic Behavior of Hemicarceplexes

Yong Liu, Merck Research Laboratories, Rahway, NJ and Ralf Warmuth, Rutgers University, Piscataway, NJ

The chromatographic behavior of over thirty five hemicarceplexes, which differed only in the nature of the incarcerated guest, was investigated with the goal to elucidate how stereochemistry, size, shape, electrostatic potential, and dipole moment of the fully encapsulated guest molecule modulate the interactions between the hemicarceplex and the chromatographic stationary phase. Our results indicated that the chromatographic retention of a hemicarceplex is mainly controlled by the size of the encapsulated guest molecule. A linear relationship between the logarithmic retention factor and the hemicarceplex length was observed for hemicarceplexes with linear guest molecules and was independent of their polarity. Partial separation was also achieved for *p*-xylene hemicarceplexes that differed only in the extent of their guest deuteration. The largest retention time difference among such isotopomeric hemicarceplexes was observed for a mixture of *p*-xylene and d_{10}-*p*-xylene hemicarceplexes and is based on the volume isotope effect of the guest. From the retention time differences of these isotopomeric hemicarceplexes the C-H bond length alteration upon deuteration of *p*-xylene was determined and provides new insight into the origin of volume isotope effects.

419. Application of Orthogonal Signal Correction and Partial Least Square for the Simultaneous Determination of Aspirin, Caffeine and Acetaminophen based on UV Spectra

Hugh Zhang[1], Weng Li Yoon[2], Janet Mashkovich[1], Benjamin Costa[1] and John Sienkiewicz[1], (1)GlaxoSmithKline, Parsippany, NJ, (2)GlaxoSmithKline, Surrey, United Kingdom

The analysis of Aspirin, Caffeine and acetaminophen is typically carried out using High Pressure Liquid Chromatography. The actives are separated in a column and quantified by comparing the peak areas of actives to the standard peak areas. This technique involves substantial time and resource.

This work aims to demonstrate an alternative method which offers rapid measurement and greater ease of use. Synthetic sample mixtures containing levels of the three actives which were varied according to an experimental design were prepared: APAP (0 to17.45 mg/ml), Aspirin (0 to 34.92 mg/ml) and Caffeine (0 to 4.3272 mg/ml). The UV spectra of these mixtures were measured with the wavelength range scanned from 210 to 320 nm. Orthogonal Signal Correction was then applied to the spectra and a Partial Least Squares calibration was constructed. This was carried out using the SIMCA-P+ software Version 10.

The calibration yielded the following values for root mean squares errors of estimate (RMSEE): Caffeine (0.1132), APAP (0.1627) and Aspirin (0.5286). These values were comparable to the values for root mean squares errors of prediction (RMSEP): Caffeine (0.0872), APAP (0.1128) and Aspirin (0.4469). Furthermore, all the calibration and prediction models gave R2 values greater then 0.99.

In conclusion, this work has shown that a rapid method for simultaneous determination of multi-actives can be successfully developed. This method offers substantial time and resource savings particularly when applied to dissolution testing. In fact, with the appropriate instrument-software interface, it can be envisaged that real-time determination of dissolution profile can be achieved.

420. Bridging Institutions through Shared Instrumentation (NSF Award #0088392)

Rebecca DeRosa, **Garrett J. McGowan**, Michele M. Hluchy and Jean Cardinale, Alfred University, Alfred, NY

Alfred University is a residential, coeducational institution that is home to about 2300 students. The University is made up of several private sector colleges as well as the publicly endowed New York State College of Ceramics (a statutory college within the SUNY system). Four unique units are involved in this project: from the private sector the division of Chemistry, the division of Biology and the division of Environmental Studies and Geology housed in the College of Liberal Arts and Sciences; from the public sector, the School of Engineering. Goals of this project were to adapt and implement a shared laboratory between these classically non-interacting academic units, increase collaboration among the students and faculty, as well as shared used of the instrumentation acquired through the NSF:DUE:CCLI program for laboratory and research activities. Student learning outcomes as well as a few of the modules/laboratory activities developed through this grant are presented.

421. Examination of Yeast Cell Parameters Using Optical Techniques

Julio Cesar Romero, Jessenia Burges, Karen Leon, Alvaro Castellanos, Tak Cheung, Alex Flamholz and Patricia Schneider, Queensborough Community College, Bayside, NY

Optical technology is being explored as a non-invasive method to diagnose various cellular abnormalities associated with aging and cancer. The purpose of this study was to develop optical techniques to detect cell parameters in solid tissue using a He-Ne 633nm laser as a light source and budding yeast, Saccharomyces cerevisiae, as a model organism. Direct total and viable cell counts were used to monitor the yeast growth cycle. Cells were harvested during the log and death phases, and separated into density fractions by centrifuging. The top and bottom layers of packed cell volume (PCV) displayed a density variation of approximately 15 %. Cells were digitally photographed under 100X oil immersion lens and measured using Mitotic Imaging Plus 2.0 software. Mean free path, absorption, refractive index, speckle distribution, and speckle fractal dimension were determined. Data suggests that these techniques detect changes in cell morphology, and possibly physiology (active vs. dormant) with associated biochemical differences. Julio Romero, Jessenia Burgos, Karen Leon, and Alvaro Castellanos are participants in the QCC-NIH Bridges to the Baccalaureate Program (grant 1 R25 GM65096-03).

422. Simultaneous Determination of Sulforaphane and its Major Metabolites with Liquid Chromatography-Tandem Mass Spectroscopy

S. Agrawal[1], B. Winnik[2], B. Buckley[2] and T.J. Cook[1], (1)Ernest Mario School of Pharmacy, Rutgers, The State University of New Jersey, Piscataway, NJ, (2)Rutgers, The State University of New Jersey, Piscataway, NJ

Purpose: Sulforaphane (SFN) is a naturally occurring isothiocyanate present in cruciferous vegetables that has received substantial attention for cancer chemopreventive activity. In order to understand and correlate intestinal disposition of SFN to chemoprotective activity, we have carried out single pass intestinal perfusion studies with mesenteric vein cannulation. For this purpose, sensitive and specific LC-MS-MS assay was developed for simultaneous determination of SFN and its major metabolites (glutathione and N-acetyl cysteine conjugates) from perfusate and plasma samples.

Methods: After solid phase extraction with C2 cartridges, extracts were separated on Waters Symmetry RP-C8 column over a 35 min run. Mobile phase is a gradient of 10mM ammonium acetate buffer (pH 4.5) and acetonitrile with 0.1% formic acid. Analytes were detected with tandem mass spectroscopy in selected reaction monitoring in positive mode using electrospray ionization technique. SRM of glutathione, N-acetyl cystine conjugates and SFN was done at m/z of 356, 212 and 178, respectively at 30 eV collision energy.

Results: The retention times of glutathione conjugate, N-Acetyl cystine conjugate and SFN were 8.4, 11.0 and 28.2 min, respectively. This method was linear for SFN and its metabolites with correlation coefficient of >0.999 over concentration range of 20 to 1000 ng/mL. The limit of quantification was 20 ng/mL whereas mean recoveries from spiked plasma and perfusate samples were greater than 90%.

Conclusions: The developed LC-MS-MS method can be used for quantitative analysis of SFN and its major metabolites from biological samples such as plasma and intestinal perfusate.

Financial support from NCI R03 CA105465-01 (TJC).

423. Helium: Effect on Wisconsin Fast Plants

Mitesh R. Patel, John F. Kennedy Memorial High School, Iselin, NJ

Helium composes of about .0005% (5.25 ppm) of the Earth's atmosphere (Ruscher et al, 2001). It has increased in the last eleven years because of a fluctuating temperature rate in the Earth's atmosphere (Malcolm, 1994). Helium has been known to distort an animal cell's physical appearance, but the effect on plant cells is unknown. This research examined the effect of helium on Wisconsin Fast Plants. It was hypothesized that plants exposed to varying concentrations of helium would show a decrease in overall health. In this study, Wisconsin Fast Plants were exposed to varying concentrations of helium, 3.92mL and 6.1mL. The overall health of each plant was evaluated, such as height and leaf quality of each individual plant. The two experimental groups were statistically analyzed (t-test), compared each other, and to the control. Preliminary data indicated that helium decreased the overall health of a plant. As helium begins to accumulate in the Earth's atmosphere, the threat of a decreasing plant population is evident.

424. Water Quality Experiment

Rafay Abbasi, Woodbridge High School, Fords, NJ and Michael Kreisel, Woodbridge High School, Woodbridge, NJ

A previous government study of rivers and streams throughout America has shown that many bodies of water have been contaminated with small amounts of common household chemicals such as coprostanol, a fecal steroid, N-N-diethyltoluaminde, an insect repellent, and triclosan, an antimicrobial disinfectant. Some of these rivers and streams are used in our drinking water. If people were to consume even small amounts of these dangerous chemicals over a long period of time, the chemicals may have a negative effect on communities across America. We have tested the rivers and streams in our area, as well as bottled water and tap water for traces of the chemicals found in the government study. We first used a spectrophotometer to check for any impurities in the water samples. We then took any impure water samples

and extracted the impurities using a solvent. We ran this solvent through a High Pressure Liquid Chromatograph and compared the peaks with peaks from chemical samples to determine if those specific chemicals were present in the water.

425. A Pilot Study of Arsenic Speciation and Its Bioaccessibility in Rice

Yi He[1], Yan Zheng[2], Zhongqi Cheng[3] and David C. Locke[2], (1)John Jay College, City University of New York, New York, NY, (2)Queens College, City University of New York, Flushing, NY, (3)Lamont Doherty Earth Observatory of Columbia University, Palisades, NY

Arsenic is a ubiquitous, potentially toxic trace element, which occurs naturally in many chemical forms. The different forms exhibit a wide toxicity spectrum ranging from the hazardous inorganic forms through the relatively harmless organic compounds. Dietary inorganic arsenic intake from foods of terrestrial origin is of increasing concern because of its potential impact on public health even at trace levels. Arsenic speciation and bioaccessibility in rice, a staple food in many areas in the world, was studied. Arsenic species extracted from powdered raw rice were analyzed by liquid chromatographic (LC) separation combined with high resolution inductively coupled plasma mass spectrometry (HR ICP-MS) detection. In order to gain insight into arsenic bioaccessibility, extractable arsenic in cooked rice after treatment with synthetic gastric fluid and small intestinal fluid incubation was evaluated. DMA and As(III) were detected as the major extractable species. However, we are yet to confirm the nature of the As(III) specie because As(III)-thiol complex can dissociate to inorganic arsenite at neutral and slightly basic chromatographic separation condition (Zhang W.H., et.al. Anal. Chem., 2003, 75, 7030), which was used in this study.

426. Characterization of Unsaturated Perfluoro-Carboxylic Acids

Shirley Fischer-Drowos[1], Linda Betz[2], Justin Miscavige[1], **Nisreen Madhoun**[1] and Joe Di Bussolo[3], (1)Widener University, Chester, PA, (2)Widener University and West Chester University, PA, (3)Cohesive Technologies, Franklin, MA

There has been considerable interest in attaining the physical characteristics of fluorinated carboxylic acids. Currently the data available on these species is sparse. However, an increased interest in these materials has generated a need for physical property data such as melting point and solubility. Melting point data was ascertained on traditional melting point apparatus. Solubility data was attained utilizing a LC/MS/MS system with a heated nebulizer.

Computers in Chemistry

Organizer: Wendy D. Cornell Merck & Co., Rahway, NJ

427. Relative Strengths of Se-N,O Interactions: Implications for GPx-like Activity

Craig A. Bayse, Old Dominion University, Norfolk, VA

Natural bond order (NBO) studies of model compounds of glutathione peroxidase and its mimics are used to examine the relative strengths of nitrogen and oxygen donor groups. Nitrogens are generally better donors, but depend upon the functionality. The carbonyl of acetamide is shown to be preferred to the amide N, suggesting that the glutamine of the GPX catalytic triad may influence activity through the carbonyl oxygen.

428. Advances in Conformational Sampling and Free Energy Calculations via Adiabatic Dynamics

Jerry B. Abrams, Lula Rosso and Mark E. Tuckerman, New York University, New York, NY

Conformational sampling of peptide backbone dihedrals has been studied using the recently introduced adiabatic free-energy dynamics (AFED) approach, introduced by Rosso et al. (J. Chem. Phys. 2002, 116, 4389), in which variable transformations are combined with an imposed adiabatic separation of time scales in the configurational space. The ramachandran surfaces for the alanine di- and tripeptides in gas phase and solution have been mapped out with an order of magnitude of greater efficiency using the AFED approach than using the popular umbrella sampling method. Further advances in adiabatic dynamics has led to a novel molecular dynamics method for calculating the free energies associated with transformations of the system potentials between thermodynamic states. An extension of the AFED method, this new approach introduces an additional dynamical degree of freedom, λ, that parameterizes the switching functions in the potential. In addition to allowing λ to evolve, we have developed a novel scheme using switching funtions that lead to a barrier in free energy space combined with adiabatic separation between λ and the physical system. This new scheme was used to study the chemical potential of a Lennard-Jones liquid. Here, the method was benchmarked against the blue moon ensemble approach and was shown to have a five fold increase in efficiency.

429. Combined use of local and global models for improving the accuracy of in silico ADME/Tox prediction

Michelle D'Souza, Gregory Banik, Yann Bidault, Jeff Oakes, Kevin Scully and Deborah Kernan, Bio-Rad Laboratories, Phila, PA

Improvements in model availability and performance have led to more widespread acceptance of in silico modeling of ADME/Tox properties during the drug candidate evaluation process. This paper demonstrates how drug discovery professionals can improve the accuracy of their in silico investigations by conducting predictions for multiple properties simultaneously on either one or many candidate structures. The paper includes a review of in silico tools for global models, local models, and consensus models that combine local and global models.

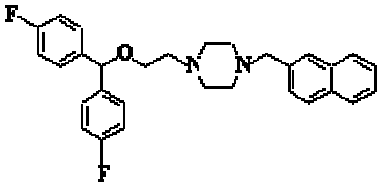
Computers in Chemistry Posters

Organizer: Wendy D. Cornell Merck & Co., Rahway, NJ
Organizer: Anita J. Brandolini William Paterson University, Wayne, NJ

430. Conformational Analysis of Piperazine and Piperidine analogs of GBR12909: Effect of Force Field and Solvent

Deepangi Pandit, William Roosma, Milind Misra, Kathleen M. Gilbert, William Skawinski and Carol A. Venanzi, New Jersey Institute of Technology, Newark, NJ

GBR analogs are an important class of dopamine reuptake inhibitor that appears to be useful in the treatment of cocaine abuse. As the first step in the modeling of a pharmacophore for binding to the dopamine transporter, we carried out conformational analysis to locate local minima on the potential energy surface of the molecule in vacuum phase and implicit solvent using the Tripos and MMFF94 force fields. The sensitivity of the conformational potential energy minima to solvent and force field was explored.



431. Computation of Through-Space NMR Shielding Effects in Peptides

Ned H. Martin[1], Kristin L Main[1], Amy K Pyles[1] and David M. Loveless[2], (1)UNCW, Wilmington, NC, (2)Duke University, Durham, NC

We have used GIAO within Gaussian03 to calculate NMR shielding effects of simple test molecules representing functional groups common to peptides. Diatomic hydrogen was employed as a probe molecule. Through-space shielding increments were computed at various points above the test molecules by subtracting the computed isotropic shielding value of the proximal hydrogen at that point from the computed isotropic shielding value of hydrogen in diatomic hydrogen alone. These shielding increments were plotted vs. Cartesian coordinates relative to the test molecule to give the NMR shielding surface. Previous work in our group has shown that the most accurate NMR shielding results are obtained when a molecule having a covalent bond to hydrogen is used as a probe. In this poster we present the results of our study.

432. Rebuilding the Computer-Instrument Interface of an ESR Spectrometer

Kathleen Hummel and Dr. Donald J. Hirsh, The College of New Jersey, Ewing, NJ

Modern Electron Spin Resonance (ESR) spectrometers operate on the same principles as those created thirty years ago. The difference lies primarily in the capabilities of the computer controlling the instrument. This project involved rebuilding the instrument-computer interface of a thirty-year-old ESR spectrometer, the Bruker ER 200D. The instrument required a new computer. The former software written to control the instrument and record the data was extensively rewritten in the newest version of LabView (National Instruments). The LabView software allows the user to pictorially observe the procedure and progress of the application. This software was designed to aid the integration of a computer and instrument, by configuring the hardware and software of a new computer interface. Besides the obvious advantages of the improved performance of modern software and hardware, upgrading allows future replacement of parts to occur with greater ease. The time and money spent rebuilding or creating a computer-instrument interface is justified if the existing instrument is sound and serviceable and if the cost of a new instrument is high.

433. Vibrational Circular Dichroism: Absolute Configuration Determination

Linda M. Phillips, Jack Z. Gougoutas, Stephen K. Gozo and Michael Galella, Bristol-Myers Squibb, Princeton, NJ

No abstract available.

434. Fuzzy relational clustering of molecular conformations using novel features based on DNA base-pair step parameters

Milind Misra[1], Deepa Pai[1], Rohan Woodley[1], Amit Banerjee[1], Rajesh N. Davé[1], Liang-Yu Shih[1], Xiang-Jun Lu[2], A. R. Srinivasan, Ph.D.[2], Wilma K. Olson[2] and Carol A. Venanzi[1], (1)New Jersey Institute of Technology, Newark, NJ, (2)Rutgers University, Piscataway, NJ

Six rigid-body parameters (Tilt, Roll, Twist, Shift, Slide, Rise) are commonly used to describe the relative orientation and positioning of any two base pairs in a nucleic acid structure. The present work generalizes the algorithms of the 3DNA software package (*Nucleic Acids Res.*, **31**, 5108-21, 2001) to describe the relative orientation of *any* two planes in a molecule--for example, planes which contain important pharmacophore elements. Fuzzy relational clustering is used to classify molecular conformations using the six base-pair step parameters as features. This approach is applied to an analog of GBR 12909, a flexible inhibitor of the dopamine transporter potentially useful in the treatment of cocaine abuse. The results of this approach provide representative conformers to be used as templates for future 3D-QSAR (CoMFA) analysis.

435. Comparative Study of Docking Programs GLIDE and GOLD for Virtual Screening

Zhiyong Zhou[1], Anthony K. Felts[2], Matt Repasky[3], Ronald M. Levy[2] and Richard A. Friesner[1], (1)Columbia University, New York, NY, (2)Rutgers University, Piscataway, NJ, (3)Schrodinger LLC, New York, NY

Computational chemistry has been playing a more and more important role in drug discovery. In particular, computational high-throughput docking has become a powerful tool for screening and identifying novel lead compounds. Two molecular docking programs widely used by the pharmaceutical industry are Glide and GOLD. The sampling methods used by these programs are significantly different. Glide employs a deterministic algorithm to search for the correct binding conformation of the ligand; GOLD utilizes a stochastic genetic algorithm for the conformational search. In this work, we have carried out a comparison to evaluate the relative performance of Glide and GOLD using 3 scoring functions with 21 receptor targets from a diverse set of 16 protein families. To make the library screens as realistic as possible, the simulated screening deck consists of 1000 drug-like decoy ligands that have been selected to be representative of a compound collection found at a pharmaceutical company. The results are presented for the latest releases of Glide (version 3.5) and GOLD (version 2.2). All screenings were performed using 2 different performance settings for Glide and 4 different settings for GOLD. Both Glide and GOLD are able to predict the protein-ligand complex conformation with reasonable accuracy and speed. A detailed comparison demonstrates that Glide appears to outperform GOLD in accuracy and speed for almost all cases studied here.

436. Modeling of triclosan analogs for enoyl reductase inhibition

Jeffrey P. Wolbach, Jonilyn Longenecker and Paul Schettler, Juniata College, Huntingdon, PA

Triclosan is an effective antibacterial agent, acting by breaking the bacterial synthase cycle through inhibition of enoyl reductase. However, recent wide-spread use of triclosan has raised concerns about the possibility of development of triclosan-resistant strains of bacteria. In this work, we have used molecular dynamics to study the binding of 20 triclosan analogs to E. coli enoyl reductase (1QSG). Free energies of binding were determined by modifying the triclosan molecule in the X-ray crystal structure of 1QSG to form each analog and by using a solvent-cap MM/PBSA procedure. Automated docking studies were also conducted on each analog and additional MD simulations were run on the seven analogs with suggested alternative, lower-energy poses than the "triclosan-like" configuration. Comparison of experimental binding energies for a subset of the analogs is used to verify the accuracy of the method. Results of this study will be used to suggest alternative anti-bacterial agents to triclosan.

437. Investigating targets of antibacterial cysteine protease inhibitors

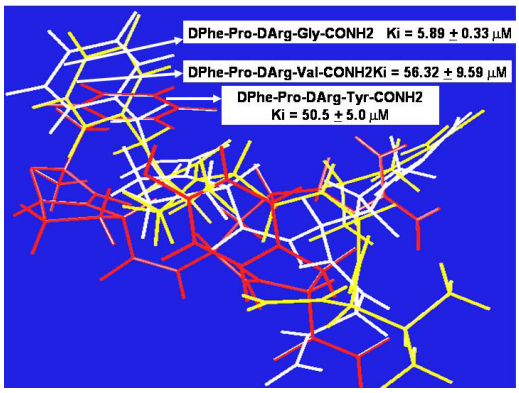
Jeffrey P. Wolbach and Leslie Vogt, Juniata College, Huntingdon, PA

Streptococcal pyrogenic exotoxin B (SpeB), a highly conserved cysteine protease secreted by Streptococcus pyogenes, is inhibited by several peptidic compounds. Some, but not all, of these compounds also exhibit anti-bacterial activity against S. pyogenes, suggesting that SpeB is not the only target of inhibition. Recently, a second cysteine protease of Streptococcus has been identified. This cysteine protease displays remarkable selectivity for cleavage of IgG, and is known to be inhibited by a specific tripeptide that also inhibits SpeB. Molecular dynamics simulations have been performed to investigate the mode of inhibition, as well as to investigate potential inhibitory capacity of other ligands.

438. Molecular docking and analysis of conformation adopted by tetrapeptide inhibitors into active site of thrombin

Cristina C. Clement and Manfred Philipp, Lehman College, City University of New York (CUNY), NYC, NY

In silico screening of reversible tetrapeptides inhibitors [sequence space: D-Phe-Pro-D-Arg-P1'-CONH2] for thrombin was performed by docking into active site of target 1ABJ.pdb candidate compounds using the software “SCULPT”–from MDL. The molecular mechanics (MM) force–field provided by the same software was used to assess the structural fitness of the ligand into each of the S1', S1, S2 and S3 subpockets of thrombin (based on van der Waals and electrostatics interactions). A structure-activity relationship (SAR) for tetrapetides was performed using in vitro standard assays for thrombin inhibition. The analysis of the structural models together with the Ki obtained experimentally suggests that the tetrapeptides differing in one single amino acid at P1' position are adopting different conformations into active site of thrombin. These different conformations might be related with significant differences in their inhibitory potential.



Electronic Structure in Chemistry I

Organizer: Kieron Burke Rutgers University, Piscataway, NJ
Organizer: Karsten Krogh-Jespersen Rutgers University, Piscataway, NJ
Presider: Kieron Burke Rutgers University, Piscataway, NJ

439. Keynote Address: The H-bond Network in Water

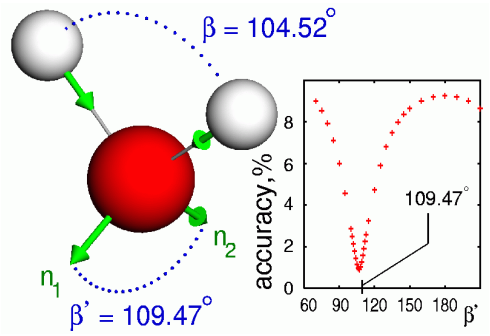
Roberto Car, Princeton University, Princeton, NJ

Hydrogen bonds are at the origin of many special properties of water and ice. In this talk I will show how simple theoretical models and extensive ab-initio molecular dynamics simulations give insight on the structure and dynamics of the H-bond network. I will focus, in particular, on the dielectric properties that make water a very special solvent, and on the molecular origin of the hydrophobic effect, which is crucial to biophysics.

440. MAME water model: Coulomb, induction and dispersion interactions in water dimer

Eugene V. Tsiper, George Mason University and Naval Research Lab, Washington, DC

The Minimal Atomic Multipole Expansion (MAME) substitutes the ab-initio or DFT density with the *minimal set* of atomic multipoles, which eliminates redundancies and reproduces molecular electrostatic potential everywhere beyond the molecular volume. We apply MAME ideas to construct a new polarizable water model, which appears to be transparent, intuitive and accurate at the same time. Hydrogen bonding, electrostatic, induction and dispersion interactions in the water dimer are reproduced by only three multipoles μ(H), μ(O) and θ(O) and two polarizabilities α(O) and α(H), which characterize a single water molecule and can be deduced either from single-molecule data or from DFT MAME calculation. The model agrees with the two best water pair potentials, VRT(ASP-W)III and SAPT-5s, and compares favorably to popular water models, such as TIP4P-FQ.



441. Ab Initio MD studies of hydrogen bonding in water and peptidic fragments

Glenn Martyna, IBM Research, Yorktown Heights, NY

Liquid water is a ubiquitous solvent whose importance cannot be underestimated. However, much remains unknown about the radial and angular structure of this hydrogen bonding liquid both at room temperature and physiological temperatures. Therefore, large scale ab inito MD simulations have been performed to examine neat water and a novel analysis of the results yields insight into the hydrogen bonding patterns and changes in these patterns induced by temperature. N-methylacetamide or NMA, CH3-CO-NH-CH3,is of interest as a model of the peptide linkage. Its behavior at points along the cis-trans isomerization pathway contributes to our understanding of the nonprolyl peptide C(O)-N bond, a ubiquitous structural proteinaceous element that can be involved in the rate-limiting steps of protein restructuring. Measurement of the radial and angular dependence of the solvation shell structure of NMA(aq) is helpful in elucidating the effect of water solvent on protein function and is now feasible experimentally, making theoretical structural studies particularly relevant. Increasingly powerful computing platforms and algorithms, now, permit, for the first time, an ``ab initio'' computational study of NMA in vacuum and in explicit water solvent at finite temperature to address these issues. A pictorial description of the amide group emerges that enhances our understanding of chemical bonding, and a detailed analysis of NMA(aq) provides structural data for comparison to anticipated new experiments.

442. Efficient evaluation of nonlocal pseudopotentials via Euler exponential spline interpolation

Hee-Seung Lee[1], Mark E. Tuckerman[1] and Glenn Martyna[2], (1)New York University, New York, NY, (2)IBM Research, Yorktown Heights, NY

An Euler exponential spline (EES) based formalism is employed to derive new expressions for the electron-atom nonlocal pseudopotential interaction (NL) in electronic structure calculations performed using a plane wave basis set that can be computed more rapidly than standard techniques. Two methods, one that is evaluated by switching between real and reciprocal space via Fast Fourier Transforms, and another that is evaluated completely in real space, are described. The reciprocal-space or g-space based technique, NLEES-G, scales as NMlogM ~ N^2logN, where N is the number of electronic orbitals and M is the number of plane waves. The real-space based technique, NLEES-R, scales as N^2. The latter can potentially be used within a maximally spatially localized orbital method to yield linear scaling while the former could be employed within a maximally delocalized orbital method to yield NlogN scaling. This behavior is to be contrasted than standard techniques which scale as N^3. The two new approaches are validated on several examples, including solid silicon and liquid water and demonstrated to be improvements on other reduced order nonlocal techniques. Indeed, the new methods have low overhead and become more efficient than the standard technique for ≥ 20 atoms. Both NLEES methods are shown to work stably and efficiently within the Car-Parrinello *ab initio* molecular dynamics framework due to the existence of p-2 continuous derivatives of a p^{th} order spline.

443. Spatial and coupling constant scaling in time dependent current density functional theory

Maxime Dion and Kieron Burke, Rutgers University, Piscataway, NJ

Time dependent density functional theory (TDDFT) is widely used to calculate excitation energies of molecules. It is however not amenable to local-type approximate exchange-correlation functionals which are commonly used in density functional theory. Using the *current* instead of the density as the basic variable (time dependent current density functional theory (TDCDFT)) remedies this problem. We derive scaling relations for TDCDFT similar to relations previously given for TDDFT: we obtain the behavior of the exchange-correlation potential and kernel under simultaneous scaling of space and the electron-electron coupling constant. This can be used to verify that approximate functionals satisfy the scaling or to obtain the exchange-correlation potential at various densities by simply knowing the potential as a function of the coupling constant. The scaling relation can also give the *ground-state* exchange-correlation energy through the adiabatic connection formula.

444. Density-functional-based methods for calculations of intermolecular forces

Krzysztof Szalewicz[1], Alston J. Misquitta[1], Rafal Podeszwa[1] and Bogumil Jeziorski[2], (1)University of Delaware, Newark, DE, (2)University of Warsaw, Warsaw, Poland

Ab initio wave-function(WF)-based methods can predict intermolecular force fields very accurately for monomers containing a few atoms, but applications to systems with tens of atoma are too time consuming. The density-functional theory (DFT) methods would be fast enough, but are currently not able to predict the very important dispersion component of the force field. We have developed a method based on a DFT description of monomers but computing intermolecular forces using expressions beyond DFT, originating from symmetry-adapted perturbation theory (SAPT). To obtain accurate predictions, it was necessary to fix the wrong long-range behavior of DFT monomer densities by applying an asymptotic correction to the exchange-correlation potential. The dispersion energies are computed from coupled Kohn-Sham frequency-dependent susceptibility functions. SAPT(DFT) calculations require only a small fraction of computer resources used by the regular SAPT and converge much faster in the size of the basis sets. Calculations for model compounds have shown that the new method reproduces all components of the intermolecular force, including dispersion, extremely well. Moreover, although initially SAPT(DFT) was expected to be a method providing medium quality results for very large molecules, it turned out that in some cases the accuracy of SAPT(DFT) surpasses that which can be reached with the currently programmed WF-based SAPT and reasonable size basis sets. The method is able to handle interactions of molecules containing 20 and more atoms. It has already been applied to several fairly large system like the benzen dimer or the RDX dimer (42 atoms). Examples of applications will be presented.

445. Undoing static correlation: long-range charge transfer in time-dependent density functional theory

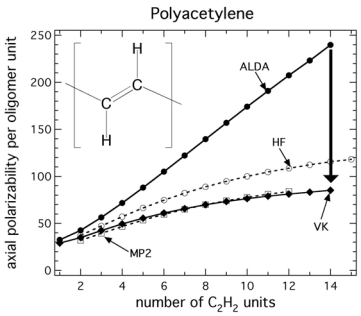
Neepa T. Maitra, Hunter College of CUNY, New York, NY

Long-range charge transfer excited states are notoriously badly underestimated in time-dependent density functional theory (TDDFT). This can have serious consequences. For example, as shown by Dreuw and Head-Gordon, charge-transfer quenching of excited-state fluorescence in light-harvesting bacteria is predicted, contrary to observation. We study how exact TDDFT captures charge transfer between two widely-separated open-shell species in a molecule: in particular the role of the step in the ground-state potential and the severe frequency-dependence in the exchange-correlation kernel. An expression for the latter is derived that becomes exact in the limit that the charge-transfer excitations are well-separated from other excitations. The exchange-correlation kernel has the task of undoing the static correlation in the ground state that is introduced by the step, in order to accurately recover the physical charge-transfer states.

446. Time-dependent current-density-functional theory: excitation and response properties of polymers

Meta van Faassen[1], Robert van Leeuwen[1], Kieron Burke[2] and Paul L. de Boeij[1], (1)University of Groningen, Groningen, Netherlands, (2)Rutgers University, Piscataway, NJ

Conjugated polymers are interesting for their large nonlinear optical properties. Time-dependent density-functional theory is a very versatile method to calculate such properties of large systems. However, even the linear axial polarizability of conjugated oligomers is greatly overestimated when using the standard adiabatic local density approximation (ALDA). This approximation, but also more advanced approximations, is unable to describe the highly nonlocal exchange-correlation found in these systems. We use time-dependent current-density-functional theory, in which we describe this ultranonlocal exchange-correlation within a local current description. The static axial polarizability of polyacetylene (see figure), and similar polymeric systems, obtained using the Vignale-Kohn (VK) [G. Vignale and W. Kohn, Phys.Rev.Lett. 77, 2037 (1996)] current-functional is in excellent agreement with MP2 results. For these systems and a set of benchmark molecules we obtained the excitation energies and oscillator strengths, and from these we explain the large reduction of the static polarizability by the VK-functional.



Enabling Technologies in the Analytical Laboratory

Organizer: Bruce A. Weber Johnson & Johnson Pharmaceutical Research & Development, LLC, Raritan, NJ
Presider: Adam M. Fermier Johnson & Johnson Pharmaceutical Research & Development, LLC, Raritan, NJ

447. Introduction

Adam M. Fermier, Johnson & Johnson Pharmaceutical Research & Development, LLC, Raritan, NJ

Streamlining the analytical laboratory processes is becoming increasingly important as corporations move towards high throughput screening and processing. This session is designed to cover the entire analytical workflow management including sample preparation, analysis and reporting. The speakers will provide real-world solutions to each of these areas to give the attendees a good overview of this process.

448. General Principles & Challenges in Automated Sample Preparation for Pharmaceutical Analysis (or: Robots Save the World!)

Mark J. Dryfoos, Novartis Pharmaceuticals Corp., East Hanover, NJ

Robotic sample preparation has been around in the pharmaceutical laboratory for more than 20 years. After all of the promise of the 1980's and the hype of the 1990's, are we now entering the POST-ROBOTICS Era? Has laboratory automation lived up to its promise? In the emerging world of PAT (Process Analytical Technology), will the very concept of putting “tablets in blenders” become obsolete? Just what is the future role of automation in the Pharmaceutical Quality Control and Analytical R&D Lab?

In this presentation we will examine the fundamental question: What are we trying to automate and why? We will survey common laboratory tasks to identify those operations that are amenable to automation, with an emphasis on the primacy of WORKFLOW in making this evaluation. We will briefly review developments in lab automation over the past quarter-century, tracing its evolution from the custom robotic systems of the early 80's, through the modular systems of the late 80's and early 90's, to the current workstation approach of the last decade.

While our focus will be on sample preparation of solid dosage forms for assay, other opportunities to apply automation will be considered. The primary tablet-extraction techniques will be discussed, and we will address the differences between automated and manual methods. We will explore various approaches to overall method design and consider some of the practical challenges faced when automating methods, with the ultimate goal of assuring reliability while providing adequate throughput.

449. New Technologies for the Sample Preparation of Organic Compounds

Ronald E. Majors, Agilent Technologies, Inc., Wilmington, DE

Sample preparation is one of the more time-consuming, labor-intensive, and error-prone steps in the analytical cycle. Newer techniques that are faster, safer, easier to perform, provide better recovery and reproducibility, are more easily automated, and use smaller amounts of sample and organic solvent are receiving increased attention.

For liquid samples, solid-phase extraction (SPE) has received more attention with development of: 1) miniaturized formats (i.e. low bed mass cartridges and disks, 96-well SPE plates, and SPE micropipette tips); 2) new highly selective, application-specific, and water-wettable SPE phases; 3) new techniques such as stir-bar sorptive extraction and solid-phase microextraction. Increased application of liquid-liquid extraction techniques on a microscale using supported membranes, supported inert packed columns and in-tube microextraction systems has given a “rebirth” to this age-old method. Even simple systems using protein precipitation followed by filtration using 96-well filter beds can help the high-speed purification of biological fluids.

For solid samples, technologies such as microwave assisted-, pressurized-fluid/accelerated solvent-, and supercritical fluid-extraction are used as direct replacement techniques for classical extraction techniques. Even Soxhlet extraction,

over 100 years old, has seen significant improvements. A little known technique "matrix solid-phase dispersion (MSPD)" has potential as a solvent-less extraction technique for solids such as tissue and food matrices.

This lecture will focus on the advantages, disadvantages and applications of some of these newer sample preparation technologies with particular reference to the needs of automation and mass spectrometry. I will speculate on why some of these techniques have not yet received the acceptance that was predicted.

450. New Column Technologies - Looking beyond C18

Matthew Przybyciel, ES Industries, West Berlin, NJ

Reversed-phase HPLC is one of the most utilized forms of chromatography. The C8 and C18 stationary phases are the most widely used for reversed-phase HPLC. However, analysts occasionally encounter difficult separations for which selectivity, ruggedness, or reproducibility are not obtained easily using traditional C8 and C18 phases. These separations might require the use of selective or novel stationary phases such as pentafluorophenyl, phenyl hexyl, C30, polar-embedded and alkyl fluoro bonded phases. These types of stationary phases separate compounds based upon selective stationary phase interactions such as steric recognition, charge transfer or pi-pi interactions. These types of interactions have lead to the development of many new unique stationary phase technologies. In this presentation the unique capabilities for novel stationary phases will be shown in several applications. These applications will be show how unique novel phases can provide alternative and complementary separations for many analyses performed on C18 columns. Information will also be provided to show that novel phases offer the chromatographer the flexibility to use simpler mobile phases, thereby avoiding ion-pair reagents, exotic buffer systems, extreme pH conditions, and complex mobile preparations. A discussion on the mechanisms of interaction for many novel phases will also be presented. The separations discussed in this presentation rely on a unique stationary phase-solute interaction. Many of the separations could not be accomplished on C18 columns.

451. Small Particle Technologies

Luis A. Colon, University at Buffalo, Buffalo, NY

Text Not Available

452. Ultra-High Pressure Liquid Chromatography and Pharmaceutical R&D Laboratories

Kelly Swinney, Johnson & Johnson Pharmaceutical Research & Development LLC, Raritan, NJ and Adam M. Fermier, Johnson & Johnson Pharmaceutical Research & Development, LLC, Raritan, NJ

The inability of the typical LC system to sufficiently separate chemically similar compounds is often encountered during drug development. With only subtle differences between a drug substance and its possible impurities/degradants, separation is often very difficult exacerbating such tasks as impurity profiling and structure elucidation. Recently, short columns (L < 5 cm) packed with <2 um material have been introduced and shown to have increased peak capacity per unit length relative to columns packed with 5 or 3 um material. Therefore, it would be advantageous to work with longer columns packed with smaller particles to further increase the peak capacity alleviate some of the difficulties encountered in drug development. For this to be possible, a LC system capable of pressures > 6000 psi is required. In 2004, Waters released the UPLCTM (P = 15,000 psi). However before the availability of a commercial system and realizing this need, a pressure conversion kit was designed and developed at PRD for standard LC systems to increase the system's pressure capabilities upto 20,000 psi. The design and the development considerations of the pressure conversion kit will be discussed and the separation performance of the system demonstrated with test mixtures and drug research samples. Experimental results obtained on the Waters UPLCTM will also be presented.

453. A Software Automation Strategy for the Analytical Laboratory

Eric Milgram, Advanced Chemistry Development, Inc. (ACD/Labs), Toronto, ON, Canada

Analytical laboratories have made great strides towards becoming more productive. For example, just 10 years ago, chromatographic runtimes of 1 hour or more were very common. Currently, cycle times (time between successive sample analyses) of 30 seconds or less are relatively common for LC/MS/MS methods. Because of the high-cost of capital equipment, the goal of laboratory personnel should be to achieve duty cycles (i.e. fraction of time spent performing useful analysis relative to total analysis time) that are as close to 100% as possible. Obviously, as the duty cycle improves, the number of samples analyzed per unit time will increase. An increased sample load necessitates a greater reliance on software automation for processing and reviewing the data, otherwise the rate at which data can be collected would exceed an analyst's ability to process the data and make use of it. The goal of any automated data processing methodology should be to minimize the amount of data that a human must review while simultaneously maximizing one's confidence in the automated process. The selection of an appropriate threshold can be subjective, but the interpretation of whether data passed or failed based on the threshold should never be subjective. Most laboratory personnel use a combination of commercial and in-house developed software as part of their software automation strategy. The aim of this presentation is to review some of the challenges and some strategies for meeting them.

Environmental/Green Chemistry Posters

Organizer: Anita J. Brandolini William Paterson University, Wayne, NJ
Presider: Wen-Chung Shieh Novartis Pharmaceuticals, East Hanover, NJ
Presider: Sanjay V. Malhotra New Jersey Institute of Technology, Newark, NJ

454. Using Mössbauer Spectroscopy to Study the Effects of Salinity on the Speciation of Tributyl- and Triphenyltins in Anacostia River Anaerobic Sediments

Xueqing Song, Alejandra Zapata and George Eng, University of the District of Columbia, Washington, DC

Tributyltins (TBTs) and triphenyltins (TPTs) can leach into various water systems from their use as antifouling paints. While these compounds have been found to inhibit barnacle formation, they are also known to be toxic to non-targeted species such as fish and oysters. To complete earlier studies the species of triorganotins in sediments as a function of salinity was initiated. To this end, anaerobic sediments obtained from five different sites in the Anacostia River were spiked with either tributyl- or triphenyltins at salinity conditions of 0, 20, 40 and 60 percent. Results from the Mössbauer studies indicated that changes in salinity did not affect the speciation of the compounds. With the exception of triphenyltin acetate, the Mössbauer results of all the compounds from the different sites were within experimental error, indicating that the speciation of the compounds is independent of the characteristics of the sediments as well. Results showed that tributyltin chloride, bis-tributyltin oxide and tributyltin acetate were converted to the tributyltin hydroxide in anaerobic sediments. For the triphenyltin compounds, triphenyltin hydroxide (TPTOH) remained unchanged while triphenyltin chloride was converted to TPTOH in all sites. Triphenyltin acetate, on the other hand, was converted to TPTOH in sites IV and V sediments. However, in sites I, II and III it was converted to the same but unidentifiable species.

455. Identification and quantitative determination of Polychlorinated Biphenyls in the Urban New York City areas

Queen Golder, Manhattan Center for Science and Mathematics, Bronx, NY

Polychlorinated biphenyls, PCBs, consist of 209 congeners that is, a class of 209 different molecules based on the biphenyl structure with various arrangements and degrees of chlorination. PCBs are composed of carbon, hydrogen, and chlorine. These compounds have a harmful effect on our environment and to living organisms because they have been shown to be carcinogenic.[i] Some of the sources of PCBs include storm water and the yellow paint on streets and major highways. I plan to measure the amounts of PCBs in storm water and major streets in New York City. I have decided to focus on New York City to collect my data because the city's harbors are already polluted with PCBs. I hypothesize that there will be a significant amount of polychlorinated biphenyls in a New York City apartment as well as the New York City streets. To conduct this study I will need to determine the concentration of PCBs within each site I am going to test. Gas chromatography-electron capture detector (GC-ECD) and gas chromatography-mass spectroscopy (GC-MS) are two instruments that I will use to determine the levels of PCBs in each area. All of the GC-ECD results and the GC-MS results will be plotted versus a calibration curve on graphs to show the amount of PCBs extracted from the two different areas. These results will then be compared and the graphs will help us determine if the amount of PCBs in the home will be greater than the amount of PCBs on the street.

456. The Effect of Nitrogen Fixing Bacteria on Light Absorption in Plants

Arvind Srinivasan, John F Kennedy Memorial High School, Iselin, NJ

Light absorption and an effective growing medium are certain necessities for good plant growth. Soil and hydroponics are two different methods used to grow plants. Nitrogen Fixing Bacteria serve as an important variable between the two growing mediums. Although much research has been conducted in this area, the efficiency of the plants with relation to light absorption has not yet been tested. For this research purpose, leguminous pea plants were studied as they cooperate best with nitrogen fixing bacteria to absorb nitrogenase which helps plant growth. The two primary groups were those that had a growing medium of soil and hydroponics respectively. However, another group was added which had a growing medium of a mixture of soil and sulfur solution to increase N2 fixing activity. It was hypothesized that the group with no nitrogen fixing bacteria (hydroponics) will have the best light absorption while the group with plants that grow in the soil will have the worst. This is because the hydroponics group, without the N2 fixing bacteria do not lose proteins and certain other minerals whereas the plants in the group with soil as the growing medium do lose the proteins. Twelve plants in each group were grown and their mass was measured after 2 weeks. The average for each group was taken and the t test was used to calculate the relation between the two groups. Thus, through this experiment, the productiveness of the different growing mediums of plants was observed and the best medium was found

457. Pb and Cd based recrystallized phases on calcite surfaces

Douglas B. Hausner[1], Daniel R. Strongin[1] and Richard J. Reeder[2], (1)Temple University, Philadelphia, PA, (2)State University of New York, Stony Brook, Stony Brook, NY

The adsorption and retention of divalent metals by calcite surfaces is of significant environmental relevance due to their prevalence and documented affinity for divalent metals. Analysis of divalent Pb and Cd and their interaction with the {10$\bar{1}$4} cleavage planes of calcite was carried out with X-ray photoelectron spectroscopy (XPS) and atomic force microscopy

(AFM) after exposure to divalent metal-bearing solutions in the 0.1-100μM concentration range for times ranging from 1 - 24 hr. The majority of the divalent metal was postulated to exist in a recrystallized phase, and a relatively small fraction of the Cd and Pb was associated with an incorporated and/or sorbed state. AFM results showed that the exposure of calcite to a 1 μM Pb2+ solution resulted in ellipsoidal surface growths that were attributed to the nucleation of a PbCO3 bulk phase. In comparison AFM results for Cd showed flat growth features forming on the calcite surface, these features were attributed to a (Ca,Cd)CO3 solid solution.

458. Mechanistic Aspects of Pyrite Oxidation in an Oxidizing Gaseous Environment: an In Situ HATR-IR Isotope Study

Courtney R. Usher[1], Daniel R. Strongin[1] and Martin A. A. Schoonen[2], (1)Temple University, Philadelphia, PA, (2)State University of New York at Stony Brook, Stony Brook, NY

The reaction of metal disulfides with water and oxygen has been shown to cause enormous damage to the environment in coal mining regions. The reactions of FeS_2 (pyrite) and NiS_2 with gaseous H_2O, O_2, and H_2O/O_2 were investigated using attenuated total reflection Fourier-transform infrared spectroscopy (ATR-FTIR) to further understanding of the mechanism by which disulfides are oxidized. Reaction of pyrite in gaseous H_2O led primarily to the formation of iron hydroxide on pyrite. Exposure of the pyrite to gaseous O2 after exposure to H_2O vapor led to the formation of sulfur oxyanions that included SO_4^{2-}. If, however, pyrite was exposed to gaseous O_2 prior to pure H_2O vapor (no O_2 reactant), both SO_4^{2-} and iron oxyhydroxide became significant products. Results derived from experiments that exposed pyrite to gaseous mixtures of H_2O and O2 led to the conclusion that H_2O and O_2 exhibit a competitive adsorption on pyrite, with H_2O blocking surface sites for O_2 adsorption. Based on results of isotopic labeling experiments, the extent of oxygen incorporation from either the H_2O and O_2 component into the surface-bound sulfur oxyanion product appears to be a strong function of the relative concentration ratio of the reactant H_2O and O_2. The reaction of NiS_2 with gaseous H_2O or O_2 alone yielded little change to the surface; however, when the surface was exposed simultaneously to water vapor and oxygen gas, sulfate species were formed. Results show H_2O and O_2 do not seem to compete for reactive sites on the NiS_2 surface.

459. Synthesis of Beta-Amino alcohols in Pyridinium-based Ionic Liquid

Sanjay V. Malhotra and Richard P. Andal, New Jersey Institute of Technology, Newark, NJ

Beta-Amino alcohols are versatile intermediates in natural product synthesis. Also, they are used as Beta-blockers and as chiral ligands in asymmetric synthesis. One of the synthetic procedures for the preparation of Beta-amino alcohols involves the ring opening of epoxides with amines, commonly carried out with excess of amine and in organic solvents. Ionic liquids are emerging as viable, environmentally friendly alternative to volatile organic solvents. Interest in these solvents is largely due to their unique characteristics such as non-volatility, non-flammability, high thermal stability and tunable properties such as polarity, hydrophobicity, miscibility etc. In the present study we have synthesized Beta-amino alcohols by cleavage of epoxides with amines in Ethylpyridinium trifluoroacetate a pyridinium-based ionic liquids. A simple protocol has been developed and used in synthesizing representative Beta-amino alcohols. A comparative study in the absence of ionic liquid reveals that the medium plays an important role to aid the reaction. Ionic liquid enhances the rate of reaction significantly. This study demonstrate the potential of ionic liquids

460. Pyrite oxidation in the environment: the effect of bacteria

Jun Hao[1], Daniel R. Strongin[1], Eelin Lim[1] and Martin A. A. Schoonen[2], (1)Temple University, Philadelphia, PA, (2)State University of New York at Stony Brook, Stony Brook, NY

Metal sulfide oxidation in the environment during and after the mining of coal results in the environmental problem known as Acid Mine Drainage (AMD). Acidithiobacillus Ferrooxidans (A.F.) bacteria can thrive in the low pH regions associated with AMD. The presence of A.F. can markedly increase the oxidation rate of the metal sulfide, pyrite, one of the most abundant materials in nature and a major contributor to AMD. Research has investigated the interaction of A.F. with pyrite by measuring the rate of pyrite oxidation with and without bacteria. Furthermore, our studies have quantified the bacterial populations on the surface of the pyrite powder and in the solution in contact with the pyrite under various experimental conditions. Our studies have also focussed on methods to protect the metal sulfide from oxidation in the environment.

461. Pyrite oxidation in the environment and the effect of bacteria

Jun Hao[1], Daniel R. Strongin[1], Eelin Lim[1], Martin A. A. Schoonen[2] and David Vuong[1], (1)Temple University, Philadelphia, PA, (2)State University of New York at Stony Brook, Stony Brook, NY

Metal sulfide oxidation in the environment during and after the mining of coal results in the environmental problem known as Acid Mine Drainage (AMD). Acidithiobacillus Ferrooxidans (A.F.) bacteria can thrive in the low pH regions associated with AMD. The presence of A.F. can markedly increase the oxidation rate of the metal sulfide, pyrite, one of the most abundant materials in nature and a major contributor to AMD. Research has investigated the interaction of A.F. with pyrite by measuring the rate of pyrite oxidation with and without bacteria. Furthermore, our studies have quantified the bacterial populations on the surface of the pyrite powder and in the solution in contact with the pyrite under various experimental conditions. Our studies have also focussed on methods to protect the metal sulfide from oxidation in the environment.

Graduate Posters

Organizer: Anita J. Brandolini William Paterson University, Wayne, NJ
Organizer: Yorke Rhodes New York University, New York, NY
Presider: Yorke Rhodes New York University, New York, NY

462. Cooperative binding of 1,2 substituted ferrocene based bidentate Lewis acids

R. Boshra[1], JA Gamboa[1], A Sundararaman[1], F. Jakle[1], Arnold L. Rheingold[2] and Lev Zakharov[2], (1)Rutgers Univ., Newark, NY, (2)University of California at San Diego, La Jolla, CA

Lewis acids have been the subject of much recent academic and commercial research. Driven by the need for asymmetric and enantioselective synthesis, researchers have focused their efforts towards the development of new stereo- and regio-selective catalysts.

In particular, hetero nuclear bidentate Lewis acids present new opportunities in asymmetric catalysis as well as anion and neutral ligands recognition. A practical way for the synthesis of planar chiral hetero nuclear ferrocene-based bidentate Lewis acids has been developed by our group. Our model compound displays both boron and tin centers occupying the 1,2 positions of one of the cyclopentadienyl (Cp) rings. Single crystal x-ray diffraction and multinuclear NMR studies revealed significant interactions between both metal centers. Coordination of halide and neutral ligands to both acid centers will be discussed. Thermodynamic parameters pertaining to the rotational barrier of the Cp-B bond before and after nucleophile binding have also been obtained

463. Current Efforts Towards the Preparation of 2'-Aminotaxol

Hengqun Shen and Guillermo Moyna, University of the Scineces in Philadelphia, Philadelphia, PA

Current Efforts Towards the Preparation of 2'-Aminotaxol

As the most promising anticancer drug Taxol® has been the subject of intense research for almost four decades. SAR studies showed that the presence of 2'-hydroxyl group is crucial for good bioactivity and is believed to be due to its hydrogen bonding capacity. Two different hypotheses exist: One stipulates that a hydrogen bond is formed between the 2'-hydroxyl and 1'-carbonyl groups that fixes the flexible side chain in its active conformation; the other proposes that the 2'-hydroxyl group interacts directly with residues at the microtubule binding site. To investigate these two different hypotheses the synthesis of a 2'-amino derivative is being attempted. This poster presents the current status of the project.

464. Neighboring Group Participation in the Syntheses and Reactions of 4-X-*exo*-8-*anti*-Iodo-6-azabicyclo[3.2.1]octanes (X=F, Cl, OH). Selectfluor and Mercuric Fluoride as Nucleofuges

Deepa Rapolu[1], Grant Krow[1], Ryan A. Centafont[1] and Kevin C. Cannon[2], (1)Temple University, Philadelphia, PA, (2)Penn State Abington, Abington, PA

Stereoselective syntheses of novel 4-*exo*-8-*anti*-difunctionalized-6-azabicyclo[3.2.1]octanes containing *anti*-iodo in the methanobridge and *exo*fluoro, chloro, hydroxy substituents in the other larger bridge have been carried out by reaction of Selectfluor and mercuric fluoride with the appropriate halide. Retention of configuration was observed in all displacement reactions. Precursor halides were synthesized by addition/rearrangement of dihalides or halohydrins to *N*-alkoxycarbonyl-6-azabicyclo[2.2.2]oct-5-enes.

465. Synthetic Studies Towards Ustiloxin Natural Products

Cory D. Evans, Pixu Li and Madeleine M. Joullié, University of Pennsylvania, Philadelphia, PA

The ustiloxin family of heterodetic cyclopeptides were isolated from the parasitic false smut balls on the panicles of rice plants in 1992. Although only moderately cytotoxic, the ustiloxins are highly potent inhibitors of microtubule assembly. The ustiloxins share a common 13-membered peptide macrocycle with a chiral tertiary alkyl-aryl ether linkage. Two total syntheses of ustiloxin D have been reported to date. Development of a new method for the synthesis of chiral tertiary alkyl-aryl ethers and a synthetic approach towards incorporation of the sulfinyl sidechain of ustiloxin A will be described.

466. Solvent-Dependent Chemoselectivities in Ce(IV)-Mediated Oxidations of 2,4-Diketones : Fragmentations Vs. Intramolecular Cyclizations

Yang Zhang, Jingliang Jiao and Robert A. Flowers II, Lehigh University, Bethlehem, PA

Ce(IV) reagents have been extensively utilized in organic synthesis, however, their use in intramolecular C-C bond-forming reactions is very limited. In our recent work exploring the utility of Ce(IV) reagents in the oxidations with 2,4-diketones, we found that solvents played an important role in determining the chemoselectivity of the reactions. In an initial experiment, 6-phenyl-hexane-2,4-dione was treated with 2 equiv of Ceric Ammonium Nitrate (CAN) in both acetonitrile and MeOH at room temperature. The reaction in acetonitrile produced 3-phenyl-propionic acid exclusively,

whereas, the same reaction in MeOH afforded the expected Friedel-Crafts cyclization product. This solvent dependent chemoselectivity was found for a number of substrates and results showed that cyclized products or carboxylic acids were obtained as the major or only products in MeOH or acetonitrile respectively. While the formation of carboxylic acids through fragmentation is known, they normally require high temperature and an acidic medium. Considering the advantage of neutral and mild reaction conditions with CAN, the scope of this new acid preparation method was studied. Compatibilities of functional groups were also investigated. Mechanistic studies were carried out with Stopped-Flow Spectroscopy and React IR. Initial results showed that nitrate group participated in the carboxylic acid formation. Further mechanistic studies indicate that the solvent dependent chemoselectivities may arise from the stabilities of the radical cations formed between 2,4-diketones and CAN in these two solvents.

467. Synthesis and Novel Homolagation Reactions of 1,2-Cyclopropanated Carbohydrates

Cecilia H. Marzabadi, Seton Hall University, South Orange, NJ and **Jamie Talisman**, Seton Hall University, New York, NY

The goal of the research is to incorporate cyclopropanated carbohydrate elements into drug-like molecules for the treatment of epilepsy and depression. Towards this end, homologation reactions of 7,7-dihalo-1,2-cyclopropanated carbohydrates are being explored. In particular, generation of reactive carbenoids via lithium-halogen exchange followed by an electrophilic quench is of interest. Also, we are pursuing carbohydrate analogues of biologically-active examples in the literature that contain cyclopropane and tetrahydropyran moieties. Thus, carbohydrate derivatives of 7-(hydroxyimino)cyclopropa[b]chromen-1a-carboxylate, an agonist for the metabotropic glutamate receptor, are current synthetic targets.

468. Synthesis of novel nucleosides as potential anti-tumor or antibiotic drugs

Irene Negrete and Dr. Cecilia H. Marzabadi, Seton Hall University, South Orange, NJ

The purpose of this research project is to make nucleosides, to be used as potential antibiotics or anticancer drugs. Since the chemistry of carbohydrates is pertinent to the process of cell recognition and regulation of cell growth, developing novel nucleosides may result in enhanced binding and interaction with cellular targets. Our proposal is to use a variation of protecting groups at the C-2' position of the sugar Thymine and Adenine for the nucleosides. These molecules will then be tested for anti-tumor or antibiotic properties.

469. Asymmetric Transfer Hydrogenation of Allylic Compounds: a Novel Reaction with Homogeneous Chiral Ruthenium Catalysts

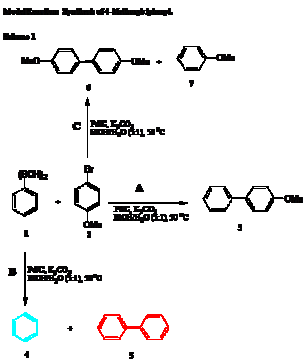
Marie G. Beauchamps and John Sowa Jr., Seton Hall University, South Orange, NJ

Asymmetric catalysis has been many chemists interest for its use in the preparation of chiral alcohols that are very important in the biological and pharmaceutical areas. There has been recent interest in asymmetric transfer hydrogenation (ATH) reactions that avoid gaseous hydrogen; the hydrogen source comes from solvent (isopropyl alcohol). Many examples of ATH of aldehydes and ketones have been reported but there has not been any report of this reaction for allylic alcohols. We were able to convert geraniol and gamma-geraniol to citronellol in 95% and 91% yield respectively using Ru-(S)-tol-binap as a chiral catalyst in the presence of KOH. The reaction with geraniol resulted in high enantiomeric excess (90% R), where gamma-geraniol resulted in 0% ee. The results of these reactions brought some insights for the mechanism of the ATH reaction and also encouraged us to apply this chemistry to a new class of substrates, allylic amines. Preliminary results of this new class of substrates will also be presented.

470. Protodeboronation investigation in Heterogenously catalyzed Suzuki-Miyaura cross-coupling reaction

Lubabalo T. Bululu and Dr. John R. Sowa, Seton Hall University, South Orange, NJ

The high reactivity towards activation of C-X bond in aryl halides has earmarked the heterogenous Pd catalyst as a useful catalyst for suturing new c-c bonds in the Suzuki-Miyaura reaction (scheme 1, pathway **A**). Unfortunately, in some cases, the catalyst is not as selective as it is anticipated. For example, the reaction can follow 3 separate pathways: **A**, **B**, and **C** (scheme 1). Of course, these pathways have different rates, usually in this following order: **A** > **B** >>> **C**. Protodeboronation, **B**, is typically the competitive side reaction to the desired pathway **A**.



Although the cause of protodeboronation is known, the mechanism is still obscure. We intend to investigate how this process occurs. That is, we examine how the metal center, solvent ratio, base, and substitution effects on the boronic acid, influence protodeboronation. Lastly, we would like to isolate the source of the proton since there are potentially three different donors i.e. **1**, ethanol, and water.

471. MFCC-DM: An Approximate QM Method to Study Large Biomolecules

Xihua Chen, Yingkai Zhang and John Z.H. Zhang, New York University, NEW YORK, NY

We propose an efficient approximate quantum mechanical approach to study large biomolecular systems such as proteins and nuclear acids. The method is based on the Molecular Fractionation with Conjugate Caps (MFCC) which is used to systematically decompose large biomolecules into fragments and concaps and on the scheme of density matrix (DM) which is approximately assembled from those of fragments and concaps. By this MFCC-DM method, the self-consistent field procedure can be avoided and the electronic energy and other molecular properties of large molecules can be evaluated efficiently. Numerical test results are also presented.

472. Controlling the Crystal Growth of Polymorphs with 2-Dimensional Templates

Rupa Hiremath, Stephen W. Varney, Joseph A. Basile, Megan J. Carroll and Jennifer A. Swift, Georgetown University, Washington, DC

A polymorph is a solid crystalline phase of a given compound resulting from the possibility of at least two different arrangements of the molecules of that compound in the solid state. Polymorphs can have different physical properties including solubility, melting point, flow characteristics, and bioavailability. Controlling and/or limiting the number and type of drug polymorphs are of paramount importance to pharmaceutical and commercial industries. Specially functionalized 2D self-assembled monolayers (SAMs) developed in our laboratory have been used as templates to (A) exhibit orientational control over crystal growth direction (B) selectively reduce the number of polymorphic forms obtained, and (C) discover new polymorphic phases. Examples of each phenomenon will be presented.

473. Study of pH-response of Bacillus subtilis spores

Elizabeth M. Bonvouloir, Pace University, New York, NY and Sergey V. Kazakov, Pace University, Pleasantville, NY

An approach to study electrochemical behavior of bacterial spores is proposed and tested by measuring pH in the exterior to Bacillus subtilis spores. The approach is based on the statement that properties of an ionic reservoir can effect on the properties of the external solution and can change the concentration of ions in the exterior to spores. The structure of Bacillus spores, particularly, the properties of the spore cortex, a peptidoglycan cross-linked polymer (negative net charge, high level of mobile ions, high degree of freedom of ions movement, ability to change volume in response to ionic changes or water content), allow one to consider a spore as a natural ionic reservoir. The objective of the present work is to examine the ability of Bacillus subtilis spores to accumulate and release ions and to expand or contract in response to external conditions. The potentiometric titration curves for Bacillus subtilis spores were obtained to show that each spore behaves like almost infinite ionic reservoir capable of accumulating billions of protons. The parameters of protonation/deprotonation kinetics were extracted from the time-resolved measurements of establishing an equilibrium pH in spores' suspensions carried out at different conditions effecting on spore germination (extreme pH, temperature, and nutrients). The spore size and shape were monitored using dynamic light scattering and phase contrast optical microscopy. Electrochemical properties of bacterial spores are of great potential for new methods of spore detection and identification and for understanding the phenomenological and molecular mechanisms of germination and sporulation of the Bacillus bacteria.

474. Sonication and Electrodeposition of Rhodium: Effects on Surface Morphology and Cathode Efficiency

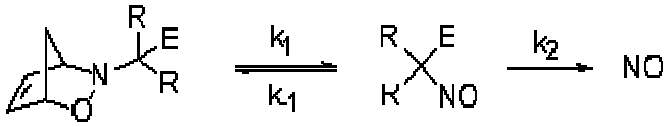
Michael D. Hatton Jr., Robert Hesketh and Stephanie Farrell, Rowan University, Glassboro, NJ

Rhodium is used in the jewelry industry to brighten metal and make it more corrosive resistant. A very thin layer is electroplated over less expensive base metals, such as platinum, white gold, or silver, shielding the less resistant metal from the elements. Rhodium electroplating is usually 8-12% efficient, with much of the energy used in side reactions that produce hydrogen and oxygen. An attempt has been made to raise the efficiency and change the grain structure by introducing the electrodes to ultrasonic waves while electroplating. A 750 Watt, 20 kHz ultrasonic processor is used to transmit ultrasonic waves to the rhodium plating solution through a sonic horn. The pressure waves then produce cavitations and mixing in the solution. The observed effects of the ultrasonic waves on the process are close to 3 times the plating efficiency and altered surface morphology.

475. Synthesis and NO-related Properties of Cycloadducts of C-Nitroso Compounds

Harinath Chakrapani and Eric J. Toone, Duke University, Durham, NC

Nitric oxide is a ubiquitous signaling molecule that has been identified to be involved in a plethora of biological processes including regulation of smooth muscle relaxation, inhibition of platelet activation, stimulation of immune response against bacterial pathogens and tumor cells, neurotransmission, and control of gene regulation. Despite the widespread medical use of several NO donors, selective and controlled delivery of NO is still a major research focus area. *C*-nitroso compounds (CNOs) with one or more geminal electron acceptors are good exogenous nitric oxide donors. CNOs reversibly form Diels-Alder adducts and the position of the equilibrium depends on the nature of the diene. In an attempt to regulate the rate of NO release, we synthesize and study the NO-related properties of cycloadducts of CNOs.



476. Electron Deficient C-Nitroso Compounds as Donors of Nitrosonium (NO+)

David M. Gooden and Eric J. Toone, Duke University, Durham, NC

The fundamental role of nitric oxide in myriad biochemical processes is well established. Our understanding of nitric oxide biology has largely been deduced from studies using relatively stable synthetic agents that contain nitric oxide and demonstrate "NO-like" bioactivity. The development of such agents, the so-called "NO donors", has received considerable attention and the primary literature is now replete with examples of compounds whose bioactivities are based on their ability to release nitric oxide or a redox-related species. *C*-nitroso compounds offer several significant advantages as NO donors relative to other classes of compounds. Most importantly, incremental alteration of substitution patterns at the nitrogen-bearing carbon facilitates precise control over both the rate of NO release and the redox form of the released species. We have established that electron deficient *C*-nitroso compounds serve as selective donors of nitrosonium (NO^+) in transnitrosation experiments with simple aliphatic thiols. Preliminary kinetic analysis of the transnitrosation reaction indicates dimer dissociation to the monomeric species is rate limiting.

Graduate Presentations

Organizer: Yorke Rhodes New York University, New York, NY
Presider: Yorke Rhodes New York University, New York, NY

477. Enantioselective synthesis of majusculone

M. Inthikhab Sikkander, University of Delaware, Newark, DE

No abstract available.°

478. The Effect of Fuel Type and Aftertreatment Devices on Mobile School Bus Emissions from Diesel Powered School Buses

Andrew Toback, Sarina Colligan, Anthony J. Marchese and Robert P. Hesketh, Rowan University, Glassboro, NJ

The New Jersey Department of Transportation (NJDOT) is currently sponsoring a research study at Rowan University to develop strategies for reducing diesel emissions from mobile sources such as school buses. Experiments have been performed to quantify the emission reduction capabilities of various alternative fuels, including biodiesel and ultra low sulfur diesel blends, as well as aftertreatment devices such as diesel oxidation catalysts (DOC) and diesel particulate filters (DPF). Three school buses equipped with an International T444E, an International DT466E, and a Cummins 5.9L ISB engine were instrumented and tested. Emissions of CO, CO2, NO2, NO, O2, unburned hydrocarbons, and PM were measured. A school bus cycle was developed by acquiring Global Positioning System (GPS) data from actual school bus

routes from different municipalities within the state of New Jersey. Alternative fuels produced minor reductions in CO, HC, and PM while the use of a DPF eliminated almost all PM.

479. Influence of Bead Size on Activity and Distribution of Candida Antarctica Lipase B (CAL-B) Adsorbed on Macroporous Polyacrylic Beads

Bo Chen and Richard Gross, Polytechnic University, Brooklyn, NY

Adsorption of Candida Antarctica Lipase B (CAL-B) on macroporous polyacrylic beads under the trade name of Amberchrom™ with various diameters but uniform pore size and surface area has been studied. A decrease in particle size results in a increase of CAL-B adsorption as well as the increase of the specific activity in ring-opening polymerization of å- caprolactone in deuterated toluene and polycondensation of adipic acid and 1,8- octanediol in bulk. The amount of enzyme retained activity was determined by active site titration using a organic phosphate, methyl p-nitrophenyl n-hexylphosphonate (MNPHP) as the inhibitor. Moreover, a change of protein distribution upon adsorption is observed using IR microscope by scanning the concentration of amide bond on the film which is cut from CAL-B immobilized beads. CAL-B entered the center of beads when their size decreases to 35 ìm while it stayed on the shell (~40ìm) of beads when their size is more than 120ìm. These results indicate that the size of beads influences the concentration, distribution and the activity of adsorbed CAL-B.

480. New Fluorogenic Calix[4]arene-bis-crown-6 Ether for Selective Recognition of Cs^+

Ebony D. Roper[1], Galina G. Talanova[1], Maryna G. Gorbunova[2], Richard A. Bartsch[3] and Vladimir S. Talanov[4], (1)Howard University, Washington, DC, (2)Oak Ridge National Laboratory, Oak Ridge, TN, (3)Texas Tech Unviversity, Lubbock, TX, (4)National Cancer Institute, NIH, Bethesda, MD

A new dansyl-group containing calix[4]arene-biscrown-6 ether has been obtained and investigated as an optical chemosensor for metal ions. In acidic CH_3CN/H_2O (1:1, v:v) solutions, the fluorogenic ligand exhibits appreciable selectivity for Cs^+ over K^+ and Na^+. Coordination of Cs^+ is followed by hypsochromic shift of the ligand's emission band along with increasing fluorescence intensity.

481. Removal of Depleted Uranium from Water Using Titanium Dioxide

Christine Chin Choy, Mahmoud Wazne and Xiaoguang Meng, Stevens Institute of Technology, Hoboken, NJ

Groundwater contamination with depleted uranium (DU) is a concern in many areas where uranium mining or uranium processing and recycling have occurred. Uranium typically migrates with groundwater as uranyl carbonates and uranyl hydroxides complexes. Soluble U(VI) has been found to strongly adsorb onto the reactive surface of nanocrystalline titanium dioxide. This presentation addresses the formation of a chemically reactive barrier by injecting TiO2 adsorbent into a sand column. Tests were performed at varying influent concentrations and flow rates. Optimal conditions for homogeneous TiO2 distribution in the sand column were determined and used to saturate a column with adsorbent. A second influent of contaminated groundwater was subsequently passed through the sand column and the U distribution in the effluent was monitored.

482. A New Biological Fluorescent Probe: PheCN

Matthew J. Tucker and Feng Gai, University of Pennsylvania, Philadelphia, PA

Recently, nitrile-derivatized amino acids have been used as infrared probes of local environment. Here, we show that phenylalanine-CN (PheCN) also exhibits interesting fluorescent properties. For example, its fluorescence quantum yield is roughly 4 times larger than that of Phe and its fluorescence spectrum is sensitive to solvent and, therefore, allowing measurements of local environment through PheCN fluorescence. In addition, its emission spectrum overlaps significantly with the absorption spectrum of Trp. Thus, PheCN and Trp make a good fluorescence resonance energy transfer (FRET) pair. Using a series of synthetic peptides that contain a single Trp and a single PheCN residue at different positions, we verified that indeed Förster energy transfer takes place between these two amino acids. Moreover, the distance-dependent FRET signals allowed us to obtain structural information on the peptides.

Green Chemistry I

Organizer: Wen-Chung Shieh Novartis Pharmaceuticals, East Hanover, NJ
Organizer: Sanjay V. Malhotra New Jersey Institute of Technology, Newark, NJ
Presider: Sanjay V. Malhotra New Jersey Institute of Technology, Newark, NJ

483. A Green Future for HMPA?

Peter Wipf, University of Pittsburgh, Pittsburgh, PA

Hexamethylphosphoramide (HMPA) has been used extensively in organic synthesis due to its unique properties as a dipolar aprotic solvent and its superior ability to form cation-ligand complexes. For example, HMPA coordinates approximately 300 times better to lithium ions than THF. HMPA has also been used catalytically, stoichiometrically, or in

excess to control the stereochemistry of the product or to bias the reaction regio- and chemoselectivity. However, HMPA is also a highly toxic chemical with considerable potential carcinogenicity. Its use has been severely restricted, and there is continued need for more environmentally benign and biologically innocuous analogs. We have systematically tested polymer-linked variants and studied their synthetic properties in order to develop a green alternative to HMPA.

484. Development of an environmentally sound process for production of the new carbapenem antibiotic ertapenem sodium

J. Michael Williams, Merck Research Laboratories, Rahway, NJ

INVANZ is a new carbapenem antibiotic developed at Merck for treatment of serious bacterial infections. Ertapenem sodium, the active ingredient, is unstable in solution presenting a difficult challenge for development of an environmentally responsible manufacturing process. Our strategy led to an efficient, environmentally sound process that is now used in the commercial production of INVANZ for sale worldwide. Innovative chemical reactions and a novel method for improving product stability served to reduce the burden on purification. A highly selective low temperature reaction is used in assembly of the carbapenem. Hydrogenolysis of a p-nitrobenzyl ester gives ertapenem in 90% yield for two steps. Use of bicarbonate was key in improving reaction performance and stability of the product through formation of the sodium carbamate. An extraction makes use of a reaction by-product as an ion-pairing agent simultaneously purifying and concentrating the aqueous product stream. Crystallization affords 65% overall yield of ertapenem sodium.

485. Development of a 2nd generation process for Gleevec®

Mark Meisenbach, Novartis Pharma AG, CH-4002 Basel, Switzerland

Gleevec® (or Glivec®, STI571) is a new drug effective in the treatment of chronic myeloid leukaemia (CML) and gastrointestinal stromal tumors (GIST) marketed by Novartis. It possesses a unique mode of action by the inhibition of the BCR-ABL tyrosine kinase, a key-player in the signalling cascade responsible for CML. Gleevec® is also an inhibitor of the receptors for platelet-derived growth factor (PDGF) and stem cell factor (SCF) which explains the drug's property to inhibit proliferation and to induce apoptosis in GIST cells. The drug was developed and approved in record time. The current production synthesis is very effective and robust but has some drawbacks in terms of throughput and potential mutagenicity of several intermediates. A new synthesis tackling these deficiencies was developed and scaled up. It turned out that a simple change in the order of assembling the molecule applying almost the same chemistry as the previous synthesis could avoid most of the aforementioned problems. This lecture summarizes the different phases of this Technical Live Cycle Project starting from brainstorming, basic screening, route selection and finally process development and scale-up of the new synthesis.

486. Maraviroc (UK-427,857) The Process chemists tale

Jens Ahman, Sarah J. Haycock-Lewandowski, Nicola Mawby, Alex Wilder and Steve Challenger, Pfizer, Sandwich, United Kingdom

This talk will detail the development of an environmentally friendly synthesis of CCR-5 receptor antagonist UK-427,857 from the medicinal chemistry route through a bulk enabling route to a route operating in a commercial production plant. The use of Green-Chemistry metrics to guide process development towards a more environmentally friendly synthesis will be detailed

487. Green Chemistry: Current Status and Future Challenges

David Highfield, American Chemical Society, Washington, DC

Green chemistry is a science-based, non-regulatory and economically driven approach to environmental protection and sustainable development. The approach has been utilized in a number of industrialized and developing nations with extremely positive results in terms of both protection of human health and the environment as well as significant economic benefit to the industrial interests involved.

Green chemistry is chemistry for pollution prevention which strives to reduce or eliminate the use and generation of hazardous substances. This scope explicitly does not include approaches such as waste treatment, waste control or re-mediation even though these elements are recognized as important, but separate, elements of an environmental

protection programs. There is a need for initiatives that design products and processes such that these environmental problems never occur. This is the focus of green chemistry.

Green chemistry includes products and processes. This means that not only the final product can be designed to be non-hazardous but also each of the intermediate transformations are designed so that they don't use or generate hazardous substances. There is an implicit consideration life cycle impacts with the scope of sustainable chemistry. Although traditionally pollution prevention was thought to focus on waste reduction sustainable chemistry includes and expands this focus to all stages of the life cycle. The importance of this expansion is seen through commonly reported achievements from industry where the greatest economic and environmental benefits are being realized as much in the early stages of production or product life cycle as they are in the latter stages.

In-Line Analytics for Reaction Monitoring

Organizer: John A. Grosso Bristol-Myers Squibb Co., New Brunswick, NJ
Organizer: John Wasylyk Bristol Myers Squibb Co., New Brunsick, NJ

488. Building Process Knowledge Through the Use of In-line/On-line Reaction Monitoring - Case Studies

Srinivas Tummala, Simon Leung, Ehrlic Lo, John Shabaker and San Kiang, Bristol Myers Squibb, New Brunswick, NJ

Mid-infrared spectroscopy and Raman scattering are two popular techniques used for chemical process development in the pharmaceutical industry. Inline use of these monitoring tools can provide not only valuable information about a chemical reaction, but may also improve the safety and robustness of the chemical process. There are several areas where application of PAT tools can have a unique and positive impact. For highly hazardous processes, these tools may be used as a saefety measure. For unstable and reactive species, direct monitoring of its formation or disappearance may be vital to the chemical process. For extreme conditions, inline monitoring will eliminate or reduce traditional sampling and errors associated with it. Furthermore, data collected by these techniques may provide insight into the mechanism of the process, which may not normally be obtained by other means. Finally, PAT tools can be an important component for feedback control of a continuous or highly automated process. In this presentation, several examples will be used to illustrate the applications of PAT in the aforementioned areas. Pros and cons of some of the common implementation setups in the plant will also be discussed.

489. Process Development and Scale-Up with In-Line FTIR Monitoring

George Zhou and Zhihong Ge, Merck and Co, Rahway, NJ

Process analytical technologies (PAT) play an important role in process development and optimization throughout the pharmaceutical industry. With the encouragement of recent PAT initiatives by FDA, PAT is becoming more and more recognized and embraced by pharmaceutical companies in both research and manufacturing areas. Online spectroscopic techniques, such as FTIR, are popular PAT tools widely used in the development and optimization of bulk drug processes to measure quality parameters and performance attributes of raw and in-process materials. In this presentation, the benefits of employing FTIR will be demonstrated through several case studies. Applications of FTIR for optimization of a synthetic process and online measurement of initiation, progress, and potential stalling of a hazardous reaction will be presented. Utilization of FTIR for online monitoring headspace gas of a reaction process to map out a timely strategy for safe processing while adhering to environmental regulations in the pilot plant will also be illustrated.

490. Development and Implementation of an In-Line Quantitative Raman Method for In-Process Pharmaceutical Monitoring

Robert G. Wethman, Charles Ray and John Wasylyk, Bristol-Myers Squibb Company, New Brunswick, NJ

The use of Raman spectroscopy as an in-process monitoring tool has gained increasing utilization in the pharmaceutical production plant. Reactions that present issues with regard to intermediate stability and sampling down time lend themselves particularly well to an in-line method. A quantitative in-situ Raman method was successfully developed and transferred from development lab to pilot plant for monitoring of a Schiff's base formation and subsequent reduction. The presentation will discuss chemometric model development, installation into the pilot plant, as well as instrument to instrument method transfer.

491. Development of a Laboratory Crystallization System with In-line Sensors

Boris Gordonov and Benoit Vanasse, Sanofi-Aventis, Bridgewater, NJ

Recent developments of in-line sensors and instrumentation have enabled developers to use powerful tools in order to better understand and optimize crystallization processes. Skyrocketing amounts of real-time data acquired in the laboratory by simultaneous use of various instruments manufactured by different vendors dictates the need to develop an integrated and synchronized data acquisition system with a flexible architecture and data processing/process control capabilities. This paper presents an in-house laboratory suite assembled for the study and development of crystallization processes for manufacturing active pharmaceutical ingredients. The system integrates the following: laser Focused Beam

Reflectance Measurements (FBRM) probe for particle size monitoring, in-situ Raman spectrometer, pH, conductivity and temperature sensors, liquid loss-of-weight feeds, agitation and ultrasound processor control. The data acquisition and process control software has been written in-house in Visual Basic to allow synchronized data recording, analysis, flexibility and further expansions (including incorporation of machine vision/image analysis tools). We will present examples that demonstrate the utility of this approach to conduct solubility/meta-stable zone measurements, to synchronously monitor processes in the liquid and solid phases, including solid phase transitions and evolution of a meta-stable solid form.

492. Real Time, On-Line Analysis of Flow Reactions using Impedance

Mike C. Hawes, Syrris Ltd, Royston, United Kingdom

Flow chemistry is an emerging technology with great potential for both discovery and process development. Flow chemistry allows reactions to be analyzed in real time and conditions varied in a fast serial approach. This presentation discusses impedance, a novel method of analysis ideally suited to flow and its application to closed loop reaction optimization.

Inorganic and Organometallic Polymers III

Organizer: Frieder Jaekle Rutgers University, Newark, NJ
Presider: Robert B. Grubbs Dartmouth College, Hanover, NH
Presider: Qiao-Sheng Hu City University of New York-College of Staten Island, Staten Island, NY

493. Reactive Organometallic Polymers Containing Metallacyclopentadiene Repeating Units in the Main Chain

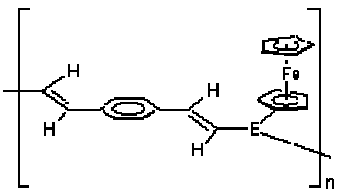
Ikuyoshi Tomita, Tokyo Institute of Technology, Yokohama, Japan

Polymers containing functional groups with versatile reactivity in the main chain are expected to serve as useful reactive precursors for main chain functional polymers. In the course of our studies to create polymers having reactive organometallic units in the main chain, we describe herein the synthesis and reactions of organometallic polymers containing cobaltacyclopentadiene and titanacyclopentadiene units in the main chain. Polymers having metallacyclopentadiene units were prepared by the reaction of diynes with low-valent organometallic complexes. Especially, polymers produced from aromatic terminal diynes such as 2,5-dialkoxy-1,4-diethynylbenzenes and a low-valent titanium complex generated in situ from titanium(IV) isopropoxide have the regioregular main chain linkage whose polymer reactions proved to be suitable for production of p-conjugated organic polymers. For example, polymers containing conjugated diene, thiophene, phenylene, and phosphole systems in the main chain were produced by the reactions of the polymers with hydrochloric acid, sulfur monochloride, propargyl bromide, and dichloroalkylphosphines, respectively. Polymers obtained through these reactions exhibited p-conjugated characters judging from their UV-vis absorption and photoluminescence spectra.

494. Polymerisation of Ferrocenylboranes via BH_3 Elimination or Hydroboration Reactions

Matthias Wagner, Matthias Scheibitz and Julia B. Heilmann, J. W. Goethe-Universität, Frankfurt (Main), Germany

Syntheses, structures and reactivities of the ferrocenylborane adducts $FcBH_2$-Do (Do = NMe_2Et, SMe_2) and of the corresponding 1,1'-disubstituted species are described (Fc = ferrocenyl). Thermolysis of $FcBH_2$-NMe_2Et gives the dinuclear hydroboration reagent Fc_2BH and B_2H_6. The thioether adduct $FcBH_2$-SMe_2 undergoes a similar condensation reaction in solution even at room temperature. X-Ray crystallography revealed Fc_2BH to be a rare example of a diorganylborane which is monomeric in the solid state. Ferrocenylborane derivatives $FcBH_2$-Do may be used in the hydroboration polymerisation of aromatic diynes which yields π-electron deficient conjugated polymers with ferrocenyl substituents at the boron atoms (e.g. **1**). Treatment of $FcBBr_2$ with Et_3SiH leads to the formation of diferrocenylbromoborane Fc_2BBr in quantitative yield. Similarly, 1,1'-$Fc(BBr_2)_2$ and Et_3SiH give the BBr-bridged polymer **2** (chain length: approximately 30 – 50 repeat units) which can be derivatised in a variety of ways to generate poly(ferrocenylenes) with cationic, neutral and anionic three- or four-coordinate boron bridges.



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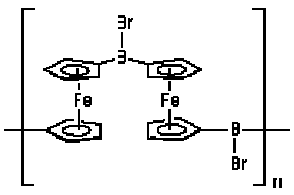

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495. Synthesis of Ferrocenylmethylphosphine-Containing Polymers for Transition Metal Catalysis

Qiao-Sheng Hu, Cheng-Guo Dong, Yong Lu, Hanako Hirosi, Elizabeth Plocher and Zhen-Yu Tang, City University of New York-College of Staen Island, Staten Island, NY

Transition metal-catalyzed cross-coupling reactions have emerged as extremely powerful tools in organic synthesis. The development of highly efficient transition metal catalysts remains as one of the important goals in this field. In our laboratory, we interested in developing rigid, site-isolated monodentate ligand-containing polymers as highly efficient ligands for transition metal-catalyzed cross-coupling reactions. Our ongoing effort focuses on understanding the nature of the Pd(0) catalyst system derived from rigid, site-isolated monophosphine-containing polymers, In this presentation, the synthesis and study of a series of bisphosphine-containing molecules including polymers will be described.

496. Synthetic approaches to hybrid polymer/small-molecule materials for solution processed organic light emitting diode (OLED) devices

Nora S. Radu, Norman Herron, Frank Uckert, Eric Smith and Dan LeCloux, DuPont Co., Wilmington, DE

The preparation of highly efficient and long-lived multilayer solution processed OLED devices is a difficult challenge. Some of the most important issues encountered in this area are thermal and morphological stability, solubility and film-forming ability of materials employed. Specifically, transport and emitter materials that combine the high OLED device performance demonstrated by phosphorescent small-molecules with the solution processing advantages offered by polymers are in high demand. We will present our synthetic approaches to hybrid polymer/small-molecule materials for use in solution processed organic light emitting diode devices

497. Luminescent Organoboron Quinolate Polymers

Yang Qin, Cynthia Pagba, Piotr Piotrowiak and Frieder Jäkle, Rutgers University at Newark, Newark, NJ

Aluminum quinolates (Alq3) were first reported by Tang and VanSlyke in 1987 to possess electroluminescent properties and are currently widely used as materials for emission and electron-conduction layers in organic light emitting devices (OLEDs). The recent discovery by Wang and coworkers that certain organoboron quinolates such as Ph2BQ show efficient luminescence while at the same time providing good stability triggered new research efforts into boron quinolates and related species. We have developed a novel modular synthetic route to the first example of well-defined luminescent organoboron quinolate polymers. Solutions and thin films of PS-B5HTQ and PS-B3HTQ show luminescent properties similar to those of the respective molecular model compounds with bright green emission at ca. 508 - 511 nm upon excitation at 395 nm. Our new approach is highly versatile since the polymer properties can readily be fine-tuned. Thus, we have shown that substitution of the pendant aryl rings with hexyl groups leads to enhanced polymer processability. Moreover, the emission characteristics can readily be fine-tuned through the substitution pattern of the chelating ligand and the boron substituents.

Ion Channel

Organizer: Robert Goodnow Hoffmann-La Roche, Nutley
Presider: Thomas J. Caufield Sanofi-Aventis, Bridgewater, NJ

498. Blocking Ion Channel KCNN4 Alleviates the Symptoms of Experimental Autoimmune Encephalomyelitis in Mice

Chuan-Chu Chou, Eva-Pia Reich, Long Cui, Lily Yang, Catherine Pugliese-Sivo, Andrei Golovko, Mary Petro, Galya Vassileva, Inhou Chu, Amin A. Nomeir, Li-Kang Zhang, Xian Liang, Joseph A. Kozlowski, Satwant K. Narula and Paul J. Zavodny, Schering-Plough Research Institute, Kenilworth, NJ

The KCNN4 potassium ion channel was reported to play an important role in regulating antigen-induced T cell effector functions in vitro. We present here the first evidence that a selective KCNN4 blocker, TRAM-34, confers protection against disease in a mouse model of experimental autoimmune encephalomyelitis (EAE). Treatment with the KCNN4 blocker did not prevent infiltration of T cells in the spinal cord. However, there was a reduction in pro-inflammatory cytokine levels in this targeted tissue. Furthermore, RNA analysis showed a dramatic decrease of the messages of several cytokines and chemokines in the spinal cord of TRAM-34-treated mice. Plasma concentrations of TRAM-34 within a 24-hour period were between the in vitro IC50 and IC90 values for the KCNN4 channel. The effect of TRAM-34 was reversible, as indicated by the development of clinical EAE symptoms within 48 hours after withdrawal of treatment. In summary, our data support the idea that KCNN4 channels play a critical role in the immune response during the development of MOG induced EAE in C57BL/6 mice.

499. Ion Channel Modulation: Can it Enhance Neurotransmission, Conduction, and Myelination for New Therapeutic Interventions?

Craig P. Smith, Sanofi-Aventis, Bridgewater, NJ

Text Not Available

500. De novo design of potent T-type calcium channel blockers

Daniel L. Cheney, Jon Hangeland, Todd Friends and Paul Levesque, Bristol-Meyers Squibb PRI, Hopewell, NJ

An increasing body of evidence suggests that selective T-type calcium channel blockers may be clinically efficacious while incurring significantly fewer side-effects than current therapies involving blockade of the L-type calcium channel. In this report, we describe the development of a qualitative activity model, and its successful application in the de novo design of novel and selective T-type calcium channel blockers. Prototype scaffolds fitting the constraints of the activity model were generated by the program Sprout, and iteratively refined into drug-like chemotypes, representatives of which were synthesized and found to exhibit moderate to high potency in in-vitro assays.

501. Identification of Ion Channel Modulators

Maria L. Garcia, Merck Research Laboratories, Rahway, NJ

Ion channels participate in numerous cell functions and modulation of their activities could have important physiological and therapeutic consequences. The preclinical development of drugs that selectively target a particular ion channel requires the combined efforts of several fields of expertise, such as biology, chemistry, pharmacology, and drug metabolism. During the past few years, technologies have become available for assaying ion channel function in a high throughway fashion with the goal of identifying potent and selective modulators of these proteins. Peptide inhibitors of voltage-gated potassium channels have been purified from venoms of different organisms. These molecules have contributed to proof of concept studies for defining the physiological role that a given channel plays in native tissues. Small molecule potassium channel modulators have also been identified and characterized. The family of indole diterpene blockers represented by paxilline, aflatrem and penitrem A are all potent and selective blockers of the high-conductance, calcium-activated potassium channel, whereas correolide and a series of disubstituted cyclohexanones (DSC), are selective inhibitors of the Kv1 family of voltage-gated potassium channels. In addition, water-soluble, tetraphenyl porphyrin derivatives have been designed to mimic the known interaction of peptide inhibitors with potassium channels. Knowledge of the detailed molecular determinants of drug-channel interactions will allow the design of more potent and selective channel inhibitors with appropriate characteristics for becoming clinical development candidates.

Laboratory Experiences in the Undergraduate Curriculum

Organizer: Christine M. Ingersoll Muhlenberg College, Allentown, PA

502. Quantitative NMR Experiments

Kurt Rublein, Lock Haven University, Lock Haven, PA

A variety of samples have been used in the Instrumental Analysis Laboratory to demonstrate quantitation of mixtures by proton NMR spectroscopy. Sample preparation, results, and exemplary calculations will be presented. Samples that have proved to be particularly difficult will also be discussed.

503. Introducing Statistics and Nonlinear Least-Squares into the Physical Chemistry Lab

Carl Salter, Moravian College, Bethlehem, PA

Data reduction using statistics and least squares fitting is much easier nowadays in the teaching physical chemistry lab thanks to microcomputers and data acquisition. This paper presents several experiments spanning gas behavior, kinetics, and spectroscopy that are designed to introduce students to statistical analysis, especially nonlinear least squares fitting. The common theme is that each experiment asks a question that must be answered through statistical analysis; in addition, the experiments are simple, fast, and reproducible.

504. Academic Choice Coupled to Open-Ended Exercises in the Analytical Chemistry Lab

Thomas A. Betts, Kutztown University of PA, Kutztown, PA

Science educators not only have the responsibility of providing students with an understanding of the fundamental concepts of scientific disciplines, but also to develop problem solvers. Over the past several years, I have been modifying my analytical laboratory exercises in small ways to attempt to provide students with laboratories that match their interests, and encourage the development of problem-solving skills. Students have some choice in the laboratory exercises that are executed to become familiar with an analytical technique. Once students become familiar with a technique, open-ended assignments or problems are posed. This cycle can be repeated for a variety of analytical techniques, and provides several pedagogical advantages over a continuous stream of “cookbook” laboratory exercises.

505. An Interdepartmental Offering in Instrumental Analysis

Donald Mencer Jr. and J. Michael Case, Wilkes University, Wilkes-Barre, PA

For several academic years Wilkes University has offered a cross-listed three-credit course (CHM244/GES244) entitled "Applications of Instrumental Analysis". The course draws half its enrollment from among Chemistry and Biochemistry majors and half from among Earth and Environmental Science majors. The course focus is on the applications of quantitative instrumental techniques. Lab work includes chromatographic, spectroscopic and electrochemical techniques. Team-taught by two instructors, the course strives to exploit the interdisciplinary learning possibilities and to more effectively promote active learning. As a central part of the course, students tackle a multi-week of seawater. Characterization of the seawater samples for a wide variety of analytes includes: total dissolved solids, pH, conductivity, Na^+, K^+, Ca^{2+}, Mg^{2+}, Cl^-, Br^-, SO_4^{2-}, trace organic analysis, and more. Students learn the fundamental physical operating principles of instrumental methods of analysis through exposure to data that illustrate those principles. The interdisciplinary work broadens the academic perspective of the students (and faculty). The challenge and opportunities of this course are related to providing a richer learning experience through a curriculum that encourages students to think beyond their discipline-specific interests. Many techniques are required for the water analysis: UV-Vis spectroscopy, Gas Chromatography-Mass Spectrometry, electrochemical methods (pH, selective ion analysis, conductivity, dissolved oxygen, etc.), atomic absorption/emission, and others. Application of statistical techniques and computer based data treatment are emphasized. Students assess the precision and accuracy of their work and evaluate trends in the data.

506. Molecule Day: Laboratory Projects Based on an Interdisciplinary Theme

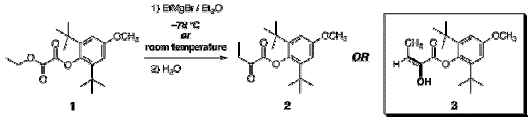
Christine M. Ingersoll, Muhlenberg College, Allentown, PA

Each year, the chemistry department at Muhlenberg College organizes an interdisciplinary minisymposium based on a ‘molecule' that is not only of scientific interest, but is a topic that can be investigated across the disciplines. To date, we have celebrated eight annual symposia based on the following: methyl bromide, ethanol, nicotine, caffeine, norethindrone, porphyrin, DNA and sucralose. The highlight of each Molecule Day minisymposium is a student poster session based on various projects students undertake in their classes, as independent study or research projects, or as literature exploration assignments. For example, Ethanol Day consisted of student posters on social and religious issues of drinking, ethanol as an alternative fuel, economic analyses of alcoholic beverages, and fermentation processes of wine. Nicotine Day examined chemical and physiological aspects of nicotine and nicotine addiction as well as ethical issues faced by the tobacco industry. In the upper level chemistry laboratories, students propose and carry out independent projects involving experiments on the molecule of the year to be presented at the poster session. This presentation will focus on specific examples of team-based laboratory projects centered on yearly molecule day themes conducted by students in instrumental analysis.

507. Maximize your research: Teach it!

Olivier J.-C. Nicaise, Southern Connecticut State University, New Haven, CT

Our current interest in stable enols originates from an accidental discovery that we made in the context of one of our research projects. When treated with EtMgBr, 1,2-diester **1** affords quantitatively either the α-ketoester **2** or the corresponding (*E*)-enol form **3** depending on the reaction conditions. The enol ester **3** has been spectroscopically characterized, and both methyl carbonate and trimethylsilyl ether derivatives have been prepared. We have also documented the kinetic stability of **3**, and verified the generality of this observation using other Grignard reagents in the presence of **1**. More recently, we have initiated a systematic study of the effect of substituent size on the generation, stability, and stereochemistry of the enol ester. Owing to the simplicity of the experimental procedure involved, the generation of enol ester **3** has formed the base for the development of a new laboratory experiment that requires combining synthetic organic chemistry and spectroscopic knowledge in order to determine the structure of the reaction product, and also suggest a mechanism for its formation. This experiment introduces the students to the concept of stability of the tetrahedral intermediate in acyl-transfer reactions, and it also gives them a taste of the unexpected. This presentation will describe a discovery that was made in the research laboratories and how it made its way to the undergraduate teaching laboratories.



508. Does the Solvent Affect the Relative Nucleophilic Strength of Halide Ions in an SN2 Type Reaction?

Terrence P. Sherlock, Ralph Fleming, Ryan Oesterle and Jared Styer, Burlington County College, Mount Laurel, NJ

As part of our first semester organic chemistry laboratory course, our students have traditionally run a version of a classic textbook experiment that complements their study of mechanisms in nucleophilic substitution reactions. In the experiment, bromide and chloride ions are competing nucleophiles in an SN2 type reaction with 1-butanol in aqueous solution. Typical results indicate the ratio of brominated product to chlorinated product to be on the order of 10:1. Students have been

curious whether, as their textbook predicts, this ratio could be affected by proper selection of solvents. Experiments were designed and conducted to test this theory, and the results will be presented.

509. Development of Inexpensive Nucleic Acid Kinetics Experiments

Jamie Burns[1], Madeley Alcala[2], Syeda Islam[2] and **Amber Flynn Charlebois**[3], (1)Montclair Kimberley Academy, Montclair, NJ, (2)J.F.K. High School, Paterson, NJ, (3)William Paterson University, Wayne, NJ

This laboratory exercise will provide an opportunity for undergraduate students to be exposed to modern concepts in RNA research while using standard biochemistry and molecular biology techniques. It seems that most often nucleic acid experiments of this type involve sophisticated and/or expensive techniques that are not practical for undergraduate laboratories, including electron microscopy, and the use of radioactive or fluorescent labeling. We have developed an undergraduate laboratory that allows the student to measure the kinetics of a DNA enzyme. The 10-23 DNA enzyme, isolated by G. F. Joyce in 1998, is a single stranded DNA molecule that cleaves a strand of RNA site specifically. In the exercise the standard assay is completed and the products are separated using denaturing polyacrylamide gel electrophoresis and are visualized by the use of a dye staining process. We have optimized this dye staining process. This exercise can be completed in two three-hour laboratory periods.

510. Advantages of Microwave-Enhanced Reactions in the Organic Lab

Marsha R. Baar, Danielle Falcone and Christopher Gordon, Muhlenberg College, Allentown, PA

The educational benefits of utilizing microwave heating in the sophomore organic chemistry lab will be discussed. Already success with rate enhancement and yield improvement associated with a Diels-Alder cycloaddition, a Williamson ether synthesis and a Wittig salt formation allowed the incorporation of additional experiments, more in-depth spectral analyses, easier purification and exposure to an environmentally friendlier heating technique. Additional reactions currently under investigation aim to introduce chemistry previously unavailable due to prohibitive reflux periods, as well as concepts of asymmetric syntheses.

NanoScience and Technology Posters

Organizer: Anita J. Brandolini William Paterson University, Wayne, NJ
Organizer: Yves J. Chabal Rutgers University, Piscataway, NJ
Organizer: Eric Garfunkel Rutgers University, Piscataway, NJ

511. Simulations of Thiol Terminated Dendrimers

Shyam Vyas, Accelrys Inc, Morristown, NJ

Dendrimers are a novel class of polymers that have proved important for a range of nanotechnology applications. One such dendrimer is a thiol terminated fourth generation dendrimer, G4-SH, which has been used a template for the production of gold nanoparticles [1]. As an initial first step to understanding this process at a theoretical level we perform molecular dynamics calculations of the isolated dendrimer and present the results of these calculations. These include the free volume, radius of gyration as well as other geometric properties.

1. G. Schmid, W Meyer-Zaaika, R. Pugin, T. Sawitowski, J-P. majoral, A-M Caminade & C-O Turrin. Chem. Eur. J., 2000 Vol 6[9] 1693 “Naked Au55 Clusters: Dramatic Effect of a Thiol Terminated Dendrimer”

512. Formation of Nano-sized Lead Sulfide and Cadmium Sulfide by Using Ionomers

Kayla A. Lu, Roshan Deen and Masanori Hara, Rutgers University, Piscataway, NJ

Semiconductor nano-particles have been studied extensively in the past few decades. The blue-shifts occur in their band-gap compare to those of the bulk, known as the quantum size effect. These nano-sized semiconductors also exhibit unique electrical, optical, and mechanical properties that have potential applications in electronic devices. Semiconductors such as lead sulfide (PbS) and cadmium sulfide (CdS) were synthesized in various concentrations of poly(methyl methacrylate-methacrylic acid) (MMA-MAA) ionomer by a solid-state method that we have developed. Ions in the ionomer were exposed to Hydrogen sulfide (H2S) for a sufficient amount of time to completely convert Pb2+ and Cd2+ ions to PbS and CdS. The changes in color (blue shift) were apparent, reflecting the formation of the nano-sized semiconductors. One of the tests used was Differential Scanning Calorimeter (DSC) to measure the glass transition temperatures (Tg). The increase in Tg with the increase in ion content was observed. UV-vis spectroscopy was used to determine the sizes and size distributions of the nano-particles. The UV-spectrum showed that the size of the nano-particles decreases with decreasing ion content.

513. Molecular Self-Assembly Processes between Vesicles and Nanotubes for Device Fabrications

Ipsita A. Banerjee, Stephanie Colleti and Rose L. Spear, Fordham University, Bronx, NY

Here we report the study of two new classes of peptide bolamphiphiles containing the bis (N-alpha-amido-His-Glycine-)1,5 pentane dicarboxylate moiety and the bis (N-alpha-amido-Leu-Leucine-)1,5 pentane dicarboxylate moiety. The self-

assembly process of the molecules was studied in different solvents as well as at varying pH. It was observed that the His-Gly containing bolamphiphile tends to self-assemble into nanospheres in aqueous solutions within a week. However, in the presence of Ni or Co ions, they tend to fold to form nanotubular structures. Upon reduction, these materials lead to the efficient formation of Ni and Co nanocrystals on the surface of the nanotubes. However the Leu-Leu bolamphile self-assembled to form nanorod like structures in the presence of organic solvents. The nanosphere, nanorod as well as the nanotube formation mechanisms were probed by Raman microscopy. The size and shape of the materials obtained was analyzed by TEM and AFM. Such materials can be used for device fabrications for sensors, electronics and magnetic materials.

514. Probing the Intrinsic Electrical Properties of Individual Nanowires With Electric Force Microscopy

Jianming Zhang, Oleh Taratula, Jowairia Chaudhry and Huixin He, Rutgers University, Newark Campus, Newark, NJ

One-dimensional nano-structures are attractive building blocks for the next generation nano-electronics. Although significant progresses have been made in nanowire fabrication, challenges still exist to fully exploit their potential applications for the future nano-devices. One of the challenges is to study the intrinsic electronic properties of individual nanowires without average effect, because it is always difficult to separate the contributions in the measured resistance from the nanowire itself and from the wire/metal electrode contact. Methods based on scanning probe microscopic techniques have been developed and widely used, such as, conducting atomic force microscope (AFM), electrical force microscope (EFM) and scanned gate microscope, etc. Advantages and disadvantages exist in each of the methods. We studied the electrical properties of Pd nanowires with conductive AFM and EFM. In the EFM studies, we surprisingly found that Pd nanowires showed a negative-positive-negative phase shift. In this report, we will present the electrical properties of individual Pd nanowires studied by these two techniques. To understand the new phenomenon that occurred in the EFM studies, comparison was made with different one-dimensional nanostructures, such as carbon nanotubes, CdS nanowires and DNA.

515. Generation and Stabilization of Copper Nanoparticles

Moni Chauhan[1], **Wayne Narain**[1], Umar Latif[2] and Bhanu P.S. Chauhan[3], (1)Queensborough Community College, Bayside, NY, (2)bNanomaterials Laboratory of Center for Engineered Polymeric Materials, Department of Chemistry and Graduate Center, City Univer, Staten Island, NY, (3)Nanomaterials Laboratory of Center for Engineered Polymeric Materials, Department of Chemistry, City University of New York, Staten Island, NY

Nanometer-sized particles of metals and semiconductors have been investigated intensively in recent years.1 Generation of Copper Colloids has great and diverse uses because of its catalytic, electrochemical, magnetic and optical properties.2 In our approach to generating copper colloids, a variety of copper salts, stabilizing agents, and solvents were used in order to investigate. In our synthetic approach, we have used PMHS as reducing agent for the generation and in-situ stabilization of nanosized copper reservoirs in organic solvents. This method enables routine formation of stable nanosized copper particles, avoiding particle aggregation during the storage as well as nucleation and growth process. We also demonstrate the utility of such reservoirs in grafting the surface properties of nanoparticles by ligand exchange reactions with a variety of surfactants. Effect of different stabilizing agents was studied in order to investigate the stability profile of copper nanoparticles. Samples analyzed by Transmission Electron Microscope (TEM) reveal copper colloids with particle size between five (5) to ten (10) nanometers (nm). The oxidation state was confirmed by X-ray Photoelectron Spectroscopy (XPS) to be in zero oxidation state which coincides with the UV-visible spectroscopy that revealed copper colloids at 570 nanometers (nm).

1. a. Bhanu P.S. Chauhan, Jitendra Singh Rathore, Moni Chauhan and Alexandra Krawicz. J . Am. Chem. Soc. 2003,125, 2876-2877. 1, b. Bhanu P. S. Chauhan, Jitendra S. Rathore, and Tariq Bandoo J. Am. Chem. Soc. 2004, 126, 8494 2 Chauhan, B. P. S.; Rathore, J. S.; Sardar, R.; Tewari, P.; Latif, U. J. Organomet. Chem. 2003, 686, 24

516. Functionalized Polyaniline/Carbon Nanotube Composite for Sensitive Detection of Glucose by a Non-Enzymatic Approach

Yufeng Ma, Ali Shah and Huixin He, Rutgers University, Newark, NJ

The ability to detect trace level of glucose not only allows for early diagnosis of diabetes, it also dramatically reduces the blood volume needed for regular monitoring of diabetic patients.

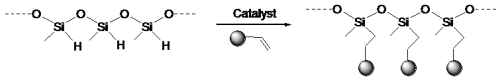
Although the development of glucose sensors for use in battling diabetes has been the focus of intense research since the 1960's, most advanced sensors are based on the enzyme glucose oxidase (GOx) coupled to electrochemical systems, and the sensitivity is still in the millimolar range. In this presentation we will report a non-enzymatic approach to detect glucose, the concentration as low as 1 nM can be detected by modifying the gold electrode with a thin layer of poly (aniline boronic acid) /carbon nanotube composite. Glucose chemically binds to the boronic acid groups, which greatly influences the electrochemical activity of the polyaniline backbone due to steric effects. The carbon nanotubes in the composite not only increase the effective electrode surface area (thereby increasing the density of boronic acid groups for glucose binding), they also greatly increase the stability of the film. Glucose concentrations as low as 1 nM was detected with cyclic voltammetry, and the electrochemical current decreased as the concentration of glucose increased from 1 nM to 10 nM, and leveled off in higher concentrations for some films. The sensitivity is four orders of magnitude greater than

the current glucose sensors. It holds great potential for early diagnosis of diabetes, and it could also dramatically reduce the pain of diabetic patients by reducing the blood volume needed for regular monitoring.

517. Platinum and Rhodium Nanoclusters as Catalyst in Hydrosilylation of Alkenes and Alkynes

Bhanu P.S. Chauhan[1], Moni Chauhan[2], **Gilchris O. Burton**[2] and Umar Latif[3], (1)Nanomaterials Laboratory of Center for Engineered Polymeric Materials, Department of Chemistry, City University of New York, Staten Island, NY, (2)Queensborough Community College, Bayside, NY, (3)bNanomaterials Laboratory of Center for Engineered Polymeric Materials, Department of Chemistry and Graduate Center, City Univer, Staten Island, NY

Platinum (Pt) and Rhodium (Rh) metal nanoclusters can be envisioned as efficient and recyclable catalyst in the hydrosilylation reactions of alkenes and alkynes.[1] Pt and Rh are electron rich transition metals that are part of the largest group of catalyst used in hydrosilylation and allow synthetic manipulation over the selectivity of product formation. Hydrosilylation is a considerable reaction type in the production of organosilicon compounds and polymer chemistry. We are interested in designing new hybrid materials by the grafting of various functionalities on silicon-based polymers via hydrosilylation (Scheme 1).[2] Scheme 1 We envision that materials with unique properties can be devised in this fashion. Numerous reactions were carried out under various conditions especially that of temperature and reaction time to determine the optimum conditions of maximum yield in product and selectivity. All products were analyzed and confirmed utilizing UV-vis Spectroscopy, Infra-red (IR) Spectroscopy, Transmission Electron Microscope (TEM) and Nuclear Magnetic Resonance (NMR) Spectroscopy which clearly describes Si-C bond formation and alpha (&alpha) or beta (&beta) selectivity.



518. Synthesis and Characterization of Iron Oxide Nanoparticles Derived from Ferritin

Gang Liu, Hazel-Ann Hosein, Sudeep Debnath, Douglas Hausner and Daniel R Strongin, Temple University, Philadelphia, PA

Metal oxide nanoparticles are of great importance due to their unique size- and shape-dependent optical, magnetic, electronic and chemical properties. Herein we report a novel biological approach to synthesize iron oxyhydroxide nanoparticles (2-6 nm). The general morphology of nanoparticles as well as the electronic structure of a single nanoparticle on Au(111) were characterized with a combination of Atomic Force Microscopy (AFM), Scanning Tunneling Microscopy (STM) and Scanning Tunneling Spectroscopy (STS). The chemical reactivity towards SO_2 adsorption of FeOOH nanoparticles were examined using Attenuated Total Reflection Infrared Spectroscopy (ATR-IR). The size dependent properties, e.g,, the band gap energy and geometrical structure, on the chemical performance of FeOOH nanoparticles are discussed.

519. The LIterature of Nanoscience

Howard M. Dess, Rutgers University, Piscataway, NJ

The literature of nanoscience and technology has experienced rapid growth in recent years. This presentation offers an overview of this growth with specific attention to the following areas:

* Principal journals used by researchers in this area of R&D * Institutions active in research in the field * Countries of origin of the work * Major non-print sources of information * Current trends in the growth rate of the literature * Search tools available for finding needed information

520. Substrate-Assisted Phase Transitions of Au Nanorods

Oscar R. Miranda and Temer S. Ahmadi, Villanova University, Villanova, PA

Phase transition of metals in the nanodimensions is of both scientific and technological interest. In this work, we have studied the role of substrates on the melting of gold nanorods (AuNRs). Gold nanorods were prepared using a photochemical method. The melting process was induced by two CW UV-irradiation sources with energies of 4.13 eV and 4.89 eV. Polymer, glass, and quartz substrates were employed in this study. Phase transition was monitored with UV-visible spectroscopy and transmission electron microscopy (TEM). Our findings indicate that the nature of the substrate strongly affects the kinetics of melting of AuNRs. A simple model for energy transfer from the substrate to AuNRs is presented.

521. Electroanalytical study of anti-*S. aureus* enterotoxin B and enterotoxin B reaction on nano-patterned aluminum surface

Changhoon Chai and Paul Takhistov, Rutgers, The State University of New Jersey, New Brunswick, NJ

Immunosensing system for *Stapylococcus aureus* enterotoxin B, based on electrochemical impedance spectroscopy (EIS), was developed. To achieve the sensitivity, the nano-porous aluminum substrate was electrochemically fabricated. Then, anti-*S. aureus* enterotoxin B was immobilized on the nano-porous aluminum substrate through a specific method, which was developed for the stability of antibody on immunosensor. Morphological changes by the binding of enterotoxin B on immunosensor was studied using atomic force microscope (AFM) and the attachment resulted in a morphological change. Especially, Z value was increased and the difference was 2nm. Even though there was only 2nm increase in Z value as enterotoxin B attachment, there was significant changes in cyclic voltammogram as well as EIS analysis of immunosensor in enterotoxin B solution showed a huge difference in resistance ranging from 20 kohm to 100 kohm at 0.25Hz. As the biological reaction between anti-*S. aureus* enterotoxin B and enterotoxin B, resistance decreased as time function and enterotoxin B concentration. The presence of enterotoxin could be detected in 10 minutes and linear relationship between enterotoxin B concentration and resistance could be seen after 60 minutes. This study exhibits that immunosensing system for *S. aureus* enterotoxin B based on EIS is sensitive and fast.

522. Metal-molecule nano-junctions with organic self-assembled monolayers

Weirong Jiang[1], Eric Garfunkel[1], Nikolai Zhitenev[2] and Zhenan Bao[3], (1)Rutgers University, Piscataway, NJ, (2)Bell Laboratories, Lucent Technology, murray hill, NJ, (3)Stanford University, Stanford, CA

The metal-molecule junction plays a critical rule in molecular electronics applications. In the work presented here, various methods were used to make metal-molecule nano-junctions on self-assembled monolayers (SAM), including vacuum evaporation of metal, nano-transfer printing (nTP), shadow angle deposition on a quartz tip, e-beam lithography based nano-fabrication, as well as direct interaction in conductive atomic-force microscopy (CAFM). The junctions were characterized by both structural (SPM, SEM, TEM) and electronic methods for different thiol molecules. A comparison of results is discussed.

523. Substitutions of the amino-capped aniline trimer and potential applications in nanotechnology

Matthew C.R. Zagorski, Amber J. Reilly and Yen Wei, Drexel University, Philadelphia, PA

The aniline trimer at the emeraldine oxidation state, N, N'–bis(4'-aminophenyl)-1,4-quinonenediimine, has been synthesized via an oxidative coupling method developed in our group. Resent research efforts have been made to find suitable conducting oligomers for nano size electronic devices using this aniline oligomer. Our recent work involves substitution modifications of the above trimer oligomer in two ways: 1) by introducing n-alkyl chain(s) to the terminal amine ends of the trimer in an effort to make potential electroactive surfactant molecules; 2) by introducing thiol group(s) to one or both terminal amine ends, which may be useful in making electronic nanojunctions. An alternate method for making substituted trimers has also been implemented by using cross coupling aromatic substitution using N, N'-dichloro-1,4-benzoquinonediimine and N,N-disubstituted aniline compounds. This method may represent an economical and convenient route to N-alkyl and N-alkyl thiol substituted oligoaniline molecules.

524. Water Intrusion: A New Technique to Characterize Hydrophobic Porous Surfaces and Wetting in Nano-Confinement

Roy Helmy and Alexander Y. Fadeev, Seton Hall University, South Orange, NJ

Characterization of wetting and adhesion in nano-confined environment is of great fundamental interest due to its application in material science. This work describes a new experimental technique that provides insight into the wetting of hydrophobic surfaces in mesopores. This method utilizes the intrusion of water into the pore space of hydrophobic porous solids. The applicability of the method has been demonstrated for a series of well defined mesoporous silicas (SBA-15) hydrophobized with a monolayer of trimethylchlorosilane (pore radii of 2.5-4 nm). It is shown that capillary pressure for water in hydrophobic pores can not be described by classical models. Work of adhesion, however, for water in pores and on flat hydrophobic surfaces are in a very good agreement.

Novel Instrumentation and Applications of Mass Spectrometry in ADME studies

Presider: Dr. Walter Korfmacher Schering Plough Research Institute, Kenilworth, NJ

525. Special Applications of MS for Metabolite Identification as Part of Drug Development

Ragu Ramanathan and Swapan Chowdhury, Schering-Plough Research Institute, Kenilworth, NJ

The introduction of atmospheric pressure ionization (API) techniques, as the interface between high performance liquid chromatography (HPLC) and mass spectrometry (MS), has established LC-MS as an important characterization and quantification tool in the pharmaceutical industry. Specifically, LC-MS has dramatically changed the approaches necessary in assessing the metabolism of a novel drug candidate. For example, from a simple LC-MS analysis, the metabolic fate of a novel drug in both in vitro and/or in vivo systems can be assessed. LC-MS spectra, acquired in the full scan mode, combined with targeted searches (precursor ion and neutral loss scans) for possible metabolites, can provide information on the metabolic pathway of a novel drug. Among such metabolic modifications, oxidation of carbon (hydroxylation), nitrogen (N-oxides & hydroxyl amines) or sulfur (sulfoxides) atoms are very common and results in the shift of the LC-MS detected mass of metabolites by 16 Da from that of the parent drug. Distinguishing between hydroxylation, N-oxidation and/or sulfoxidation are important due to the N-oxide metabolites being associated with toxicity. Previously, we have shown that LC-MS, coupled with atmospheric pressure chemical ionization (APCI), can be used to distinguish N-oxides from hydroxyl and sulfoxide metabolites based on the thermal instability of N-oxides relative to other oxygenated metabolites. In this presentation, we will also show that H/D exchange, in conjunction with MS/MS, can also be used to distinguish various forms of oxide metabolites.

526. Novel LC-MS Applications for Preclinical ADME/PK Assays

Ron Kong, Dahai Dong, Kimloan Nguyen, Martha Vallejo and Gamini Chandrasena, Lundbeck Research USA, Paramus, NJ

Liquid chromatography - mass spectrometry has been extensively used as the analytical method of choice for drug level analysis of in vitro ADME screens as well as biological samples in pre-clinical animal studies. Discovery ADME/PK screens of NCEs demand robust high-throughput quantitative LC/MS/MS methods to analyze a large number of biological samples. For the quantitative analysis of plasma and brain samples, we employed a Cohesive 2300 HTLC system for on-line sample extraction. In this system, we implemented a tee-in re-focus column technique and an on-line filtering configuration that can perform automated sample cleanup as well as achieve concentration enrichment. This automated cleanup configuration significantly reduces the potential backpressure buildup. The method has proved to be robust for all calibration standards, QCs, and PK plasma samples. The statistics showed that less than 5% of all analyzed calibration standards and QCs were out of the ± 15% error range. We also automated brain tissue process by employing a Tomtec automated homogenizer (Autogizer), which eliminated all manual intervention in the tissue homogenization procedure to meet the analytical throughput demand. In the in vitro metabolic stability screen, we are implementing high-throughput LC/MS analyses using a fast LC method. A ballistic gradient has been employed to afford a total runtime of 1.5-minute. Such fast LC/MS methods will make it possible to analyze 900 samples per day.

527. Rapid Pharmacokinetic Analysis in Drug Discovery Utilizing Ultra Performance Liquid Chromatography coupled with the Micromass Quattro Premier

Cymbelene Nardo, Dr. Sam Wainhaus and Dr. Walter Korfmacher, Schering Plough Research Institute, Kenilworth, NJ

With the increasing number of compounds requiring pharmacokinetic analysis in early drug discovery comes the challenge of increasing throughput and turnaround time. The key to this endeavor is to “kill” compounds with unacceptable pharmacokinetic profiles as early as possible within drug discovery. We have previously reported on the use of the cassette accelerated rapid rat screen in order to facilitate this process and a similar strategy was extended to monkeys as well. Previously, ballistic gradients with microbore columns were used, but with the recent introduction of the ultra performance liquid chromatography (UPLC) this has become an option to improve turnaround time.

We utilized the Acquity Ultra Performance Liquid Chromatography (UPLC) system from Waters coupled with the Micromass Quatro Premier to analyze rat plasma, brain and liver samples as well as monkey plasma samples. This combination has become a powerful tool for rapid analysis of biological samples allowing us to provide same day turnaround time for a variety of studies.

The Quatro Premier Masslynx 4.0 software has an option package called QuanOptimize that allows the scientist to automate MS/MS method development. It has the capability of multiple compound tuning, automated acquisition and quantitation of analytical samples for multiple sets of studies. Additionally, it has the capability of simultaneously tuning in both ESI(+/-) and APCI(+/-).

The UPLC/Quatro Premier system improved our cycle time by 50-100% with improved sensitivity.

528. On-line Sample Preparation Techniques for Faster LC-MS/MS Assays of Preclinical Samples

Voon S. Ong, Memory Pharmaceuticals, Montvale, NJ

An integrated on-line solid phase extraction approach incorporating turbulent flow chromatography (TFC) with mass spectrometric detection was developed to support in-house drug discovery and development efforts. Activities such as metabolic stability/profiling and pharmacokinetic characterization support are carried out on a single unified platform. Two different TFC column-switching configurations, parallel and serial, are presented. The first, a dual, parallel TFC-column configuration, is capable of high-throughput analysis but carryover can reach as high as 0.24%. The characteristics of the instrument operating in the parallel configuration are provided for analysis of samples generated during in vitro metabolic stability assessments, a key screen during the lead optimization phase of drug discovery. Operating in this configuration, the system has the capability of performing on-line solid phase extraction and analysis of approximately 400 samples containing phosphate-buffered saline in approximately 14 hours. The second, a serial TFC-column configuration, was used to perform direct plasma injection analysis. The advantage of the serial configuration is the relatively low carryover (<0.040%). A method developed using the serial column configuration for the determination of dihydropyridines in plasma samples is given as an example. Analytical performance criteria examined during method development and validation included linearity, accuracy, precision, and recovery. The robustness of the technique was demonstrated in the analysis of over 2500 plasma samples generated during preclinical drug development studies. This approach has been further applied to combined analysis of plasma and homogenized brain tissue samples in a single analytical batch using acetonitrile precipitation as sample pretreatment for both matrices.

529. APPI-MS: Applications and Use in a Drug Discovery Environment

Ganfeng Wang and Yunsheng Hsieh, Schering-Plough Research Institute, Kenilworth, NJ

Electrospray ionization (ESI) and atmospheric pressure chemical ionization (APCI) have been widely employed as very useful tools for the liquid chromatographic/mass spectroscopic (LC/MS) analysis of polar compounds. Non-polar compounds, however, are difficult to analyze with these techniques due to their soft ionization mechanism. Recently many new approaches have been introduced. Among them, atmospheric pressure photoionization (APPI) is the last arrival in the family of atmospheric pressure ionization methods to couple mass spectrometry (API-MS). It was originally developed to broaden the range of LC/MS ionizable compounds towards less polar or non-polar compounds that cannot be analyzed by electrospray or atmospheric pressure chemical ionization. It has been used for analysis of steroidal and non-steroidal compounds in both pharmaceutical and drug metabolism assays. This talk will present a short theoretical outline on the use of a dopant and APPI sources, and describe factors that affect the performance of APPI, such as the dopant, mobile phase composition and temperature. In addition, example APPI applications and use in a drug discovery environment will be shown.

530. Drug ADME analysis, including tissue metabolite profiling, in a few rats using a combination of microplate scintillation counting, capillary LC/MS, and whole-body autoradiography

Mingshe Zhu, Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, NJ

Quantitative whole-body autoradiography (QWBA) is increasingly being used to determine drug tissue distribution. Application of the technique would be enhanced if it could also be used to distinguish between the parent drug and metabolites. A method is described for drug ADME analysis, including characterization and quantification of tissues metabolites, using microplate scintillation counting and capillary LC/MS in conjunction with QWBA. Frozen whole-body sections as well as plasma, urine and bile were obtained from rats dosed with a radioactive drug. Tissues of interest were excised from the sections, followed by radioactivity profiling by HPLC-microplate scintillation counting with a detection limit of 18 DPM. Fractions containing unknown components were recovered and further structurally characterized by capillary LC/microspray ion trap MS. This integrated method provided a tool for complete ADME analysis in a few rats, including quantitative determination of radioactivity and metabolite distribution in tissues, characterization of unknown metabolites, and correlation with metabolite profiles in the plasma, urine and bile. The technique may prove particularly useful for the study of tissue- or organ-specific drugs (e.g. CNS compounds) as well as tissue-specific toxicity.

Pharmaceutical Engineering Fundamentals (Workshop)

531. Pharmaceutical Engineering Fundamentals Workshop

Hugo Fernandez, Skanska Pharmaceutical Group, Parsippany, NJ

Course Intent: This course is an introduction to the Engineering Elements of the Pharmaceutical Industry. This course will be most valuable to individuals with an engineering/technical background seeking a familiarity with pharmaceutical manufacturing operations.

Course Syllabus:

- Introduction and Overview of the Pharmaceutical Industry with emphasis on Applicable Regulations and Definitions: - Water Systems – General Overview - Fundamentals of Heating Ventilating and Air Conditioning (HVAC) - Reactors and Pressure Vessels - Fundamentals of Reliability, Maintainability, and Availability (RAM) - Tableting Operations - Parenteral Operations - Commissioning and Validation

Pharmacokinetics in Drug Discovery and Development

Presider: Dennis Scott Pfizer, Groton, CT

532. Nonspecific brain binding as an indirect tool to assess CNS penetration

Tristan Maurer, Pfizer, Groton, CT

It has long been recognized that relative plasma and tissue binding largely determine drug distribution. In this work, we demonstrate that unbound brain (fub) and unbound plasma (fup) fraction paired with a measure of equilibrium brain and plasma exposure can be used as an indirect model for the assessment of brain penetration and for the direct estimation of free brain concentrations. Preclinical brain-to-plasma ratio's (B/P) for the majority of over 100 proprietary and marketed CNS agents examined thus far can be accurately predicted via fup/fub ratio measured in vitro. In instances where brain distribution is known to be impaired via efflux transport, the degree of impairment is quantitatively indicated by the discrepancy between B/P ratio and fup/fub. Application of this approach to multiple species suggests that the degree of tissue binding and distributional impairment (due to P-gp) are quantitatively similar among species. In addition, PK-PD exercises indicate that the concentration of drug available to interact with CNS targets can be accurately estimated through the product of fub and total brain concentrations. These results indicate that this approach offers a simple and nonspecific (species and mechanism) means for determining CNS penetration and free drug exposure.

533. Human dose projection from pre clinical CNS models: Lundbeck experience

Gamini Chandrasena, Lundbeck US Research, Paramus, NJ

It is often the practice at Lundbeck Research, USA to perform human dose projections of their discovery leads, prior to recommendation for early development evaluation. We have been using number of approaches, including microsomal and hepatocyte Clint predictions as well as allometric scaling of modeled PK parameters to predict minimum human efficacy dose. In the case of SSRI inhibitors, the corresponding CNS target occupancy will be incorporated, as well, to strengthen the dose predictions. The pre-clinical utilization of these approaches for early human dose projections will be discussed.

534. Application of Physiologically-Based Models in Drug Discovery and Development

David Plowchalk, Pfizer, Groton, CT

Although PBPK models are well-established tools for chemical risk assessment, their use in the drug discovery and development process has only recently been gaining acceptance. This presentation will illustrate advantages and limitations of PBPK modeling when applied in the pharmaceutical industry setting. Case studies will be presented in which PBPK models applied to therapeutic agents provided distinct advantages over conventional data-based PK modeling techniques. The availability and utility of in vitro, in vivo, and in silico tools and data for use in model parameterization and calibration will also be discussed.

535. Hydrophobic Drug Aggregates: Structure and Biology

Eddy Arnold[1], Yulia Frenkel[2], Arthur D. Clark Jr.[1], Kaylan Das[2], Yuh-Hwa Wang[3], Paul J. Lewi[4] and Paul A. J. Janssen[2], (1) Rutgers University, Piscataway, NJ, (2)Center for Advanced Biotechnology and Medicine, and Rutgers University, Piscataway, NJ, (3)UMDNJ, Piscataway, NJ, (4)Center for Molecular Design, Belgium

Using a variety of physicochemical approaches, we have determined that some highly hydrophobic drugs with great promise for the clinical treatment of AIDS form aggregated structures in simple aqueous solutions mimicking gastrointestinal conditions [1]. Aggregate size and oral bioavailability are correlated; compounds forming aggregate structures with 30-100 nm in radii had good bioavailability and those with aggregate sizes exceeding 250 nm in radii had poor bioavailability. The aggregates contain on the order of a million drug molecules, with size depending on the structure of the compound and the solution conditions. In the current study we have been exploring the structure and mechanisms of formation of NNRTI aggregates using diffraction, spectroscopic, and computational simulation approaches. The aggregates appear to represent an intermediate state between monomeric and precipitated forms of the hydrophobic compounds. X-ray powder diffraction measurements from the aggregates using synchrotron radiation at CHESS provided evidence for the presence of micro-crystalline domains. From our findings we are hoping to deduce an explanation of the unique biological behavior of these compounds. [1] Frenkel, Y.V., Clark, A.D., Jr., K. Das, Wang, Y.-H., Lewi, P.J., Janssen, P.A.J., Arnold, E., J. Med. Chem., 2005, in press.

536. In Silico Prediction of ADME Properties: Current Status of Predictive Models

Terry Stouch, Editor-in-Chief, Hopewell, NJ

This presentation will discuss the current state of predictive in silico ADME models and their utility in early drug discovery.

Physical Chemistry Posters

Organizer: Anita J. Brandolini William Paterson University, Wayne, NJ

537. Evaluation of shelf stability of food emulsions by Electrochemical Impedance Spectroscopy

Shiby Paul and Paul Takhistov, Rutgers, The State University of New Jersey, New Brunswick, NJ

The stability of emulsions and particle suspensions is explained by different stages, namely, creaming or sedimentation, flocculation of drops or particles, coalescence between drops and phase separation. Development of reliable and sensitive methods to monitor these changes has always interested many research groups. In this paper we propose a real time non-destructive method based on electrochemical impedance spectroscopy to describe the ageing and deterioration profile of oil-in-water emulsions. Complex impedance of the undisturbed emulsion was measured over a frequency range of 5Hz to 13MHz at different time intervals over two weeks. This methodology was applied to monitor changes in milk, a typical oil-in-water emulsion, and experimental set up was designed to measure the values of the intact system, i.e. through the package. The impedance measurements are sensitive to small changes in the phase separation and impending deterioration. The results from the proposed method were compared and the reliability verified by measurements on conductivity, reflectance measurements, gravimetric analysis, and also physico-chemical tests to test the stability of the emulsion. The simplicity and sensitivity of the proposed method makes it a useful technique in food industry with wider applications including product formulation and process control and shelf life studies.

538. Mechanistic interpretation of molecular interactions of tetracycline with clay and organic matter

Pankaj Kulshrestha, H.S. Atreya, Dinesh Sukumaran, Rossman F. Giese and Troy Wood, University at Buffalo, The State University of New York, Buffalo, NY

Tetracycline-class of antibiotics is licensed as growth promoters for livestock in United States. This has also led to increased emergence of resistant strains of pathogenic bacteria that could potentially impact human health. Tetracycline input to the soil and aquatic environments due to the use of manure and sewage sludge in agriculture as soil conditioners requires the knowledge on their fate, transport and factors that affect their mobility in soil. To determine the factors that might affect the mobility of these antibiotics in soil, the mechanisms of interaction of oxytetracycline with model clay adsorbents and organic matter were investigated as a function of suspension pH. The adsorbents used were native montmorillonite (SWy-2), Na-montmorillonite (Na-SWy-2), and hexadecyl trimethyl ammonium-montmorillonite (HDTMA-montmorillonite) and natural organic matter. Attenuated Total Reflectance Fourier Transform Infrared (ATR/FT-IR) showed that tetracycline hydrogen bonds with inter-layer water molecules in montmorillonite, Na-montmorillonite, and humic acid-montmorillonite at lower pH values whereas it directly co-ordinates with HDTMA cation in HDTMA-montmorillonite at alkaline pH values. Nuclear Magnetic Resonance (NMR) parameters such as spinspin, spin-lattice relaxation and subtle chemical shifts of 1H, 13C, 15N nuclei also provide molecular information on the predominant sites and the interaction mechanisms between tetracycline pollutants and environmental matrices.

539. Adsorption of Glyphosate on Montmorillonite, a Theoretical Study

George A. Khoury and Lorena Tribe, Penn State Berks, Reading, PA

Glyphosate (N-phosphonomethylglycine) has clearly emerged as the most used herbicide in the world. Some examples of weed killers implementing the use of glyphosate are Roundup®, Rodeo®, and Accord®. Glyphosate (GPS) is a postemergent herbicide that is effective against broadleaved and grassy weeds. Being as popular as GPS is, it is clearly of keen interest to model what occurs at the physical molecular level as this herbicide may have long term effects on the environment. Our group chose to model glyphosate relative to the smectite clay potassium-montmorillonite, using the program Spartan Pro. The glyphosate, through molecular mechanics calculations, was seen to be attracted to the layers of the clay. We found the changes in energy associated with the stabilization of six particular configurations of the system, as well as distances between key elements that are expected to bond with elements on the smectite clay. We present the correlations we observed between the equilibrium interatomic distances and the changes in energy.

540. Detection of residues of tetracycline antibiotics in soil fertilized with manure and wastewater using Enzyme Linked Immunosorbent Assay

Pankaj Kulshrestha, Rossman F. Giese and Troy D. Wood, University at Buffalo, The State University of New York, Buffalo, NY

The degradation of chlortetracycline (initial concentration of 5.0 ppm) in soil fertilized with manure and grown with and without corn plants was followed using ELISA to measure the decline in the chlortetracycline concentrations. Low levels of chlortetracycline residues (0.5 to 1.0 ppm) remained detectable in soils for up to 5 months. It was observed that the degradation of chlortetracycline followed first order degradation kinetics and its half-life was greater in the soil planted with corn than the soil in which the corn plants were not grown. Tetracycline residues analyzed by ELISA in the influent and effluent wastewater samples showed minimal degradation of the drug during biological treatment. Oxytetracycline concentrations as high as 1250 µg/Kg (0 – 2 inches soil depth) and as low as 11 µg/Kg (12 – 14 inches soil depth) were

detected using ELISA in soil fertilized with swine manure sampled from a farm. The antibodies employed in ELISA exhibited high relative affinity for tetracycline and were also characterized for their ability to detect structurally related tetracyclines such as chlortetracycline, oxytetracycline and their corresponding epimers and anhydromers. The specificity and crossreactivity of these antibodies are discussed in relation to the electrostatic potential mapped on electron density surfaces of tetracycline antibiotics and their transformed products.

541. Potential Energy Surface for ArHCN

Rudolph C. Mayrhofer, Kutztown University, Kutztown, PA

A potential energy function for the Ar-HCN complex will be presented that incorporates ab initio points that have been calculated over the full range of motion. Spectroscopic constants from the fit will be presented and compared to previous work from other groups. The goal is to develop a surface that will be used to study the isomerization reaction for HCN ---> CNH using classical mechanics.

542. Simulations of Methane in Liquid Water using ab initio force fields

Omololu Akin-Ojo and Krzysztof Szalewicz, University of Delaware, Newark, DE

Methane in water is a classical prototype to study the hydrophobic effect. This is reflected by the number of molecular simulations done on this mixture (see, e.g., Ref. [1] and references therein). Most of these simulations, however, give results different from our traditional view of hydrophobic interaction (HI) which is typically in terms of entropy. This discrepancy between our conventional view of HI and computational studies could be due to deficiencies in the force fields used in the simulations. Most of these simulations do not have explicit potentials for the CH_4--H_2O system but instead use so-called ``mixing rules'' to obtain force fields for this heterogenous dimer from those for the H_2O--H_2O and CH_4--CH_4 dimers. These mixing rules are crude approximations. In this work we develop *ab initio* force fields for the CH_4--H_2O interactions and use these in simulations. These potentals were obtained using both symmetry-adapted perturbation theory (SAPT) and the supermolecular methods at different levels of electron-correlation treatments, namely, at the second (MBPT2) and fourth (MBPT4) order levels of the many-body perturbation theory with the Moller-Plesset partitioning of the Hamiltonian as well as the coupled-cluster theory with single and double excitations and noniterative inclusion of triple excitations [CCSD(T)]. We expect that using such accurate interaction energies in molecular simulations will help us determine the truth about the hydrophobic effect in mixtures of methane and water.

References: [1] H. Shinto, S. Morisada, M. Miyahara, and K. Higashitani, J. Chem. Eng. Japan **36**, 57 (2003).

543. The Solubility of Chiral Enantiomers and Racemates as a Function of Enthalpy Differences in the Crystalline solids and Activity Coefficients in the Solution

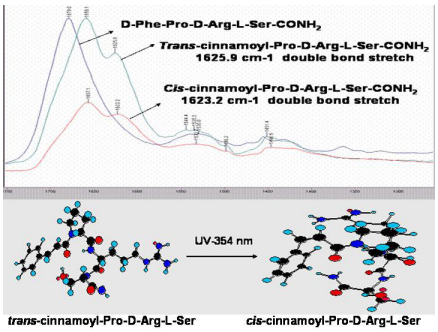
S. Alex Studniarz, Penn State University, Sharon, PA

The aqueous solubility of five chiral alpha hydroxyl carboxylic acids was measured as a function of temperature and will be given. The enthalpy difference between enantiomer and the corresponding racemate was calculated from a new derived equation and the measured enantiomer and racemate solubility at different temperatures. The enthalpy difference between the enantiomer and their corresponding racemate was found to be on the order of hydrogen bond energies; Also the enthalpy difference was either positive, negative, or nearly zero depending on the compound. The enthalpy difference is attributed to difference in the hydrogen bonding in the crystalline solid and differences in the spatial molecular packing due to the molecular asymmetry. The activity coefficients were always less than two and usually less than 1.5. Some racemates were found to behave as mixture of enantiomers and others as if they were different compounds. The results presented here should be a useful guide in determining differences in enthalpy between the crystalline solid enantiomer and racemate or in estimating the ratio of racemate to enantiomer solubility from diffences in enthalpy of formation.

544. Molecular modeling, circular dichroism and FTIR studies of conformation adopted by tetrapeptides with inhibitory activity for thrombin

Cristina C. Clement[1], Manfred Philipp[1] and Christian Matthaeus[2], (1)Lehman College, City University of New York (CUNY), NYC, NY, (2)Hunter College, City University of New York (CUNY), New York City, NY

A structure-based design of a library of tetrapeptides containing the sequence space D-Phe/X(P3)-L-Pro(P2)-D-Arg(P1)-P1' was employed to discover potential inhibitors for thrombin (X= analogs of Phe, such as constrained analogs (L)/(D)-Tic [1,2,3,4-tetrahydro-isoquinoline-3-carboxylic acid] and trans/cis-cinnamic-acids). The peptides were docked into active site of thrombin by taking the X-ray coordinates of thrombin template 1ABJ.pdb using the software “SCULPT” provided by MDL. Circular dichroism investigations are showing a sequence-dependent beta turn structures (I and III) in solution at low and neutral pH. FTIR microscopy studies using peptides solid films confirmed at least 3 wavenumber shifts for the double bond stretch frequencies of the two geometric isomers trans and cis-cinnamoyl peptides. SAR (structure-activity relationship) suggests that tetrapeptides which adopt beta turn conformation in solution are more active toward inhibiting thrombin and the trans isomers are better inhibitors than the cis-cinnamoyl peptides.



545. Scattering of Propanol off Ionic Melts: a Theoretical Study

Barbara E. Graves and Lorena Tribe, Penn State Berks, Reading, PA

Molecular beam studies of collisions and reactions at surfaces allow us to explore the fine details of energy transfer and reaction steps. We are specifically looking at shooting both argon and propanol onto a surface of molten sodium and potassium hydroxides in order to gauge the effect of a strongly basic ionic solution on alcohols.

We are simulating this experiment, which was performed experimentally by Dr. Gilbert Nathanson of the University of Wisconsin-Madison, using the Tinker software package. We modified the existing input files to model the formation of a gas-liquid interphase, and to then include scattering off the newly formed surface of the melt. We adjusted the parameters to match the experimental conditions.

We will show a preliminary density profile for the ionic melt, which shows a very clear liquid-gas interphase at 463 K and we will outline the method we have developed to gather data for the energy-dependant time-of-flight simulations.

546. Molecular Dynamics Calculations of Mg-Cu Alloys

Andrew J. Modzelewski and Lorena Tribe, Penn State Berks, Reading, PA

Copper and magnesium alloys are used in the walls of nuclear reactors. There is great interest in studying the stability of the phases of these alloys as a function of temperature and pressure. We approach this problem by developing a molecular dynamics simulation code that will allow a step-by-step analysis of the transition between phases, as a complement to previous Monte Carlo simulations of the same system. The first step of this study involves developing a molecular dynamics code for a pure substance using a simple Lennard-Jones potential. Subsequently, the second element will be incorporated into the melt and finaly, the potential will be replaced by one developed with the embedded atom method.

547. Solvation and Solvation Dynamics in Room-Temperature Ionic Liquids

Mark N. Kobrak, Brooklyn College -- CUNY, Brooklyn, NY

Room-temperature ionic liquids have generated considerable interest as environmentally benign solvents for chemical processing, but little is known about the connection between their chemical structure and their properties as solvents. We present the results of molecular dynamics simulations that indicate how ions in solution respond to the presence of a molecular solute, and develop an analytic theory that can be used to connect the chemical structure of an ionic liquid to its macroscopic liquid properties.

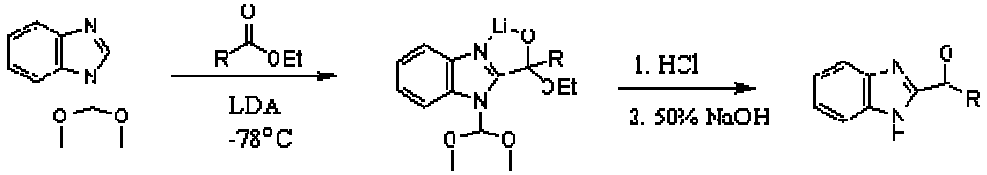
Physical Organic

Organizer: Cecilia H. Marzabadi Seton Hall University, South Orange, NJ
Presider: Simon Leung Bristol Myers Squibb, New Brunswick, NJ

548. Efficient Acylation of Benzimidazoles with Esters and Identification of a Tetrahedral Hemiacetal Alkoxide Intermediate

Kenneth J. Fitch, Merck Research Labs, Rahway, NJ

Substituted benzimidazoles are important intermediates for the synthesis of various drugs and natural products. Substituents at the 2-position are generally introduced by the reaction of the 2-litio derivative of N-protected benzimidazoles with electrophiles. In some cases when esters were used as acylating agents, the yields were low and bis addition products predominated. Here we describe a general method for the efficient acylation of 2-lithio benzimidazoles with esters, lactones and lactams and present evidence of a tetrahedral hemiacetal alkoxide interemediate responsible for the selective reaction.



549. Withdrawn

550. Polysulfane Natural Products as Evolved Chemical Warfare Agents

Edyta M. Brzostowska and Alexander Greer, The City University of New York (CUNY), Brooklyn College, Brooklyn, NY

Ascidians (tunicates) contain compounds with a large range of pharmacological activities. With the most common of chemical ingredients, elemental sulfur and dopamine, we hypothesize that an ascidian has developed a means to protect itself from predators using in essence chemical warfare. A novel aspect of this work is the idea that tunicates can filter elemental sulfur, transform solid insoluble S_x, and transfer sulfur atoms chemically into a phenolic molecule for use as a protecting agent. Our work focused on a biomimetic HS_x^- reaction with *o*-quinone as a biosynthetic generator of antimicrobial (anticancer) *o*-benzopolysulfanes. Experiments using HPLC and SIM GC/MS revealed the presence of benzotrithiole, pentathia-benzocycloheptene, and heptathia-benzocyclononane compounds. The benzo-S3, -S5, and -S7 products co-exist in equilibrium, where their relative concentrations are influenced by solvent. Detection of heptathia-benzocyclononane is an exciting new result that had been predicted by our density functional theory (DFT) computation. This suggests that natural product *o*-benzopolysulfanes exist as a mixture of the S3-, S5-, and S7-homologs. Factors controlling the formation and interconversion of the S3-, S5-, and S7-polysulfanes and possible biological implications will be discussed.

551. Does nature preferably select macrocycles based upon ring size?

Aaron R. Frank, Nicola S. Farina, Orrette R. Wauchope, Mo Qi and Alexander Greer, The City University of New York (CUNY), Brooklyn College, Brooklyn, NY

A study of ring size patterns on the natural selection of macrocycles is presented. Chemical literature provided structural information for the study. Analysis of 4000 natural products reveal that about one in five possess a macrocycle structure, where an unexpected preference exists for 14-, 16-, and 18-membered ring systems. An even-over-odd preference exists in natural product macrocycles from terrestrial and marine sources. Natural 14-, 16-, and 18-membered rings predominate in heterocycle, carbocycle, and cyclic peptide structures, implying an origin independent of a two carbon (acetate) bioinsertion pathway. The origin of the preference would be difficult to examine biochemically because of the large number of individual biosynthetic pathways. However, the results raise an interesting question concerning the limited diversity of macrocycle ring sizes and the nature of the constraints that may cause them. Implications for drug design will be discussed.

552. UV-Visible Absorption of 10-Chloro-9-Anthraldehyde as a Probe of Hydrogen Bonding in Bioorganic Systems

Josette Crout Seibles, Manhattanville College, Purchase, NY

The UV-visible absorption of halogenated anthracenyl ketones is dominated by the absorption characteristic of the anthracene moiety due to pi to pi* transitions. In certain media e.g. methanol, this absorption also exhibits the vibronic fine structure characteristic of anthracene. These vibronic bands represent the aromatic ring breathing vibrational modes. The lambda max of aromatic pi-pi* absorption is well known to red shift as solvent polarity increases. However, for anthracenyl ketones the lambda max blue shifts when solvent polarity increases and the solvent is a hydrogen bonding solvent such as methanol. This shift is as much as 18 nm (chloroform to methanol) for 10-chloro-9-anthraldehyde. This molecule can

hydrogen bond with methanol via the unshared electron pairs on the carbonyl oxygen. This intermolecular hydrogen bonding is the apparent reason for the observed blue shift. Anthracene derivatives with nitrogen atoms capable of hydrogen bonding have recently been reported to blue shift by a few nanometers in alcoholic solvents presumably also due to hydrogen bonding (J. Phys. Chem., 2004, 108, 7843-7852). In this study, selected parameters of the vibronic fine structure of the anthracenyl moiety of halogenated aromatic ketones were measured in a variety of hydrogen bonding media. Other molecules studied included 9-trifluoromethylanthryl ketone and 9-anthraldehyde. Parameters measured included lambda max (0-0 transition), band width, band separation, band shape and molar extinction coefficient. These parameters were then compared to determine which parameters would be most sensitive to monitor hydrogen bonding via the carbonyl.

553. The Concept of Protobranching and its Paradigm Shifting Implications

Matthew D. Wodrich and Paul V. R. Schleyer, The University of Georgia, Athens, GA

Branched alkanes like isobutane and neopentane are more stable than their straight chain isomers, n-butane and n-pentane (by 2.8 and 5.5 kcal/mol, respectively) due to the greater number of stabilizing 1,3-interactions. For example, there are three 1,3-interactions in isobutane but only two in n-butane. However, such attractive 1,3-interactions (which we call “protobranching”) also stabilize all n-alkanes relative to ethane (which has none). There is one in propane, two in n-butane, three in n-pentane, etc. “protobranching,” is not considered in conventional evaluations, e.g., of the strain energy of rings and of hyperconjugation. When protobranching is taken into account, the ring strain of cyclopropane is reduced from 27.7 kcal/mol (based on propane, which is stabilized by one protobranch) to 19.2 kcal/mol (based on ethane). Correction for torsional strain reduces this value further, by 3-6 kcal/mol. Values for hyperconjugation, +5.3 and +7.7 kcal/mol for alkenes and alkynes respectively, are obtained by adding the protobranching corrections.

554. Effects of Introducing a Rigid Spacer into Gemini Surfactants: Reversal of the Hofmeister Series and Evidence of Ch•••X- Hydrogen Bonding

Brian P. Regler and Laurence S. Romsted, Rutgers University, Piscataway, NJ

Cationic gemini surfactants, twin tailed surfactants with spacers between the cationic head groups, have emerged as a fascinating area of study during the last decade. There has been little research conducted to determine counterion interactions with the head group. Chemical trapping results of 1-n-1 (n = 2-4) show that Br- is bound better than Cl- and that as the spacer length, n, gets longer, counterion binding decreases. We believe that this strong counterion binding can be explained by the “pincer” binding model in which an anion can simultaneously interact with both positive charges, and the flexibility of the spacer is related to the strength of interaction. By placing the two positive charges on a rigid five membered ring, 1,1,3,3-tetramethylimidazolidinium (1-Im-1), counterion binding should be reduced. Chemical trapping of 1-Im-1 2 Br- demonstrated that the rigid spacer has weaker counterion binding than the flexible 1-n-1 cations, however, 1-Im-1 2 Cl- displayed stronger counterion binding than any of the 1-n-1 cations. Crystal structures were obtained of 1-Im-1 2 X- (X- = Cl-, Br- and I-) in which one counterion sits above the ring in position to interact with the methyl groups of the imidazolidinium. FT-IR spectra are consistent with hydrogen bonding occurring between the methyl groups and the halide ion in a CH•••X- nature.

555. Determining the distribution of an antioxidant between the oil, interfacial and aqueous regions of food-like emulsions stabilized by C12E6

Krishnan Gunaseelan and Laurence S. Romsted, Rutgers University, Piscataway, NJ

We have developed a new approach for estimating the distributions of antioxidants in opaque, surfactant based, macroemulsions based on the pseudophase model for homogenous microemulsions. The distribution of *t*-butylhydroquinone, TBHQ, in emulsions composed of tributyrin, $C_{12}E_6$, and acidic water is described by two partition constants between the oil and interfacial, P_O^I, and the water and interfacial, P_W^I, regions. To estimate values for P_O^I and P_W^I requires fitting two independent data sets with two independent mathematical relations and solving two equations simultaneously. One data set was obtained by electrochemical determination of the observed rate constant, k_{obs}, for reaction of TBHQ with an arenediazonium ion probe as a function of $C_{12}E_6$ volume fraction. The second data set was obtained by determining the partition constant, P_O^W, of TBHQ between tributyrin and water in the absence of surfactant by UV-Visible spectrometry, $P_O^W = 0.015$. The values of the partition constants in the emulsion are: $P_O^I = 11$ and $P_W^I = 7.11 \times 10^2$. Application of this approach to a variety of antioxidants in emulsions containing different food oils and emulsifiers should provide new insight into the factors controlling antioxidant distributions and may lead to a development of a new scale of antioxidant efficiency.

Surface and Interface Science I

Organizer: Yves J. Chabal Rutgers University, Piscataway, NJ
Organizer: Theodore E. Madey Rutgers, The State University of New Jersey, Piscataway, NJ
Presider: Yves J. Chabal Rutgers University, Piscataway, NJ
Presider: Theodore E. Madey Rutgers, The State University of New Jersey, Piscataway, NJ

556. Biochemical Surface Modification of Self Assembeld Monolayers

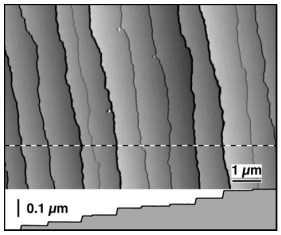
Susan C. D'Andrea and Alexander Y. Fadeev, Seton Hall University, South Orange, NJ

This work describes the use of enzymes for the modification of organosilicon monolayers supported on silica and glass surfaces. Through the use of enzymes, new surfaces can be developed whose synthesis may not be possible using conventional chemical methods. Monolayers containing adsorbed phospholipids, and proteins, with enzymatic cleavage sites for lipases, proteases, and phosphatases are investigated. The reactions produce substantial changes in wettability (from wettable to non-wettable and vice versa) of the surfaces. The progress of the reactions is investigated by ellipsometry, contact angles, and capillary rise techniques.

557. Chemical Control of Surface Morphology: Taming Instabilities in Silicon Etching

Melissa A. Hines, Simon P. Garcia and Hailing Bao, Cornell University, Ithaca, NY

Under some conditions, simple chemistry can be more precise than conventional microfabrication. For example, aqueous KOH solutions selectively attack all silicon surfaces except {111} planes. Because of this, KOH is widely used in micromachining to selectively produce precisely aligned and oriented surfaces, in some cases with near-atomic smoothness. In spite of their widespread use, KOH etchants have defied simple chemical explanation, in part because of the complex morphologies they produce. Using a combination of STM experiments and kinetic Monte Carlo simulations, we show that the KOH etching of silicon surfaces is severely affected by inhomogeneities that develop in the etchant as a result of the highly anisotropic (site-specific) etching reactions. These inhomogeneities drive a kinetic instability similar to the instability that causes traffic jams on crowded highways. The instability leads to the production of wide, nearly atomically flat terraces separated by step bunches containing tens or even hundreds of atomic steps. The instability can be “tamed” with microfabricated etch barriers, allowing the production to highly regular arrays of macrosteps. The striking effect of inhomogeneities is attributed to an underappreciated aspect of silicon etching -- the chemistry of the etch product.



AFM image of a KOH-etched vicinal Si(111) surface illustrating the chemical production of a well ordered array of macrosteps separating nearly atomically flat terraces. The orientation and spacing of the macrosteps were controlled with a microfabricated etch mask. The lower panel shows a representative image profile.

558. Wet chemistry on germanium (100) for high-κ dielectric growth

Sandrine Rivillon[1], Kenneth A. Bratland[1], Yves J. Chabal[1], Fabrice Amy[2], Antoine Kahn[2] and Marek P. Boleslawski[3], (1)Rutgers University, Piscataway, NJ, (2)Princeton University, Princeton, NJ, (3)SAFC, Sheboygan Falls, WI

Germanium is a promising semiconductor substrate for high-speed electronics due to its higher carrier mobilities. Control of its Ge/GeO_2 interface and Ge surface chemistry is critical because it is difficult to establish reliable wet chemical cleaning and passivating methods, particularly for the growth of high-κ dielectrics. Controlling the chemical nature of the surface is essential to achieve an abrupt interface between Ge and high-κ dielectrics. We have investigated different wet chemical methods for cleaning, oxidizing and H-terminating germanium substrates, using infrared absorption spectroscopy (IRAS) and X-rays photoelectron spectroscopy (XPS) as the main characterization techniques. The native oxide is characterized by TO and LO modes at 840 and 930 cm^{-1} and can be easily dissolved in deionized water. Presence of GeO is also observed is some cases. The native oxide thickness is larger than the oxide created by exposing a H-terminated Ge(100) wafer to room air, to UV-ozone or to H_2O_2. A monolayer H-termination can be achieved on Ge(100) using HF-etching after a cleaning process involving deionized water and hydrogen peroxide. This monolayer is composed of both Ge-H at 1990 cm^{-1} and $Ge-H_2$ at 2020 cm^{-1}, as expected on Ge(100). The morphology of the etched surfaces depends on the initial defect concentration of the bulk substrate, leading for high defect density to “porous” surfaces. We have also studied in situ the initial growth of HfO_2 on H-terminated and oxide-free Ge(100), paying particular attention to the nature of the interface between Ge and HfO_2.

559. Silicon Surface Functionalization for High-κ Dielectrics Growth

Yu Wang, Ming-Tsung Ho, Leszek Wielunski, Lyudmila Goncharova, Torgny Gustafsson and Yves Chabal, Rutgers University, Piscataway, NJ

Atomic layer deposition (ALD) is one of the best methods to grow highly conformal and uniform high-κ thin films. A central issue, however, is the formation of unwanted interfacial SiO_2 during growth. In this work, we report several approaches based on surface chemical functionalization to minimize interfacial SiO_2 layer during high-κ dielectrics deposition. Specifically, we have investigated the growth of HfO_2 on silicon using tetrakis(ethylmethylamido) hafnium (TEMAH) and water vapor (or ozone) as precursors. We find that surface passivated by hydrogen, chlorine, or silicon nitride can effectively prevent silicon oxidation in the process of HfO_2 ALD, while fostering a linear growth of HfO_2. We have also identified the presence of hydroxyl incorporated in the HfO_2 film, which can be partially removed by high temperature annealing. However, when the post annealing temperature is increased above 500^{o}C, SiO_2 interfacial layer start to develop and the crystallization of hafnium oxide is observed.

560. Buried Interfaces in Thin Molecular Films and Colloids

Hai-Lung Dai, University of Pennsylvania, Philadelphia, PA

The electronic properties of molecular thin film devices are much affected by the structure and dynamics at the interfacial layer between the film and substrate. To be able to understand and even modify colloidal properties, which are controlled by particle-solvent and particle-particle interactions, requires knowledge of the functionality and structure at the surface of colloidal particles. Yet, probing the properties of these buried interfaces has been quite an experimental challenge. In this talk we will show that by using a combination of nonlinear optical, such as Second Harmonic Generation, and surface science techniques we can probe the structure and charge transfer bonding of the interfacial layer between an thin semiconducting organic film and a metal substrate and the structure and adsorption characteristics of the interfacial layer of a colloidal particle.

561. The Potentiometric response during Layer-by-Layer Deposition

Manju Manju and Kalle Levon, Polytechnic University, brooklyn, NY

It has been reported that polymer absorption through layer-by-layer deposition lead to appreciable changes in the electrical conductance of devices, making a label-free high potential detection of biomolecules .The potentiometric responses of alternate depositions of negative and positively charged polymer layers on the surface of polyaniline are measured with increasing number of layers. As compared to previous result, our new approach makes a significant change in the potentiometric responses. Further research uses this electrode to determine the response of biopolymer for a more significant contribution to the electronic biosensing signal.

Surface and Interface Science Posters

Organizer: Anita J. Brandolini William Paterson University, Wayne, NJ
Organizer: Yves J. Chabal Rutgers University, Piscataway, NJ
Organizer: Theodore E. Madey Rutgers, The State University of New Jersey, Piscataway, NJ

562. Faceting of O/Re (1 2 -3 1): a model system for catalytic study

Hao Wang, Wenhua Chen, Ally S.Y. Chan and Theodore E. Madey, Rutgers, The State University of New Jersey, Piscataway, NJ

The adsorption of oxygen on Re (12-31) has been studied by low energy electron diffraction (LEED), Auger electron spectroscopy (AES) and scanning tunneling microscopy (STM). The atomically rough Re (12-31) surface remains planar at room temperature after being exposed to oxygen. However, the O/Re (12-31) surface can undergo drastic morphological changes to become completely faceted upon annealing at 700K or higher temperatures. With low oxygen coverages (~0.5ML), the facets form 2-sided ridge-like structures. The size of the ridges grows with annealing temperatures. The typical dimensions for the ridges are ~8nm wide and >50nm long upon annealing at 1000K. The orientations of the two facets of the ridge are identified as (11-21) and (01-10) by LEED measurements, which are consistent with kinematical simulations of the LEED patterns and confirmed by STM measurements. When the oxygen coverage is about 1ML, the ridge-like structure is found to be truncated by a third set of facets in the annealing temperature range between 900K and 1300K. The orientation of the third facet is identified as (10-10). The faceted O/Re surfaces may not only provide us templates to grow ordered nano-structures but also are possible candidates to study structural sensitivity in catalytic reactions. Recent studies on methanol oxidation over planar and faceted Re surfaces reveal differences in reactivity of these two surfaces.

563. Ion scattering study of oxygen diffusion and reactions in high-κ dielectric films on Si

Lyudmila Goncharova[1], Dmitri Starodub[1], Robin Barnes[1], Eric Garfunkel[1], Torgny Gustafsson[1], Genadii Bersuker[2], Brendan Foran[2] and Pat Lysaght[2], (1)Rutgers University, Piscataway, NJ, (2)International Sematech

We have used high-resolution medium energy ion scattering (MEIS) to investigate the atomic oxygen transport in the model systems, including hafnium and cerium oxides, silicates and oxynitrosilicates as a function of composition, crystallinity and post-deposition annealing conditions. Oxygen diffusion and reactions were studied by re-oxidation of as-grown and annealed films in $^{18}O_2$. Annealing of dielectric films in oxygen-containing atmospheres even at soft CMOS processing conditions may result in oxygen diffusion and interaction consequently in the (i) near-surface, (ii) bulk high-κ and (iii) near high-κ/Si interfacial regions. This is in contrast to vitreous SiO_2, which thermal stability is high and simply determined by the Si-O phase diagram. We found that at 500oC and $p_{O2}=10^{-2}$Torr the interface oxidation in hafnium dielectrics was minimized, and reaction with oxygen was predominated by exchange in the bulk silicate film. Oxygen exchange rate decreases with an increase of SiO_2 fraction in Hf silicate films and is almost fully suppressed for the (HfO2) : (SiO2) = 1 : 1 ratio. Exchange reaction saturated with time and appeared to be enhanced after film recrystallization, perhaps due to the enhancement of grain boundaries. Annealing in a nitrogen-containing atmosphere and nitrogen intake results in a reduced level of oxygen incorporation. In comparison to hafnium dielectrics, cerium oxides and silicates exhibit rapid interface growth.

564. Characterization of Wettability of Hydrophobic Dispersed and Porous Solids and A Model-Free Method to Determine Macroscopic Contact Angles for Hydrophobic Powders

Jeffrey J. McElwee, Roy Helmy and Alexander Y. Fadeev, Seton Hall University, South Orange, NJ

This work investigates wettability of hydrophobic surfaces supported on dispersed and porous materials using a water intrusion technique. Intrusion of water into the pore space under external pressure is studied, and the pressure-volume curves are analyzed. Hydrophobic surfaces were prepared via surface modification of porous and non-porous metal oxide powders (silica, titania, zirconia, alumina) with monolayers of n-alkylsilanes (1-18 carbon atoms in alkyl chain). Volume of hydrophobic pores and the work of adhesion of water to hydrophobic surfaces are determined directly from the intrusion experiments. A model free method to determine macroscopic contact angle (through the work of adhesion) for porous and dispersed solids is described.

565. Reactive, thin copper foils are readily prepared by controlled chemical etching of rotating disks of heavier copper sheet

Karen Root Caldwell, Pace University -- Westchester, Pleasantville, NY

Clean, reactive metallic copper surfaces can be prepared in a well-defined manner by using the rotating disk system. Copper disks can be corroded uniformly to produce thin, reactive metallic foils, to which organic materials adhere. The rate of corrosion of rotating copper disks follows expected kinetics. Disk thickness is reduced from 0.13 mm to ca. 20 µm (by ca. 70-85%) within ten minutes by using this recently patented process (U.S. Patent #6,464,893, October 15, 2002). Foils thus prepared readily react with chemical substances, apparently by chemisorption. The resulting organic films on copper, as examined by spectroscopic and microscopic methods, show the same properties and the same corrosion and wetting behavior as those prepared by other means. They readily undergo additional functional group transformations, as well. This process might be useful for investigating various aspects of copper surface chemistry, e.g. corrosion, corrosion inhibition, adhesion, lubrication, specialty coating and finishing.

566. Structure sensitivity in oxidation of CO and decomposition of NH3 over Ir surfaces: relevance to environmental applications of Ir catalysts

Wenhua Chen, Ivan Ermanoski and Theodore E. Madey, Rutgers, The State University of New Jersey, Piscataway, NJ

We report on catalytic oxidation of CO and decomposition of NH3 on two different kinds of catalytic surfaces, clean planar Ir(210) and clean nanoscale-faceted Ir(210) containing 3-sided pyramidal facets with {311} and (110) faces, which are prepared reversibly from the same crystal in situ. Both planar and faceted Ir(210) are very active for CO conversion to CO2 and NH3 conversion to carbon-free H2. At low coverages of pre-adsorbed oxygen (<0.4ML O), the temperature Ti for the onset of CO2 desorption is 460K at low CO coverage, and Ti decreases with increasing CO coverage. At high coverages of pre-adsorbed oxygen (>0.5ML O), Ti is <330K, and independent of CO coverage. CO oxidation is structure sensitive on planar Ir(210) versus faceted Ir(210); at all initial coverages of CO and oxygen, distinct evidence for structure sensitivity is seen in the CO2 formation rates over planar and faceted Ir(210). However, no evidence has been found for size effects in CO oxidation over faceted Ir(210) for average facet size ranging from 5nm to 14nm. NH3 decomposition is also structure sensitive on planar Ir(210) versus faceted Ir(210). Moreover, the decomposition kinetics of NH3 on faceted Ir(210) exhibit size effects on the nanometer scale; this is the first report of size effects in surface chemistry on an unsupported monometallic catalyst with controlled and well-defined structure and size.

567. Displacement of Organosilicon Monolayers Supported on Si

Joseph W. Krumpfer and Alexander Y. Fadeev, Seton Hall University, South Orange, NJ

This work studies the dynamic equilibria of Si supported organosilicon monolayers at solid-liquid interface. It is demonstrated that covalently-attached monolayers of octadecyldimethyl-, trimethyl-, and perfluoroalkyldimethyl- silanes can be qualitatively displaced in presence of different alkylsilanes in the solution. The kinetics of these reactions were studied using optical ellipsometry and contact angles of water and hexadecane.

Thermochemistry and Chemical Kinetics I

Organizer: Joseph W. Bozzelli New Jersey Institute of Technology, Newark, NJ
Presider: Joseph W. Bozzelli New Jersey Institute of Technology, Newark, NJ

568. Thermochemical and Kinetic Analysis of CH3S + O2

Li Zhu and Joseph Bozzelli, New Jersey Institute of Technology, Newark, NJ

The reaction paths of CH3S + O2 abstraction and association reaction systems are calculated using a wide range of computation theory levels including B3LYP with 6-311++G(d,p), 6-311++G(2d,p), 6-311++G(3df,2p), and 6-311++G(3df,3pd) basis sets. Sulfur is in a lower row of the periodic table than carbon and oxygen, so other density function and ab initio calculations are studied to determine an accurate potential curve and a density functional method for use on larger sulfur molecules. These include: CCSD(T)/6-311G(d,p)//MP2/6-31G(d,p), QCISD/6-31G(d), B3P86/6-311G(2d,2p)//B3P86/6-31G(d), B3PW91/6-311++g(3df,2p), G2, G3, G3MP2, G3B3, G3MP2B3, and CBS-QB3. Enthalpies of formations are determined and compared with literature using results at CBS-QB3 level with isodesmic reactions. Contributions to entropy and the heat capacity from translation, vibration, and external rotations are calculated using the rigid-rotor-harmonic-oscillator approximation based on B3LYP/6-311++G(d,p) structures. Hindered internal rotational contributions to entropies and heat capacities are calculated by summation over the energy levels found using the internal rotor potential from B3LYP/6-31G(d,p) level. Rate constants for the chemical activation and dissociation reactions are estimated as a function of temperature and pressure using quantum RRK analysis for k(E) and master-equation for pressure fall-off. Data are compared with experiment results. The higher-level ab initio results and B3PW91 density functional with a large basis set show the best results. The reaction system has a relatively shallow well, only 9-11 kcal/mol and most of the CH3SOO adduct dissociates back to reactants. Abstraction to form CH2=S + HO2 and intramolecular isomerization of CH3SOO to form CH3SO2, which dissociates to CH3 + SO2 are the important products.

569. Experimental and Computational Studies of the Kinetics of Chlorinated Hydrocarbon Radicals

Vadim D. Knyazev, The Catholic University of America, Washington, DC

A series of reactions of chlorinated hydrocarbon radicals (C2Cl3, CCl2, CH2CClCH2, CH2Cl, CHCl2, CCl3) were studied experimentally in the gas phase using the laser photolysis – photoionization mass spectrometry technique. Rate constants of these reactions were obtained in direct real-time experiments as functions of temperature and pressure. Experimental studies were complemented by computational investigations of the potential energy surfaces using quantum chemical methods and transition state theory and RRKM/master equation calculations of the rate constants. Experimental and computational results were used for extrapolation of the rate constant values to conditions outside the experimental ranges of conditions.

570. Reaction Pathways and Kinetic Analysis on Xylene Radical dissociation

Joseph W. Bozzelli[1], **Eric E. Moore**[1] and John T. Farrell[2], (1)New Jersey Institute of Technology, Newark, NJ, (2)ExxonMobil Research and Engineering, Annandale, NJ

Ab initio and density functional calculations are performed to determine thermochemical and kinetic parameters for hydrogen elimination and dissociation reactions from ortho- meta- and para-xylene benzylic radicals. The elimination is shown to proceed most rapidly in the para- isomer, primarially due to the favorable energetics in creating a quinoid-like structure in the bis(methylene) cyclo hexadiene product. The ortho- isomer is energetically favored over the meta- isomer because it can form a bond-alternated structure not possible in the meta- case. In all three isomers the reactions are calculated to occur with no discernable barrier to the reverse association / addition. Energies are determined at the MP2/6-31+G(d,p) and B3LYP/6-311g(d,p) levels, the potential energy surface for the reactions is obtained at the B3LYP/6-311g(d,p) calculation and used to calculate the reaction rates using variable reaction coordinate transition state theory.

571. Reaction Paths to Gas Phase Perfluoropropene Formation: A CASMP2 Investigation

Edward Ritter, William Kohler and Dorothy Skaf, Villanova University, Villanova, PA

We have performed ab initio calculations to compare the following three pathways to perfluoropropene, C3F6, formation from difluoromethylene, CF2, and tetrafluoroethylene, C2F4: addition of CF2 to C2F4 to form a singlet biradical with subsequent fluorine migration, direct insertion of CF2 into C2F4, and isomerization of C2F4 to a C2 carbene with subsequent carbene combination. Calculations were performed using the Gaussian 98W and Gaussian 03W program suites, at the CASMP2(6,6)/cc-pVDZ//CAS(6,6)/cc-pVDZ level of theory. The barriers to transition states for CF2 addition

to C2F4 and fluorine migration in the biradical lie 15.7 and 16.4 kcal/mole above the reactants, respectively. This is consistent with reported activation energies for CF2 addition to C2F4 to form C3F6. Results also suggest that the carbene combination pathway may be favorable if the C2 carbene is formed, as in pyrolysis of chlorotetrafluoroethane. However, in pyrolysis of chlorodifluoromethane, C2 carbene formation is unfavorable, and the formation of C3F6 is likely to proceed through the addition pathway.

572. Thermochemical and Kinetic Analysis on Tertiary Alkyl Radicals with Oxygen: 2-Hydroxy-1,1-Dimethylethyl and 1,1-Dimethylpropyl Radicals

Hongyan Sun[1], Joseph W. Bozzelli[2] and Chung K. Law[1], (1)Princeton University, Princeton, NJ, (2)New Jersey Institute of Technology, Newark, NJ

The reactions of two tertiary alkyl radicals, 2-hydroxy-1,1-dimethylethyl and 1,1-dimethylpropyl, with molecular O2 are analyzed with ab initio and density functional calculations to evaluate reaction paths and kinetics in the oxidation systems. The entropies (S°298) and heat capacities Cp(T)'s (0 < T/K < 1500) from vibrational, translational, and external rotational contributions are calculated based on statistical mechanics, and the hindered internal rotor contributions to S°298 and Cp(T)'s are from analysis of rotational potentials. The potential energy surfaces for the two reaction systems are computed at the composite CBS-Q//B3LYP/6-31G(d,p) level with species enthalpies of formation determined by isodesmic reaction analysis. Thermochemistry, reaction paths, barriers and Arrhenius pre-exponential factors are compared for these two similar reaction systems. Rate constants for chemical activation reactions are calculated as function of pressure and temperature using quantum Rice-Ramsperger-Kassel (QRRK) analysis for k(E) and master equation for pressure fall-off.

573. Experimental and Computational Study on Preignition Chemistry of SI Primary Reference Fuels in a Pressurized Flow Reactor

Xiaohui Gong, David L. Miller and Nicholas P. Cernansky, Drexel University, Philadelphia, PA

In this study, a skeletal chemical kinetic model for spark ignition primary reference fuel (PRFs) and their blends has been developed and tested against data from a Pressurized Flow Reactor. The model was developed as an extension of our previous preignition model by modifying several reactions to incorporate recent advances in our understanding of the relevant chemistry. The model was also reformulated to be compatible with the standard CHEMKIN simulation package. The model consists of 29 reactions and 35 species. n-Heptane, iso-octane and three of their mixtures corresponding to PRF20, PRF63 and PRF92 were examined. The reaction rate parameters for the modified model were selected initially as those used in our previous work or based upon similar reactions in the case of the new reactions. The rate parameters were then “tuned” using the PRF data from the flow reactor. These “tuned” reaction rate parameters included only three fuel-sensitive reaction rates, which were correlated to the octane number of the specific hydrocarbon mixture. The model was able to satisfactorily reproduce the negative temperature coefficient region and general reactivity behavior observed in the PFR, as well as the measured CO species evolution profiles. Compared to the detailed model, this modified skeletal model reduced the CPU time by almost 3 orders of magnitude.

Visions in Chemistry I

Organizer: Philip Wientraub sanofi aventis, Bridgewater, NJ
Organizer: Tahir N. Majid sanofi aventis, Bridgewater, NJ

574. Lewis Base Activation of Lewis Acids: New Concepts and Applications

Scott E. Denmark, University of Illinois, Urbana-Champaign, Urbana, IL

Although the concepts of Lewis acid-base interactions have been developed and understood for nearly 80 years, the implications for catalysis of organic reactions have still not been fully realized. In recent years we have outlined the conceptual framework for the counter-intuitive ability of electron-pair donors (Lewis bases) to enhance the electrophilic character of the electron-pair acceptors (Lewis acids) along with the unique opportunities for enantioselective reactions promoted by the catalytically active species thus generated. The main themes of this lecture are the conceptual development, structural basis and preparative application of chiral Lewis base catalysis. The first part will describe the structural (X-ray, NMR) and mechanistic investigations (kinetics, stereochemistry and computations) on the origin of catalysis and stereoselection in a number of Lewis-base catalyzed processes. This section will be followed by the illustration in a number of different reactions (allylation, aldol addition and Passerini reaction) of the scope and generality of the concept.

575. Peptidoconjugates as cellular and molecular probes of DNA damage

Shana Kelley, Boston College, Chestnut Hill, MA

The preservation of genomic integrity is essential for cellular function. Damage caused by radiation, radicals and other reactive chemical species can corrupt the information content of genomes by changing the chemical identities of the DNA bases or causing strand scission. A newly discovered pathway for nucleic acids damage is under investigation in our laboratory that involves cleavage of the DNA backbone by amino acid peroxides. While oxidative damage involving DNA and proteins has been considered separately, the interrelationship between the two types of damage events is unexplored. Using model peptides and synthetic peptidoconjugates, we are modeling reactions occurring between

oxidized protein residues and DNA both in vitro and within human cells. Our studies have revealed that a subset of protein residues can form cyclic peroxides and promote strand breakage when presented to DNA. The observation of amino acid promoted DNA damage indicates that crossreactions within protein/DNA complexes should be considered as a significant cause of the toxicity of reactive oxygen species.

Molecular Modeling Throughout the Drug Discovery Process I

Organizer: Wendy D. Cornell Merck & Co., Rahway, NJ
Organizer: Prabha Karnachi Johnson & Johnson PRD, Raritan, NJ
Presider: Wendy D. Cornell Merck & Co., Rahway, NJ

576. Protein Ensemble Docking: A Robust, General Strategy for Greatly Enhanced Lead Docking

Daniel L. Cheney and Luciano Mueller, Bristol-Myers Squibb PRI, Hopewell, NJ

Accurate lead docking remains an elusive task in molecular modeling. Sampling (including ligand and protein flexibility), scoring, solvation, consideration of structural waters, and protonation states are among the many aspects of ligand / protein binding that must be addressed in any comprehensive lead docking protocol. Earlier, we addressed some of these issues by exploring the concept and utility of lead docking using conformational ensembles in place of a single, rigid protein. Our initial results were promising, and prompted us to investigate this methodology further. In this study, high quality ligand datasets were generated from crystal complexes spanning 5 targets (116 ligands total; 2 kinases, 3 proteases) and docked into a conformationally diverse ensemble of target protein crystal structures. Substantial improvements were observed in sampling the correct pose for all targets. Ranking based on initial dock scores was generally not successful (GLIDE v3.5 / P38 and CDK2 being an exception), but could be greatly improved by minimizing docked complexes with OPLS-AA in the presence of the SGB continuum model (Schrodinger, Inc). Overall average success rates are more than doubled, and the average RMSD of top-ranked poses cut in half.

577. Critical Assessment of Docking Programs and Scoring Functions

Greg Warren, GlaxoSmithKline Pharmaceuticals, Collegeville, PA

Docking is a computational technique which samples conformations of small molecules in protein binding sites. Scoring functions are used to assess which of these conformations best complements the protein binding site. In an effort to understand the strengths and weaknesses of docking programs and scoring functions, an evaluation of ten docking programs and 37 scoring functions was conducted against eight proteins of seven protein types for three tasks: binding mode prediction, virtual screening for lead identification, and rank-ordering by affinity for lead optimization. All of the docking programs were able to generate ligand conformations similar to crystallographically determined protein/ligand complex structures for at least one of the targets. For all of the targets at least one of the ten programs generated poses that place 31-94% of the ligands within 2 angstrom of the crystallographic conformation, and all programs were able to generate well-docked poses for at least one target. However, scoring functions were less successful at distinguishing the crystallographic conformation from the set of docked poses. For virtual screening, docking programs identified active compounds from a pharmaceutically relevant pool of decoy compounds. However, while all programs were able to identify active compounds for at least one target, no single program or scoring function performed well for all of the targets. For prediction of compound affinity, none of the docking programs or scoring functions made a useful prediction of ligand binding affinity.

578. Rapid and Accurate Protein Side-Chain Prediction

Michael Bower, Incyte Pharmaceuticals, Wilmington, DE

Fast and accurate side-chain conformation prediction is important for homology modeling, ab initio protein structure prediction, and protein design applications. The placement of side-chains within a protein model, long thought to be a problem too complex for solution because of its combinatorial nature, has recently proven tractable. The development and improvement of the SCWRL algorithm has recently yielded very accurate and rapid predictions.

579. An Ab Initio Method for Predicting the Stereochemistry of Drug Intermediates Using NMR

Keith W. Wiitala, Christopher J. Cramer and Thomas R. Hoye, University of Minnesota, Minneapolis, MN

New DFT NMR functionals for computing NMR shifts are presented. The new methods are more accurate than HF, B3LYP, PBE1PBE, and PW1PW91 for predicting training set carbon and proton NMR shifts. Accuracy of the methods were further demonstrated by predicting the relative configurations of monomethylcyclohexanol derivatives and a key beta lactam intermediate using computed shift profiles.

Surface and Interface Science II

Organizer: Yves J. Chabal Rutgers University, Piscataway, NJ
Organizer: Theodore E. Madey Rutgers, The State University of New Jersey, Piscataway, NJ

Presider: Yves J. Chabal Rutgers University, Piscataway, NJ
Presider: Theodore E. Madey Rutgers, The State University of New Jersey, Piscataway, NJ

580. Water-Hydrophobic Interface at the Nanoscale: Wetting Study Indicates That Water is Separated From the Hydrophobic Walls by the Vapor Gap

Alexander Y. Fadeev, Seton Hall University, South Orange, NJ

We report an investigation of wetting of well-defined hydrophobic nanochannels prepared by silanization of mesoporous ordered silicas (SBA-15 type) with Rpore ~2-4 nm. Wetting in these systems can not be described by the classical models. Water occupies only fraction (30-60%) of the pore volume and the values of pressure for the pore filling are ~60-90% greater than predicted by the Laplace equation. The results are explained well using Derjaguin's model of wetting films and the concept of "disjoining pressure". It is suggested that non-wetting fluid (water) is separated from the hydrophobic walls by thin film of the vapor phase (wetting fluid). The thickness of these films is estimated ~0.3-0.4 nm, or ~10-20% of the pore radius.

581. First Principles Resonance Widths and Energies for Ions Scattering off Surfaces: Neutralization Predictions for Scattered Ions

Keith Niedfeldt[1], P. Nordlander[2] and Emily A. Carter[1], (1)Princeton University, Princeton, NJ, (2)Rice University, Houston, TX

By combining a first principles periodic density functional theory calculation of adsorbate resonance widths and shifts with a many-body dynamical theory of charge transfer, we assess charge transfer rates for ions scattering off surfaces. This goes beyond previous approaches, which have been limited to modeling metal surfaces with either jellium potentials or finite clusters. Here we consider Li+ scattering from Si(001), Mg(0001), Cu(001), and Al(001) surfaces. For metals we show how the Li 2s orbital hybridizes with metal valence bands, near the surface, increasing the width of the 2s energy level. For Si(001), as expected the Li 2s orbital interacts most strongly with the dangling bonds in Si dimers. This in turn affects the charge transfer rates between the ion and the surface. Our predictions for scattering are in good agreement with the experimental neutralization fractions of scattered Li ions. These results show that lateral corrugation, neglected by the jellium approximation used in most previous calculations, should be accounted for in quantitative theories of ion-surface scattering.

582. Manipulation of nanoparticles growth on surfaces

Jan Hrbek, Brookhaven National Laboratory, Upton, NY

Several different approaches for preparation of nanoparticles supported on surfaces will be described. Chemical modification of single crystal surface, use of templated single crystal surfaces and use of reactive condensed multilayers all provide means for manipulation of growth, composition and properties of nanoparticles. Specific examples discussed will include chemical vapor deposition on gold using metal carbonyl precursors, metal growth on oxygen or sulfur modified and oxidized metal surfaces and preparation of titanium dioxide nanoparticles on ice multilayer.

583. Orbital-specific model for chemisorption

Sara E. Mason, Ilya Grinberg and Andrew M. Rappe, University of Pennsylvania, Philadelphia, PA

We present a DFT study of molecular chemisorption spanning a variety of transition metals and facets. We cast our results in a physical model for chemisorption that takes into account which metal and adsorbate orbitals interact to form chemisorption bonds. We use DFT chemisorption energies, orbital overlaps and changes in charge density induced by adsorption to track how the metal and adsorbate states interact as a function of metal identity, surface facet, and strain. We introduce strain to the adsorption systems as a probe that causes relatively small, but geometrically specific, changes to electronic structure of the metal. By taking into account orbital specific contributions to chemisrotpion, our model is able to reproduce subtle differences in chemisorption present in our DFT results and offers a means for predicting adsorption energies on different metal surfaces in different states of strain.

584. Structure in Self-Assembled Organic Thin Films: Chirality, Nano-patterns, and Interaction Energies

Steven L. Bernasek[1], Feng Tao[1] and Yuguang Cai[2], (1)Princeton University, Princeton, NJ, (2)Brookhaven National Laboratory, Upton, NY

Physisorption of substituted alkanes at the basal plane of graphite results in a wide range of self-assembled monolayer structures. Many of these structures exhibit chirality in two dimensions and patterns on the nanometer length scale. The formation and stability of these structures can be used to probe the interaction energies that control self-assembly. The structures discussed include a chiral monolayer formed when octadecanol is distorted into a chiral overlayer upon adsorption. Chiral pairing has been observed in the adsorption of diiodooctadecanol, forming a chiral monolayer from a racemic mixture without enantiomer segregation on the surface. An achiral anhydride molecule is found to form two-dimensional enantiomer domains with opposite chiralities. Quasi-phase separation and chiral pairing has been observed for self-assembled monolayers of the iodination products of oleic and elaidic acid. The resulting structures are patterned

on a nanometer length scale, in a reproducible and predictable fashion. Mixed monolayers of long-chain alkanoic acids and substituted isophthalic acids have been observed to form stable nanometer scaled meshes on the graphite surface. The structures are controlled by weak interactions between molecules. A balance between hydrogen bonding and van der Waals interactions between the adsorbate molecules and the molecule and substrate control these structures. The structures that result when substituted alkanes are adsorbed on graphite can be used to gain insight into this balance of interactions. By examining a range of long chain substituted hydrocarbon monolayers on graphite using STM, general principles for the formation of chiral overlayers and nano-structured overlayers can be deduced.

585. Second Harmonic Generation Probe of Dye Molecules Chemically Bonded to Colloidal Particles

Jun Han, Holly Hofer, Eric Meggers and Hai-Lung Dai, University of Pennsylvania, Philadelphia, PA

Surface modified colloidal particles have many applications, such as for coating materials, photonics, and biological/pharmaceutical diagnosis. In this study, a process is developed for covalently bonding the para-ethyl red dye to the carboxyl group on the surface of polystyrene carboxylated microspheres. The surface sensitive nonlinear optical probe – Second Harmonic Generation (SHG)- is applied to identify the binding of the dye molecules to the microparticle surface.

586. Self-Organizing Aromate Films: Architecture and Domain Evolution

Janice Reutt-Robey, Bo Xu, Hui Li, Diane Evans, Chenggang Tao and Ellen Williams, University of Maryland, College Park, MD

Nanophase structure impacts the charge- and energy-transfer processes that underlie all practical applications of ultrathin organic materials. We report the molecular architecture and domain mosaic of ultrathin aromate films, produced by physical vapor deposition on Ag(111). Adlayer structures for pure films of the N-heteroaromatic acids isonicotinic acid (INA) and 9-acridine-carboxylic-acid (ACA)) have common structural elements and notable differences. At coverages up to one monolayer, both ACA and INA form large 2-D islands based upon a head-to-tail H-bonding aromate network. At room temperature, these islands coexist with a molecular lattice gas, which is thermally quenched and imaged at 40 K. Orientational differences produce distinctive domain boundary structures: INA orientational domains are stabilized by tail-tail H-Bond fusion. Multilayer (1-5 ML) ACA films show a thickness-dependent reduction in domain size (from 100's nm to ~30 nm) in a mosaic pattern. The binary system, ACA+C60, was investigated as a model "donor-acceptor" organic film. These binary films show a complex multi-domain structure that is process dependent. At a particular compositional mixture, ACA and C60 spontaneously organize into a novel chiral phase, consisting of a net of widely spaced (2.6 nm) C60 and a net of chiral ACA trimers.

587. TPR and TEM Study of the Reduction of Cobalt-Silica Catalyst Precursors

Roger Barth, West Chester University, West Chester, PA

The reduction of silica-supported cobalt catalyst precursors is strongly influenced by the interaction of the precursor oxide with the silica support. In previously published work we showed that a fraction of the cobalt is permanently deactivated by support interactions, and that the catalytic activity was due to the cobalt in excess a threshold amount. If the cobalt was applied in two steps instead of all at once, more cobalt was deactivated. In this work, we study the reduction process by temperature programmed reduction (TPR), transmission electron microscopy (TEM), and selected area electron diffraction (SAD) in an effort to determine how a sample prepared in two steps differs from one prepared in a single step. The work has potential implications for many nanostructural materials prepared by reaction of a supported precursor.

Applications of LC-MS in Drug Discovery/Development

Presider: Guodong Chen Schering-Plough Research Institute, Kenilworth, NJ

588. Overview of LC/MS in Drug Discovery and Development

Birendra N. Pramanik, Schering-Plough Research Institute, Kenilworth, NJ

With advancement in ionization methods, liquid chromatography / mass spectrometry (LC/MS) has emerged as a powerful technology for the characterization of pharmaceuticals. This presentation will give an overview of LC/MS in drug discovery and development process, emphasizing problem solving skills in utilizing LC/MS and LC/MS/MS with examples from pharmaceutical research. They include structural analysis of trace-level impurities in drug substances, microwave-assisted MS analysis for proteins/peptides, and application to proteomics.

589. Applications of Small Molecule Mass Spectrometry in Drug Discovery

Manish Soni, Sanofi-Aventis, bridgewater, NJ

Today mass spectrometry, in its myriad forms, has become an indispensable analytical tool in bio-pharmaceutical research and development. Its applications span the entire drug discovery and development process from target identification to lead identification to animal and human testing. In this presentation, we will provide examples of some of the ways in which mass spectrometry is used in the drug discovery process at sanofi-aventis. We will describe some of our efforts to tightly integrate the various hardware, software and processes within and outside of our labs to achieve

optimum efficiency and throughput. This presentation will conclude with a brief look at the direction we are heading in the future. We will describe our implementation of a new LIMS for sample and analytical data tracking and implementation of expert software tools for processing, dereplication, validation and visualization of experimental data.

590. LC/MS Characterization of Intact Proteins: Open Access and High Throughput Applications

Bingbing Feng, GlaxoSmithKline, King of Prussia, PA

Rapid analysis of intact proteins by LC/MS has become indispensable for target recombinant protein confirmation at various stages of drug discovery. The important issues here are assay speed (throughput), mass accuracy, ease of use, and open-access, etc. Over the past several years, we have developed strategies to achieve good balance among these aspects, using either short-gradient serial sample injection format or high throughput parallel approaches. The rationales, the details of the analytical platforms and their applications will be discussed.

591. Identification of Impurities and Degradation Products in Pharmaceutical Development and Pharmaceutical Products Using LC-MS and LC-MS/MS

Jason X. Tang, Wyeth Research, Pearl River, NY

Identifying impurities and degradation products during the pharmaceutical development process and after market is important because of science and business interests and also because of regulatory requirements. The impurity and degradant profiles of a process or product provides us with a good understanding of that process or product. This allows us to improve processes, increase product yield at lower cost; extend product shelf life and protect process patents. All major analytical techniques such as HPLC-mass spectrometry (LC-MS) and HPLC-tandem mass spectrometry (LC-MS/MS), NMR, and IR have been used in the characterizations of drug impurities and degradation products. LC-MS and LC-MS/MS are often the techniques of choices for identifying low-level impurities and degradation products because of their high sensitivities and separation powers in addition to the rich structural information that MS/MS produces. The development of atmospheric pressure ionization, such as electrospray ionization technique, has made it possible not only to characterize a complicated mixture using LC-MS and LC-MS/MS but also to study non-covalently associated complexes in solution. ESI-MS technique is becoming a very powerful technique for identifying non-covalently associated impurities such as crystals or particulates found in liquid pharmaceutical products. We have been providing support for identifying impurities and degradation products during pharmaceutical development processes and in market pharmaceutical products. Examples of structural characterization of impurities and degradation products using MS based techniques, such as characterizations of impurities found in the manufacturing process and in liquid pharmaceutical products, will be presented and discussed.

592. LC/MS Degradation Studies in Pharmaceutical Development

Charles Pan, Frances Liu and Richard Vivilecchia, Novartis, East Hanover, NJ

Liquid chromatography mass spectrometry (LC/MS) has been widely used in pharmaceutical development over the past decade. It has become a powerful tool for identification of degradation products to support method development/ validation and elucidation of degradation pathways to support excipient selection.

Drug degradation is very critical in pharmaceutical development as it has significant impacts on drug efficacy, safety profile and storage conditions. As a result, identification of degradation compounds has become very important to formulation development. The LC/MS studies in pharmaceutical development are faced with some unique challenges. The content levels of degradation compounds are normally as low as 0.1%. The presence of excipient could cause source contamination or chromatographic interferences. The stability conditions may result in multiple chemical reactions, such as oxidation, hydrolysis, thermal decomposition, or light-induced free radical reactions. These reactions can sometimes occur in a combined manner, which makes identification more complicated and less predictable. In addition, isolation and enrichment are normally required to confirm the proposed structures for late phase projects.

This presentation will focus on the use of mass spectrometry to identify unknowns resulting from drug substance degradation, drug-excipient interaction, and excipient degradation. Using combined GC/MS and LC/NMR techniques, a degradation compound that was not detectable in LC/MS has been identified. Thermal desorption GC/MS was developed and used to understand chemical reactions responsible to weight loss in thermogravimetric analyses of salts of drug substance. In addition, the use of Ion trap LC/MS to support peptide mapping for protein analysis will be discussed.

Biotransformations

Official: Vinod Ramachandran GlaxoSmithKline, King of Prussia, PA

593. Minimizing the Potential for Metabolic Activation as an Integral Part of Drug Design

David C. Evans, Merck, Rahway, NJ

The formation of drug-protein adducts carries with it the risk of clinical toxicities that may not be predicted by preclinical safety studies. The process of minimizing the potential for metabolic activation at the lead optimization stage could therefore be viewed as one of building quality into our future generation of drug products. A perspective on how to address the issue of metabolic activation from an industry viewpoint based on in vitro and in vivo protocols adopted by

Merck Research Laboratories will be presented. Examples of efforts made within our laboratories to minimize reactive metabolite formation as a fundamental element of drug design will be discussed.

594. Recent Advances in Extrapolating Preclinical ADME Data to Humans

Keith Ward, GlaxoSmithKline, King of Prussia, PA

Prediction of human ADME properties is often conducted based on in vivo preclinical pharmacokinetic data generated during lead optimization in drug discovery. However, to date, the relative ability to accurately predict human pharmacokinetics from the preclinical species typically used in the pharmaceutical industry has not been presented. This study was conducted to comprehensively survey the available literature on intravenous pharmacokinetic parameters in the rat, dog, monkey, and human, and to compare common methods for extrapolation of intravenous pharmacokinetic parameters, identify the most appropriate species to use in pharmacokinetic lead optimization, and to ascertain whether adequate prospective measures of predictive success are currently available. Based on an exhaustive literature survey, 103 non-peptide xenobiotics were identified with intravenous pharmacokinetic data in rat, dog, monkey, and human; both body weight- and hepatic blood flow-based methods were used for scaling of clearance. The results from this investigation indicate that (1) monkey is the most qualitatively and quantitatively predictive species for human clearance, volume of distribution, and half-life; (2) generation of data in 3 versus 2 preclinical species does not always improve predictivity; and (3) some commonly used prospective measures of predictive success, including correlation coefficient and allometric exponent, do not accurately forecast allometric predictivity. The observations in this investigation have major implications for pharmacokinetic lead optimization and for prediction of human disposition from in vivo preclinical data, and support the continued use of nonhuman primates in preclinical pharmacokinetics.

595. Cytochrome P450 Reaction Phenotyping Study of Hp184 in Human Liver Microsomes

Lijuan Wang, Yongqing Huang and Peter S King, sanofi-aventis, Bridgewater, NJ

HP 184 is currently under clinical development. N-Dealkylated HP184 (HP183) and methylhydroxylated HP184 are two major metabolites observed in the in vitro metabolism in human liver microsomes (HLM) and human hepatocytes, and in the in vivo metabolism in rats and dogs. The objective of this study was to identify the major enzyme(s) involved in the metabolism of HP184 to these two metabolites in human liver microsomes. More than 80% of HP184 metabolism in pooled HLM was inhibited by 1-benzylimidazole, a non-selective P450 enzyme inhibitor. No metabolite was formed when HP184 was incubated with cDNA expressed human flavin-containing monooxygenase 3 (FMO3). Heat deactivation of FMO did not alter HP184 metabolism in HLM. The results indicated that HP184 was mainly metabolized by CYP450 enzymes in HLM. Selective CYP450 inhibitors for CYP3A4 (troleandomycin), CYP1A2 (furafylline), and CYP2D6 (quinidine) inhibited the formation of HP183 by up to 60%, 40%, and 40%, respectively, in HLM. The formation of HP183 was catalyzed by cDNA expressed human CYP3A4 and also only correlated significantly ($R2=0.887$, $p<0.05$) with CYP3A4/5 activities in a panel of HLM (n=16). The results indicated that CYP3A4 was the major enzyme responsible for the formation of HP183; CYP1A2 and CYP2D6 played a minor role. The methyl hydroxylation pathway was catalyzed by cDNA expressed human CYP1A2, 2C9, 2C19, and 2D6 enzymes. The formation of methyl hydroxylated HP184 in HLM was not inhibited specifically by selective CYP450 inhibitors for 1A2 (furafylline), 2C9 (sulphaphenazole), 2C19 (tranylcypromine), 2D6 (quinidine), 2E1 (diethyldithiocarbemate), and 3A4 (troleandomycin), and did not correlate with the activities of CYP1A2, 2C9, 2C19, 2D6, 2E1, and 3A4/5 in a panel of HLM (n=16). Overall, the results were consistent with the involvement of multiple enzymes, including CYP1A2, 2C9, 2C19, and 2D6, in catalyzing the methyl hydroxylation pathway of HP184 in HLM.

596. Glucuronosyltransferases (UGTs): Several recent examples in drug development

Donglu Zhang, Bristol-Myers Squibb, Princeton, NJ

Glucuronosyltransferases (UGTs) are a super-family of enzymes which catalyze glucuronic acid transfer from UDPGA to a nucleophilic group such as hydroxyl, carboxyl, and amino group in many endogenous chemicals and drugs. This presentation will include several recent examples describing a new reaction catalyzed by UGT2B7, reaction phenotyping of major clearance glucuronidation pathways of drugs, and effects of UGT1A1 inhibition.

College Student Award Symposium sponsored by the Chromatography Forum of Delaware Valley

Organizer: Marshall L. Fishman East. Reg. Res. Ctr., ARS, USDA, Wyndmoor, PA

597. Headspace SDME Using a Single Solvent: An Application to Residual Solvents Analysis

Derrick C. Wood and James M. Miller, Drew University, Madison, NJ

One of the newer sampling techniques, similar to SPME, is sometimes called SDME or single-drop microextraction. In its simplest form, a microliter of extracting solvent is suspended from a conventional microsyringe in the headspace of a heated sample. After a few minutes, the drop is withdrawn into the syringe and injected to a GC for analysis. In this research, headspace SDME was applied to residual solvents analysis and was found to be reliable, simple, and inexpensive.

Numerous aspects of headspace SDME were examined, including the use of N-methylpyrrolidone (NMP) as both the extraction solvent and raffinate, and a comparison of manual and automated techniques. Manual injections using an internal standard had an RSD of 2.7%, and automated injections showed similar results (2-4%) even without an internal standard. Limits of detection were in the sub-ppm level.

598. Microwave Extraction of Pectin and Characterization using High Performance Size Exclusion Chromatography

Halla Suleiman[1], Hoa Chau[1] and Marshall L. Fishman[2], (1)USDA/ARS/ERRC, Wyndmoor, PA, (2)East. Reg. Res. Ctr., ARS, USDA, Wyndmoor, PA

The goal of the research was to develop a method whereby high-quality pectin could be extracted from orange albedo. Pectin was acid extracted from early Valencia orange albedo using rapid microwave heating under pressure. The extraction times ranged from 3-60 minutes, at a constant temperature. The pectin was then characterized for molar mass (M), radius of gyration (Rgz), and intrinsic viscosity (IVw). The characterization was obtained by High-Performance Size-Exclusion Chromatography with online light scattering and viscosity detection. The molar mass, radius of gyration, and intrinsic viscosity were the highest at the lower heating times, particularly at 3 minutes. The molar mass was 480,000 Daltons, the Rgz was 40.9 nm, and the IVw was 8.1 dL/g. As heating times increased the percentage of pectin recovered increased, whereas the M, Rgz, and IVw all decreased. Analysis of the Mark-Houwink plots showed that the pectin extracted at lower heating times was more compact and spherical. As heating times increased the pectin structure fragmented and became less compact.

599. Thin Layer Chromatography to Separate Triglyceride Lipase Products

Ang Bian, Kavitha Sompalli and Peter M. Oelkers, Drexel University, Philadelphia, PA

Most organisms store energy in the form of biologically inert neutral lipids like triglyceride and steryl esters. Our lab focuses on the triglyceride lipases which hydrolyze triglycerides to a combination of fatty acids and glycerides (mono-, di-). Studies conducted on *Saccharomyces cerevisiae* involved feeding the cells with radiolabelled fatty acid which were incorporated by the organism into more complex lipids such as triglyceride. A phase separation technique was adopted for extraction of the lipids from cell extracts. These cell extracts were resolved by thin layer chromatography technique using silica coated plates and a hexane: ether: acetic acid solvent system. Lipids were separated based on size and hydrophobicity and visualized by iodine staining. The scintillation counter provided the numbers required for quantifying the lipids. Subsequent work will involve use of preparative chromatographic techniques to isolate different triglyceride species which will be used in *in vitro* assays with purified lipases.

600. Effects of Echinostoma caproni larval trematode infection on lipids in the medically important snail Biomphalaria glabrata as determined by HPTLC

Sharon R. Bandstra, Bernard Fried and Joseph Sherma, Lafayette College, Easton, PA

This study examined the effects of larval Echinostoma caproni infection on the neutral lipid and polar lipid content of whole snail bodies of Biomphalaria glabrata infected with cercariae and rediae for six weeks. Uninfected snails were used as controls. As determined by qualitative high performance silica gel thin layer chromatography, the major neutral lipids present in both snail populations were free sterols, free fatty acids, and triacylglycerols, and the major polar lipids were phosphatidylcholine and phosphatidylethanolamine. Quantitative analysis by thin layer chromatography with visible and UV scanning reflectance densitometry showed no significant difference in the concentrations of these lipids in whole bodies of infected snails versus the controls, but the concentration of triacylglycerols in the infected digestive gland-gonad complex was significantly less than that of the uninfected. Studies are in progress to examine the effects of the infection on the hemolymph and shells of infected versus uninfected snails.

601. Effect of Pseudostationary Phase on Fluorescence Intensity in Electrokinetic Chromatography

Stephanie A. Schuster and Joe P. Foley, Drexel University, Philadelphia, PA

The routine use of capillary electrophoresis as a separation technique has been hampered by its lower sensitivity compared to HPLC. Several methods have been developed to overcome this problem including preconcentration techniques (stacking), enhanced path length capillaries (bubble cell, Z cell), and the use of Laser Induced Fluorescence (LIF) as a detection method. LIF also has its disadvantages, including the need to fluorescently label non-fluorescing analytes. Researchers have discovered that the incorporation of a pseudostationary phase (PSP), such as micelles or cyclodextrins, in the background electrolyte (BGE) can enhance the fluorescence intensity of the investigated compounds. This study compares the fluorescence intensity of a set of probe analytes (derivatized amino acids) in the presence and absence of two PSPs: (i) sodium dodecyl sulfate (SDS) micelles and (ii) cetyltrimethylammonium bromide/sodium octyl sulfate (CTAB/SOS) vesicles.

602. Chiral Separations in Microemulsion Electrokinetic Chromatography (MEEKC) Utilizing a Chiral Surfactant and Chiral Co-Surfactant

Kimberly A. Kahle and Joe P. Foley, Drexel University, Philadelphia, PA

As more commercial products contain chiral compounds, in particular pharmaceuticals, the demand for chiral separation methods increases. The importance of enantiomer separation stems from the fact that the effectiveness of many drug formulations is due to only one of the enantiomers with the other enantiomer being ineffective or possibly toxic. Electrokinetic chromatography (EKC) has been shown to easily separate numerous pairs of enantiomers. Some of the advantages of EKC for this application include high efficiencies, short analysis times, miniscule sample and solvent consumption, and the availability of a wide variety of chiral recognition agents. Microemulsion electrokinetic chromatography (MEEKC) is one of the less developed avenues of EKC. In this technique, a pseudostationary phase consisting of a surfactant, co-surfactant, and oil core is employed for separations. To date, only three types of chiral microemulsions have been described in the literature using either a chiral oil, surfactant, or co-surfactant. This study explores the combination of a chiral surfactant and a chiral co-surfactant for the separation of chiral pharmaceutical compounds.

603. Separation of Metals from Water using Collagen Dispersion

Christopher S. Cohen, Widener University, Chester, PA

This paper discusses a new process for separating metals from water, which will produce a minimal amount of waste capable of being disposed into the environment without causing harm. Researchers at Widener University have discovered that high surface area collagen fibrils (HSC) have the ability to retain up to 500 times their mass in water. The mixture of collagen fibrils, organic acid and water is called a collagen dispersion. By adjusting the pH of the dispersion, the system can be made to become bi-phasic. That is, two aqueous phases exist – one rich in collagen (opaque) and the other being clear water. Contaminates contained in the water will distribute between the phases. Collagen dispersion will be added to several samples of water each spiked with a known concentration of a metal. The pH of this mixture will be adjusted and then will either be centrifuged or filtered to separate the metal absorbed in the collagen from the water. The processed water will be tested using atomic absorption to determine the concentration of metal separated from each water sample.

Electronic Structure in Chemistry II

Organizer: Kieron Burke Rutgers University, Piscataway, NJ
Organizer: Karsten Krogh-Jespersen Rutgers University, Piscataway, NJ
Presider: Karsten Krogh-Jespersen Rutgers University, Piscataway, NJ

604. Ab Initio electronic structure calculations for N-aromatic assemblies

Diane Evans and Janice Reutt-Robey, University of Maryland, College Park, MD

This study is aimed at understanding the supramolecular structure formation of a class of N-heteroaromatic molecules adsorbed on Ag (111). Scanning tunneling microscopy (STM) images of isonicotinic acid (INA), 9-acridine carboxylic acid (9-ACA) and co-adsorbed 9-ACA/C60 demonstrate basal plane pi-pi interaction, acceptor-donor hydrogen bonding (HB) and dispersive force field affects. To determine how these interactions scale relative to one another, ab initio electronic structure calculations were performed at the HF, MP, and LMP2 level of theory for the single monomer and several dimer and trimer conformers of each N-heteroaromatic class member.

This work was supported by Pittsburgh Supercomputing Center (PSC) under Grant No. CHE050007P and National Science Foundation under CHE-01-36401.

605. Organic molecules on the Si(100) surface: theory of reactivity and electronic conductance

Doug Doren, Jeff Frey and Zareh Darakjian, University of Delaware, Newark, DE

Organic molecules on semiconductor surfaces present new opportunities for studying molecular electronics. With a range of attachment chemistry available, and the ability to alter electronic states of the substrate as well as the adsorbed molecule, these systems allow new approaches to understand the factors that control conductance through molecules and the molecule-surface interface. This talk will review the current understanding of selectivity in cycloaddition reactions of organics on Si(100) surfaces. Theoretical simulations of STM images will be used to relate specific prodcut structures to the observed images. The factors that might be used to control electron tranport through molecules on semiconductors will be discussed, and new calculations of electronic conductance will be used to illustrate the relationship of molecular structure to electronic properties of the molecules.

606. First-principles studies of TiO_2 surfaces, their interactions with water and other small molecules, and their sensitization by molecular dyes

Annabella Selloni, Princeton University, Princeton, NJ

Photoelectrochemical solar cells based on nanostructured TiO2 electrodes have attracted much interest over the last ten years, as they offer the prospect of cheap fabrication, flexibility, and, at the same time, high energy conversion efficiency. These cells are complex devices, involving several different components and processes. We have studied some of these processes by a combination of first principles molecular dynamics simulations, density functional, and time dependent density functional calculations. Our results include the surface structure of the TiO2 nanocrystals, their interactions with water and other small molecules, including the carboxylic dye-anchoring groups, the optical absorption spectra of Ru-polypyridyl dye sensitizers. Recent studies of TiO2 anatase nanoparticle sensitization by the [Fe(CN)6]4- molecular dye are also reported.

607. On the fly orbital localization in ab initio molecular dynamics and its application in the reaction of organic molecules with semiconductor surfaces

Mark E. Tuckerman, New York University, New York, NY

The methodology of ab initio molecular dynamics, wherein finite-temperature dynamical trajectories are generated using forces computed ``on the fly'' from electronic structure calculations, has benefited significantly from its combination with maximally localized electronic orbitals. The latter exploit the unitary invariance of the total energy to generate orbitals with maximum spatial locality. These orbitals resemble the classic textbook picture of molecular orbitals and, hence, are useful tools for analyzing electronic structure. In addition, maximally localized orbitals, expanded in localized basis sets, are a key component in linear scaling methods. In this talk, it will be shown how techniques from quantum field theory can be used to reformulate ab initio molecular dynamics in such a way that maximally localized orbitals are generated automatically and dynamically as the calculation proceeds. It will be seen how the resulting trajectory of maximally localized orbitals can be used to elucidate the mechanism of a chemical process on the Si(100)-2x1 surface, namely, the addition of a conjugated diene. Such processes are opening new inroads into molecular electronics and nanoscale devices. Covalent attachment of organic molecules to semiconductor surfaces can yield active devices such as molecular switches as well as passive insulating layers. Finally, we will show that it is possible to ``reverse engineer'' specific molecules to yield lower free energy barriers to detachment, which hold promise for applications in, for example, surface lithography.

608. Temperature effects on magnetic resonance parameters from first principles

Daniel Sebastiani and Jochen Schmidt, Max-Planck Institute for Polymer Research, 55128 Mainz, Germany

Car-Parrinello molecular dynamics simulations can be combined with the ab-initio calculation of spectroscopic properties. The simulations are used to sample representative parts of the system's phase space, followed by calculations of linear response properties in the framework of density functional perturbation theory. This powerful combination yields a parameter-free prediction of many experimentally accessible spectra in complex systems under realistic physical conditions. The focus in this presentation will be the calculation of nuclear quadrupole coupling constants from electric fields gradients and nuclearmagnetic resonance chemical shifts of liquid and supramolecular systems at ambient temperature.

609. Implications of Symmetry Rules for the Aromaticity of Inorganic Clusters

Clémence Corminboeuf, R. Bruce King and Paul v. R. Schleyer, University of Georgia, Athens, GA

Isoelectronic clusters with the same basic cage structures may exhibit surprisingly different magnetic properties. For instance, nucleus-independent chemical shift (NICS) values, computed at cluster centers, may range considerably in magnitude and even change from diatropic to paratropic. The same is true for dissected canonical molecular orbital contributions to the total NICS values, computed by the GIAO method. Thus, HOMO-NICS values are paratropic only if the HOMO->LUMO rotational transition is allowed by symmetry selection rules derived from group theory. High symmetry inorganic cages are likely to exhibit spherical aromaticity if the HOMO->LUMO rotational transition is forbidden by these symmetry rules. Otherwise, inorganic clusters will exhibit paratropicity if this is not weakened by the insufficient overlap between the HOMO and the rotated LUMO and by a very appreciable energy difference between them. Larger cages, such a Au20 (Td), with many electrons and bonding MOs, are expected to be diatropic.

610. High pressure phase diagram of diamond from first principle molecular dynamics

Xiaofei Wang and Roberto Car, Princeton University, Princeton, NJ

We present a scheme to compute the phase diagrams of materials within Density Functional Theory (DFT). Our approach is based on the first principles molecular dynamics simulations combined with the scaling algorithm proposed by M. de Koning, et al, to improve the efficiency of thermodynamic integration techniques. This approach allows us to compute the free energy of a given material phase over a finite temperature range using a single simulation run. We have applied this scheme to quantitatively locate the melting curve of diamond at high pressures.

611. DFT studies of the active center in hydrogenase enzymes

Silviu Zilberman, Edward I. Stiefel, Morrel H. Cohen and Roberto Car, Princeton University, Princeton, NJ

Hydrogenase enzymes has been the focus of intense studies in the last decade. The interest stems not only from the quest to understand metabolism in anaerobic bacteria, but also it may help in the quest for bio-inspired catalysts for hydrogen production. Though many of the structural aspects of Hydrogenase are known quite well, there are still some important structure related open questions. We report here detailed studies of the infrared spectrum of Hydrogenase at various oxidation states. In particular we show that the bridging ligand in the di-iron cluster could be identified by means of infrared spectroscopy in a properly designed experiment. We also present preliminary studies of an extended system that include (for the first time) the Fe4S4 cubane part of the active center.

612. Modeling NQ-based molecular switch structures: A conformation-energy analysis

Jeanne W. Bundens, Eastern University, St. Davids, PA

Norbornadiene-Quadricyclane systems are of interest as molecular switches. Molecular modeling using DFT/BL3YP and high-level basis sets describes well the N-Q energetics. Various ring systems that symmetrically join two N rings were characterized and compared to the corresponding Q forms. These systems were examined as possible models for switches that simultaneously involve additional conformational change.

Green Chemistry II

Organizer: Sanjay V. Malhotra New Jersey Institute of Technology, Newark, NJ
Organizer: Wen-Chung Shieh Novartis Pharmaceuticals, East Hanover, NJ
Presider: Wen-Chung Shieh Novartis Pharmaceuticals, East Hanover, NJ

613. Microwave-promoted synthesis in water and an investigation of microwave effects in synthetic chemistry using simultaneous cooling

Nicholas Leadbeater, University of Connecticut, Storrs, CT

The talk will take two parts. The first will be an overview our work in the development of rapid, easy C-C coupling methodologies using microwave heating We will focus on Suzuki and Heck couplings in water showing the versatility of microwave heating. The second will outline our attempts to probe the evidence for and against a non-thermal microwave effect in relation to synthetic organic chemistry by using the method of simultaneous cooling. The effects of microwave heating whilst simultaneously cooling on a range of organic transformations will be discussed.

614. Breaking the Petroleum Feedstock Paradigm: 1,3-Propanediol Production from Renewable Feedstock

Mark H. Emptage, DuPont, Wilmington, DE

Increasing environmental awareness and the recognition of limited future petroleum supplies have help drive companies like DuPont into looking for alternative and sustainable feedstocks for their carbon-based products. Genetic engineering of E. coli to produce 1,3-propanediol (PDO) from D-glucose at high yields and titers is one highly successful example. This was accomplished by utilizing genes from two separate natural strains which can either ferment glucose to glycerol or utilize glycerol as a carbon source to produce PDO as a by-product. The new recombinant E. coli strain was then further genetically modified to improve yields and titers to commercially viable values. This then allowed for a commercial process based on a renewable resource corn sugar that is more economical, less capital intensive, more environmentally friendly than the current chemical process based on petroleum products. The success of the bioprocess is key to future growth of DuPont's newest polymer product Sorona®.

615. Ionic Liquids on a Large Scale. How They Can Improve Chemical Processes

Calvin J. Emanuel, BASF Corporation, Florham Park, NJ

Ionic liquids have gained significant interest as unique new materials that offer novel solutions for chemical industry problems . BASF is the first company to use ionic liquids on a multi-ton scale to improve a chemical process. Since 2002, the BASIL™ process has been used in the routine production of alkoxyphenylphosphines, handling ionic liquids on a multi-ton scale. The BASIL™ technology has proven to be applicable to a variety of chemical transformations and is now offered as a system solution to customers. The chemical transformations in which BASIL is applicable include chlorinations by nucleophilic HCL, azeotropic distillations, and extractions.

BASF is working diligently to overcome barriers by establishing the first multi-ton, large-scale operation that demonstrated the value of the use of ionic liquids in commercial production. BASF has also initiated the notification process for a new chemical substance, starting with BMIM Cl as a first ionic liquid. In addition, BASF offers a broad portfolio of ionic liquids in bulk quantities. BASIONICS™ products, BASF's commercial ionic liquids, are also available in lab quantities through Sigma-Aldrich.

The lecture will address the use and benefits of ionic liquids within BASF. Apart from BASIL™, several other examples by BASF for the use of ionic liquids will be presented.

BASIL is a trademark of BASF Aktiengesellschaft

616. Development of a Green Synthesis for Taxol® Manufacture via Plant Cell Fermentation and Extraction

Jonathan C. Walker, Bristol-Myers Squibb Company, New Brunswick, NJ

Paclitaxel, the active ingredient in the Bristol-Myers Squibb anticancer drug Taxol®, was first isolated from the bark of the Pacific yew tree, *Taxus brevifolia*. This was, however, an unsustainable supply due to the extremely low incidence of paciltaxel in the bark and the result that the trees were killed during the harvesting process. Total synthesis of paclitaxel was impractical from a commercial point of view due to the complexity of the molecule, however, a semi-synthetic process starting from naturally occurring 10-deacetylbaccatin III was developed. While commercially viable, the process required eleven chemical transformations and seven isolations and presented environmental concerns. A more sustainable process was subsequently developed in which paclitaxel was fermented directly using plant cell cultures in aqueous-based media and purified by chromatography and crystallization. The plant cell fermentation process has resulted in significant reductions in the use of hazardous chemicals, solvents and energy and is now being used commercially to manufacture paclitaxel.

617. Shades of Green Chemistry in Selected Pharmaceutical Processes

Shankar Swaminathan, Bristol Myers Squibb, New Brunswick, NJ

Bristol-Myers Squibb has developed a process greenness scorecard to evaluate its processes with considerations for safety on scale-up, operator protection, environmental emissions, waste handling and disposal and other regulatory factors. A number of examples from several processes where this assessment was performed will be presented. An alternative to a copper mediated dehydrogenation of oxazoline to oxazole will be discussed. In addition an industrial process for making chromenes under solvent free conditions will be presented. Waste minimization, reduction of the number of protecting groups and identification of an inherently safer chemistry for the omapatrilat process will be shown.

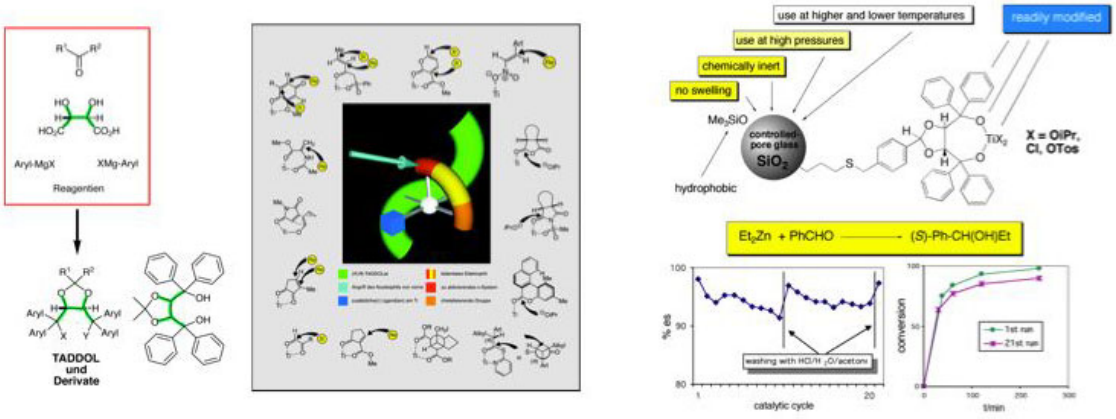
618. The Use of TADDOLs and Other Diarylmethanol Derivatives in Enantioselective Synthesis

Dieter Seebach, Eidgenössische Technische Hochschule Zürich - ETH Hönggerberg, Zürich, Switzerland

TADDOLate has been introduced as chiral ligand in organotitanium reagents as early as 1982. The TADDOLs can be prepared (in a combinatorial way) from aldehydes/ketons, tartaric acid, aryl Grignard reagents, and heteroatom nucleophiles, as to be fit for multitude of applications ranging from stochiometric chiral reagents, through chiral ligands on various organometallic centers to polymer-incorporated or silicagel-bound immobilized enantioselective catalysts. The strategy of using diarylmethanol groups as part of chiral reagents has been extremly successful in the hands of resarchers around the world. The most recent applications will be described, with emphasis on solid-support-fixed reagents and on the use of a modified Evans auxiliary (4-isopropyl-5,5-diphenyloxazolidin-2-on, DIOZ) in enantioselective syntheses.

For references we refer to a review article and to a representative full paper: – Dieter Seebach, Albert K. Beck, Alexander Heckel, Angew. Chem. Int. Ed. 2001, 40, 92 - 138: TADDOLs, Their Derivatives, and TADDOL Analogues: Versatile Chiral Auxiliaries. – Christoph Gaul, Bernd W. Schweizer, Paul Seiler, Dieter Seebach, Helv. Chim. Acta 2002, 85, 1546 - 1566.

For complete puplication lists of D.S. see Tetrahedron 2004, 60, 7455 - 7506 and the home page: http://infosee.ethz.ch/seebach/seebach.html



Inorganic and Organometallic Polymers IV

Organizer: Frieder Jaekle Rutgers University, Newark, NJ
Presider: Frieder Jaekle Rutgers University, Newark, NJ

619. Hybrid metallic nanoparticle/block copolymer systems

Robert B. Grubbs, Liliana A. Miinea, Laura B. Sessions, David S. Glueck and Benjamin R. Cohen, Dartmouth College, Hanover, NH

Alkyne functional di- and triblock copolymers have been prepared with the aid of nitroxide-mediated radical, atom transfer radical, and radical addition-fragmentation transfer polymerization. Reaction of these polymers with dicobalt octacarbonyl leads to cobalt-containing block copolymers which are of use for the preparation of microphase-separated bulk copolymers in which spatially segregated domains contain either cobalt atoms or cobalt nanoparticles. The utility of these diblock and triblock copolymer-based composites for the preparation of materials with multiple metallic nanoparticle-containing domains will be discussed.

620. Oligosiloxycynoureates Mediated Approach to Novel Metal Nano Particles and Their Catalytic Applications

Moni Chauhan[1], Richard Pantano[1], Gilchris Burton[1], Jitendra S. Rathore[2] and Bhanu P. S. Chauhan[2], (1)Queensborough Community College, Bayside, NY, (2)Nanomaterials Laboratory of Center for Engineered Polymeric Materials, City University of New York at CSI, Staten Island, NY

Nanometer-sized particles of metals and semiconductors have been investigated intensively because of their size-dependent properties and the possibility of arranging them in micro assemblies (and nano assemblies). Nanosized metal particles possess unique chemical and physical properties that can be exploited in a wide variety of technological applications, including catalysis, nonlinear optics ultra-purification and microelectronics. One of the design strategies that has shown tremendous potential as a viable route by which to produce metal nanoparticles with improved size control and colloidal stability is to employ polymeric matrixes as the form of growth media. In this presentation, we will disclose a new approach to synthesis and stabilization of nanosized novel metal nano particles. Our synthetic design is based on the need to generate catalytically active nonpassivated nanoparticles under mild reaction conditions and high yields. In this novel approach, cyclic siloxycynoureates are utilized to accomplish duel function of macromolecular stabilizing template as well as reducing agents. The details of synthetic design, nanoparticle properties and their catalytic activity will also be discussed.

621. Synthesis and binding properties of borylated oligo- and polythiophenes

Anand S. Sundararaman[1], Resmi Varughese[2], Maria Victor[1] and Frieder Jäkle[1], (1)Rutgers University, Newark, Newark, NJ, (2)Rutgers Newark, Newark, NJ

Conjugated organic polymers have received a great deal of attention due to their electrical and optical properties. Polythiophenes have become the most widely studied of all conjugated polyheterocycles. The incorporation of electron-deficient boron centers into conjugated polymer structures has recently attracted much attention following the observation that overlap between the empty p orbital of boron and the organic p-system results in unusual photoluminescent and electron-conducting properties.

The introduction of Lewis acidic centers provides an opportunity to design novel sensor materials for Lewis basic substrates. We have focused here on synthesis and characterization of bifunctional conjugated organoborane model compounds, oligomers and polymeric systems of thiophenes with Lewis acidic boron groups and their interaction with different Lewis bases.

Our studies indicate that modification of the pendant aromatic groups on the boron center from electron donating to electron withdrawing groups results in varying degree of p- orbital overlap and hence materials with different photoluminescent properties (blue, green or red emission). The binding of Lewis bases results in appreciable change of the visible absorption and emission characteristics and hence allows sensing applications.

622. Functionalilzed Polyaniline/Carbon Nanotube Composite for Sensitive Biosensor Applications

Yufeng Ma[1], Jianming Zhang[2], ali Shah[3], Afua S. Dodoo[3] and **Huixin He**[1], (1)Rutgers University, Newark, NJ, (2)Rutgers University, Newark Campus, Newark, NJ, (3)chemistry department,newark campus, rutgers university, newark, NJ

Compared to other conducting polymers, polyaniline is unique and has received considerable attention due to its straightforward polymerization, environmental stability, unique conductive properties, and potential applications in electronic devices, batteries and sensors. However, native polyaniline is not electrochemically active and is a poor conductor in neutral solutions (required for most biosensor applications). It also limited both in the number of species that can be detected and in the selectivity of the detection. A major breakthrough was the discovery of self-doped polyaniline and the polyelectrolyte anion doped polyaniline, which brought polyaniline into biosensor field due to the improved redox

activity and conductivity in neutral pH solutions. However, there are a number of tradeoffs, including reduced conductivity, chemical and mechanical stability due to steric effects.

In this presentation, we show that a self-doped polyaniline (poly (aniline boronic acid))/carbon nanotube composite is fabricated electrochemically by adding single-stranded DNA dispersed carbon nanotube into the polymerization solution. Cyclic voltammetry study of this composite demonstrates that not only the redox properties of polyaniline is reserved in neutral solutions (pH = 7.4) and the stability was greatly improved compared to poly (aniline boronic acid) itself. The morphology and the conductivity of the composite are studied by tapping mode atomic force microscopy (AFM) and conductive AFM. The interaction between the polymer and carbon nanotube is studied in a molecular structural level using Raman spectroscopy. Finally its applications in biosensor field will be presented.

Medicinal Chemistry

Presider: Joel S. Freundlich Jacobus Pharmaceutical Company, Princeton, NJ

623. Epoxybergamottin as a bioactive compound for functional foods applications

Samineh Madani and Jack N. Losso, Louisiana State University, Baton Rouge, LA

The incidence of breast cancer continues to rise and often by the time cancer is diagnosed, it is past the stage of easy curability. Treatment with traditional chemotherapy agents can provide benefits to patients, but these agents kill both malignant and normal cells and do not always provide comfortable quality and enhanced life expectancy. Since cancer lethality develops over several years, cancer prevention or management is receiving significant scientific and consumer scrutiny as one way to help reduce cases and costs. Aromatase family of enzymes catalyzes the conversion of androgens to estrogens and pro-carcinogens to carcinogenic metabolites and aromatase inhibitors are considered first-line therapy in metastatic disease. Inhibitors of aromatase show an overall superior efficacy to tamoxifen, a standard therapy used in managing hormone-receptor-positive metastatic breast cancer in postmenopausal women. Epidemiological and experimental studies show that a high intake of phytochemical-rich foods is inversely related to cancer risk and populations that consume these diets have a lower rate of cancer compared to those who do not. Grapefruit peels contain high concentration of epoxybergamottin. Epoxybergamottin is known for its ability to inhibit aromatase. Aromatase enzyme is associated with the progression of breast and prostate cancer. However, epoxybergamottin is not commercially available. Epoxybergamottin was purified from grapefruit peels using a combination of low and high pressure chromatography. The identity and purity of the isolated epoxybergamottin was confirmed by ^{1}HNMR and GC-MS. This presentation will discuss the anti-angiogenic, anti-proliferative, and other biological activities of epoxybergamottin as a functional food for breast cancer prevention.

624. Synthesis of small molecules designed to complement disease-associated thyroid hormone receptor mutants

A. Quamrul Hassan and John T. Koh, University of Delaware, Newark, DE

TSH-secreting pituitary tumor (TSHoma) and resistance to thyroid hormone (RTH) have been shown to be associated with mutations to the thyroid hormone receptor s(TR). One missense mutation (H435Y) has been found in both TSHoma and RTH. Importantly, His435 is believed to play a key role in ligand-dependant transactivation mechanism of TR. We have synthesized series of novel pyridine-based thyromimetics designed to complement TR? (H435Y). Whereas natural ligand T3 is ~400 fold less potent toward TR?(H435Y) than wild-type TR, the synthetic analog QH13 is a super agonist at nanomolar concentration towards TSHoma-associated mutant. Significantly, QH13 can selectively activate the mutant without affecting the wild-type TR subtypes. Inspired by our success with pyridine-based analogues, we currently are exploring other heterocyclic and fused ring scaffolds to improve potency and selectivity. Similarly, we have developed highly selective and potent compounds that activate the synthetic mutant TR?(H435A), which is not responsive to the endogenous ligands. Such “functionally orthogonal” ligand-receptor pairs are being explored as novel tools to study the genomic versus non-genomic actions of steroid/nuclear hormones.

625. Potent, low-calcemic, selective inhibitors of CYP24 hydroxylase: 24-sulfone analogs of the hormone 1α,25-dihydroxyvitamin D_3

Gary H. Posner, Kenneth R. Crawford, Hong Woon Yang, Mehmet Kahraman, Heung Bae Jeon, Hongbin Li, Jae Kyoo Lee, Byung Chul Suh, Mark A. Hatcher, Tanzina Mirza, **Aimee Usera**, Patrick M. Dolan and Thomas W. Kensler, The Johns Hopkins University, Baltimore, MD

Vitamin D is a secosteroid hormone which is classically known for the regulation of calcium and phosphorous absorption. By binding to the vitamin D receptor (VDR), this molecule also activates transcription, thereby regulating a number of biological functions such as cell differentiation, immunology, and cell proliferation. Thousands of vitamin D_3 analogs have been synthesized, but balancing beneficial activity against undesirable toxicity has been especially challenging. Certain analogs may possess desirable antiproliferative activity, but cause harmful hypercalcemia at therapeutic doses. In attempts to create a transcriptionally active analog with low-calcemic activity, the 24-sulfone side-chain was substituted for the traditional calcitriol side-chain. The sulfone group, though lacking the terminal hydroxyl group, may act as a hydrogen bond acceptor mimicking the structure-activity relationship of calcitriol with the VDR. Some of the new sulfones are low-calcemic, biologically potent, and selective inhibitors of P450C24 (CYP24) hydroxylase enzyme. CYP24 initiates the catabolic pathway. The inhibition of this enzyme is expected to extend the half-life of the drug and to allow a lower dosage to be administered for effective treatment while minimizing hypercalcemia. The design of analogs featuring high

antiproliferative activity with a low calcemic index could lead to potential drugs for the clinical treatment of leukemia, breast and skin cancers, prostate cancer, psoriasis, and osteoporosis.

626. Exploration of the Potential Antifilarial Activity of the Fruit, Leaf and Stem Extracts of Melia azedarach Linn. on Cattle Filarial Parasite Setaria Cervi

Qamar U. Ahmed[1], S. M. K. R. Zaidi[2], N.U. Khan[2] and K.C. Singhal[2], (1)International Islamic University Malaysia, Kuantan-25200, PahangDM, Malaysia, (2)Aligarh Muslim University, Aligarh-UP, India

Effect of aqueous and alcoholic extracts of the fruit, leaf and stem of Melia azedarach Linn. on the spontaneous movements of both the whole worm and the nerve-muscle (n.m.) preparation of Setaria cervi and on the survival of microfilariae in vitro was studied. Alcoholic extracts of fruit, leaf and stem caused inhibition of the spontaneous movements of the whole worm and the n. m. preparation of Setaria cervi, while only aqueous extract of fruit caused inhibition of the spontaneous movements of the whole worm and the n.m. preparation of S. cervi. The initial stimulatory effect was not observed by the aqueous and alcoholic extracts of fruit on n.m. preparation. The concentrations required to inhibit the movements of the whole worm and n.m. preparation for alcoholic extracts of fruit, leaf and stem were 250, 40 µg/ml; 280, 40 µg/ml and 270, 25 µg/ml respectively, whereas an aqueous extract of fruit caused inhibition of whole worm and n.m. preparation at 200 µg/ml and 40 µg/ml respectively. Alcoholic extracts of the fruit, leaf and stem and aqueous extract of the fruit of Melia azedarach caused concentration related inhibition on the survival of microfilariae of S. cervi. The LC50 and LC90 as observed after 6 hrs. were found to be 5, 15, 10, 20 ng/ml and 10, 25, 20 and 35 ng/ml, respectively. This work was designed and conducted in view of the exploration of potential antifilarial herbal drug. Keywords: Melia azedarach Linn. (Meliaceae); Setaria cervi antifilarial activity in vitro; microfilaricidal.

627. Potent, Selective and Low-Calcemic Inhibitors of CYP 24 Hydroxylase: 24-Sulfoximine Analogues of the Hormone 1α,25-Dihydroxyvitamin D_3

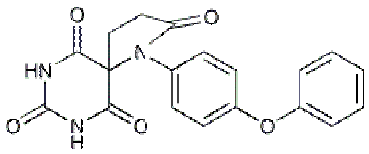
Mehmet Kahraman[1], **Sandra Sinishtaj**[1], Patrick M. Dolan[1], Thomas W. Kensler[1], Sara Peleg[2] and Gary H. Posner[1], (1)The Johns Hopkins University, Baltimore, MD, (2)The University of Texas

1α,25- Dihydroxyvitamin D_3(calcitriol) is associated with an array of biological functions such as immunomodulation, inhibition of cell growth and inducement of cell differentiation. Calcitriol shows great biological activity but its high calcemic index prevents it from being used for therapeutic purposes. This area of research proceeds with the goal of developing new synthetic analogs that have similar or greater activity than calcitriol, but without the unwanted calcemic effect. A non-traditional group of analogs that portrayed such character include some C24 side chain modified sulfone analogs. The 24-sulfone analogs lack the OH group of the calcitriol side chain necessary for hydrogen bonding with the vitamin D receptor (VDR), however, they show antiproliferative activity, low calcemic indices and are selective inhibitors of the human cytochrome P450C24 (CYP-24) hydroxylase enzyme. In the same path as the sulfone series a new group of analogs have been prepared and studied, the NH- sulfoximines. Although these new 24-sulfoximines are weakly antiproliferative and not very active transcriptionally, they are potent hydroxylase inhibitors and show low calcemic indices. One of the main enzymes responsible for vitamin D breakdown includes CYP-24 hydroxylase, whereby its inhibition will directly influence the lifetime of vitamin D and its analogs. These analogs can potentially be used therapeutically in conjunction with vitamin D analogs, extending their lifetime and making them more efficient. The chemistry and biology of these new NH- sulfoximines will be discussed.

628. Structure-based Design of a Barbiturate Containing Inhibitor of MMP-13

William Pitts, Soong-Hoon Kim, Andrew Pudzianowski, Kenneth J. Leavitt, Joseph Barbosa, Patricia A. McDonnell, Bruce M. Rankin, Richard Liu, Wayne Vacarro, William Metzler, Steven Sherriff and Bruce Jacobson, Bristol-Myers Squibb, Princeton, NJ

Computer aided drug design contributed to the discovery of a new class of spiro-barbiturates which were found to be potent inhibitors of MMP-13. The design was confirmed by a 1.75 Å resolution crystal structure of 4a complexed to MMP-13. An NMR structure of 4a complexed to MMP-13 was also obtained. A brief comparison of the two structures will be presented.



4a

Molecular Modeling throughout the Drug Discovery Process II

Organizer: Wendy D. Cornell Merck & Co., Rahway, NJ
Organizer: Prabha Karnachi Johnson & Johnson PRD, Raritan, NJ
Presider: Wendy D. Cornell Merck & Co., Rahway, NJ

629. Targeting Protein Kinases in Drug Discovery

Beth Lunney, Pfizer Global R&D, La Jolla, CA

The reversible phosphorylation process is a key driver in the regulation of protein function. Protein kinases, one of the largest gene families, are an integral part of this phenomenon. These enzymes are involved in numerous cellular mechanisms including cell cycle, signal transduction, gene expression and apoptosis. As such, protein kinases have been targeted in drug discovery spanning multiple therapeutic areas, among them, oncology, diabetes and inflammation. A major challenge facing this research is identifying small molecule inhibitors, which bind potently to the kinase of interest, while remaining selective versus other members of the family. Fortunately, the availability of X-ray structures has assisted in this endeavor, by elucidating structural and conformational features of protein kinases that might be targeted for enhanced potency and specificity. Some of these strategies will be presented herein.

630. Design of New AIDS Drugs: A Multi-disciplinary Attack on the Problem of Drug Resistance

Kalyan Das[1], Arthur D. Clark[1], Yulia Volovik Frenkel[1], Paul J. Lewi[2], Jan Heeres[2], Marc R. de Jonge[2], Lucien M. H. Koymans[2], Paul A.J. Janssen[2], Donald W. Ludovici[3], Bart De Corte[3], Robert W. Kavash[3], Chih Y. Ho[3], Hong Ye[3], Mark. A. Lichtenstein[3], Michael J. Kukla[3], Rudi Pauwels[4], Koen Andries[4], Marie-Pierre de Béthune[4], Stephen H. Hughes[5] and Eddy Arnold[6], (1)Center for Advanced Biotechnology and Medicine, and Rutgers University, Piscataway, NJ, (2)Center for Molecular Design, Belgium, (3)Janssen Research Foundation, Spring House, PA, (4)Tibotec, Mechelen, Belgium, (5)HIV Drug Resistance Program, Frederick, (6) Rutgers University, Piscataway, NJ

Drug resistance is a primary cause of AIDS treatment failure. A multidisciplinary effort [1] led to the discovery of the potent diaryl-pyrimidine (DAPY) nonnucleoside inhibitors (NNRTIs) dapivirine, etravirine, and rilpivirine that are under clinical evaluation. Synthesis of a large number of compounds, determination of efficacy of the compounds against multiple HIV-1 strains, and systematic structural and molecular modeling studies of HIV-1 reverse transcriptase (RT) in complexes with NNRTIs were the key components of the drug design effort. The structural and modeling studies revealed different modes of binding for the DAPY inhibitors [2]. The torsional flexibility ("wiggling") of the inhibitors can generate numerous conformational variants and the compactness of the inhibitors permits repositioning and reorientation (translation and rotation) within the pocket ("jiggling"). Such adaptations appear to be critical for the ability of the NNRTIs to retain their potency against a wide range of drug-resistant HIV-1 RTs. Exploitation of inhibitor conformational flexibility can be a powerful element of drug design, especially for the design of drugs that will be effective against rapidly mutating targets. [1] Janssen P.A.J. et al. J. Med. Chem. 2005, 48: 1901. [2] Das et al. J. Med. Chem. 2004, 47, 2550.

631. Cardiac Ion Channel Pharmacology and Structure-Function Analysis

Chris Culberson, Merck & Co, Inc, West Point, PA

Abstract not available.

632. Patenting 3D Structural Information in the Aftermath of the Trilateral Project

Alicia Russo, Fitzpatrick, Cella, Harper & Scinto, New York, NY

Structural genomics is a fast growing field in which large amounts of money and effort are being invested. Patents are important to ensure continued investment in this field. Accordingly, increasing numbers of structural genomics patent applications are being filed with the United States Patent and Trademark Office (USPTO). However, not that many patents have been issued. An explanation can be found in the published comments of the Trilateral Project WM4. This project was a consolidated effort by the USPTO, the European Patent Office (EPO) and the Japanese Patent Office (JPO) to try to achieve a mutual understanding of the patentability of these types of inventions. The comments suggest that most claims to these inventions are not patentable. However, these comments actually provide a useful tool for determining how to better obtain patent protection for these inventions. In addition, structural genomics patents that have been issued since the publication of these comments provide insight into the types of claims the USPTO deems patentable in light of the Trilateral Project WM4. This talk will further explore how to obtain patent protection for 3D structural inventions.

Proteinase

Organizer: Robert Goodnow Jr. Hoffmann-La Roche, Nutley, NJ
Official: Michael Angelastro Sanofi-Aventis, Bridgewater, NJ

633. A Novel Class of Non-Covalent Cathepsins Inhibitors

Tae-Seong Kim, Amgen Inc., Thousand Oaks, CA

A series of (4-piperidinylphenyl)aminoethyl amides based on dipeptide anilines were synthesized and tested against cathepsin K, cathepsin L and cathepsin B. These new non-covalent inhibitors exhibited single digit nM inhibition of the cysteine proteases. The potency of these inhibitors in both mouse and human osteoclast resorption assays was demonstrated.

Key words: Non-covalent, Cathepsin, Inhibitor

634. The Discovery and Development of Non-Covalent Cathepsin S Inhibitors

James P. Edwards, Johnson & Johnson Pharmaceutical Research and Development, San Diego, CA

The cysteine protease cathepsin S (CatS) has received much recent attention as a target for therapeutic intervention in a range of diseases of the immune system. CatS is expressed mainly in antigen-presenting cells and has been implicated in the presentation of antigens to CD4+ T-cells through the use of both knock-out animals and systemic administration of a peptidic, irreversible cysteine protease inhibitor, LHVS. The CatS inhibitors reported to date rely on covalent attachment of an electrophilic peptide-derived ligand to the active site thiol to achieve potent enzyme inhibition. In this presentation, the discovery, SAR investigations, and development of the first non-peptidic, non-covalent inhibitors of cathepsin S are described. Directed and high-through-put screening generated a set of CatS hits from which two lead structures were identified as promising starting points for a drug discovery effort. Lead optimization afforded potent (IC50 < 10 nM) and selective inhibitors of CatS demonstrating excellent cellular activity and good oral bioavailability and safety in pre-clinical species. The issues specific to this program that needed to be overcome to identify the clinical candidates will be discussed in detail.

635. Medicinal Chemistry and Properties of 1,2,4-Thiadiazoles

Tim Fat Tam, Regis Leung-Toung, Warren Li, Michael Spino and Khashayar Karimain, ApoPharma Inc., Toronto, ON, Canada

1,2,4-Thiadiazole is a distinctive class of small heterocyclic thiol trapping agents that serve as an interesting pharmacophore in the design of inhibitors targeting the cysteine residues of proteins. X-Ray crystal structures of enzyme-inhibitor complex indicate that the cysteine thiol reacts with the N-S bond of the thiadiazole moiety to form a disulfide bond resulting in the inactivation of the enzymes. This presentation addresses the medicinal chemistry and various properties of 1,2,4-thiadiazoles in their potential as new electrophilic “warheads” for targeting the cysteine residues of biomolecules (e.g, H+/K+ ATPase), and cysteine-dependent enzymes (e.g., cathepsin B and transglutaminase).

Keywords: Thiadiazole, proton pump, cathepsin B, Factor XIIIa, transglutaminase, cysteine thiol, inhibitors

Regulatory and Patent Law – the Scientist’s Perspective

Organizer: Leticia Quinones Bristol-Myers Squibb
Organizer: Jay M. Brown The Eclipse Group, Cary, NC
Presider: Jay M. Brown The Eclipse Group, Cary, NC
Presider: Leticia Quinones Bristol-Myers Squibb

636. Title: Strategies for Writing Effective Global Patent Applications and Developing Technology

Rosemary M. Miano, Pfizer Inc., Morris Plains, NJ

This talk will describe effective strategies for writing offensive and defensive patent applications and options for developing and protecting technology. Topics include how to structure patent coverage for a global patent application, the role of dominant and subservient patents, developing technology with in-house and outside resources and points to watch in the technology development process.

637. Current Developments in Federal Circuit Court Decisions on Patent Law: What Scientists Need to Know

Jay M. Brown, The Eclipse Group, Cary, NC

Key decisions over the past year by the Court of Appeals for the Federal Circuit and by other federal courts as appropriate, with respect to patent matters will be discussed. The focus will be on the perspective of the scientist as

inventor and as business manager, interested in maximizing the effectiveness of a patent portfolio. Emphasis will be placed on court decisions that shed light on measures to be taken for the preparation and prosecution of strong and enforceable patents. Developments will be reviewed as to the written description, enablement, and best mode requirements, and preservation of access to the doctrine of equivalents. Lessons will be addressed for the success of both scientists and the patent lawyers with whom they work in partnership.

638. Contrasting GMP and GLP Requirements for Pharmaceutical Development API Supplies

David Kunzinger, Proctor and Gamble Pharmaceuticals, Norwich, NY

The manufacture and testing of active pharmaceutical ingredients for use in GMP and GLP regulated activities is carried out under different regulatory and quality assurance requirements. This presentation will contrast the GMP and GLP regulatory requirements while addressing the topics of documentation, equipment qualification, QA involvement, analytical methods, cleaning and audits.

639. FDA and PhRMA's Current Thinking on Starting Materials

Sandeep, P. Modi, Bristol-Myers Squibb, New Brunswick, NJ

In January 2004, the FDA issued draft guidance for the CMC: “Drug Substance: Chemistry, Manufacturing, and Controls Information.” In this session, an overview of the FDA's current thinking on the “starting material” issue and its impact on the pharmaceutical industry will be discussed.

Research Funding Opportunities

Organizer: Alexander Grushow Rider University, Lawrenceville, NJ
Presider: Alexander Grushow Rider University, Lawrenceville, NJ

640. Writing excellent research proposals

Edward J. J. Grabowski, American Chemical Society, Westfield, NJ and Robert H. Rich, American Chemical Society, Washington, DC

Competitive proposal writing is not a skill often taught in school, but it can be learned. In this panel, Dr. Edward J. J. Grabowski from the ACS Petroleum Research Fund Advisory Board will introduce you to the ins and outs of what makes a successful proposal at ACS PRF. In addition to general comments, based upon his experience in reviewing many proposals, you will learn the specifics of preparing a proposal to ACS PRF and information about available programs. There will be an opportunity to ask questions and get answers to anything relating to the proposal writing process.

641. NSF Chemistry Division programs supporting undergraduate research at predominantly undergraduate institutions

Richard D. Foust Jr., National Science Foundation, Arlington, VA

Research is increasingly recognized as an essential component of undergraduate science education in all STEM disciplines. Predominantly Undergraduate Institutions (PUIs) play a significant role in preparing America's future workforce by educating a large fraction of the Ph.D. chemists in the United States. NSF's Chemistry Division supports undergraduate research through the following programs: (1) Research Experiences for Undergraduates (REU); (2) Research at Undergraduate Institutions (RUI); (3) Research Opportunity Awards (ROA); and (4) Undergraduate Research Centers (URC).

The REU, RUI, ROA and URC programs are complementary and provide a variety of mechanisms for supporting undergraduate research at PUIs. The REU program provides support for advanced undergraduate chemistry majors to work in the laboratory of a faculty member. The RUI program supports research by PUI faculty through funding of individual and collaborative research projects and the purchase of shared-use research instrumentation. The ROA program supports PUI faculty to work at other institutions as a means for developing long-term research collaborations. The URC program is new, and provides research opportunities to first- and second-year college students. Developments in all these programs will be discussed in the context of developing a national undergraduate research community in the chemical sciences.

642. NSF update: What's new at DUE?

Kathleen A. Parson, Susan Hixson, Harry Ungar and Herbert H. Richtol, National Science Foundation, Arlington, VA

Undergraduate education is central to the National Science Foundation's mission in human resource development. The Division of Undergraduate Education (DUE) serves as the focal point for agency-wide support for undergraduate education. The program activities of DUE aim to strengthen and continuously improve the vitality of undergraduate education for all students in science, technology, engineering and mathematics (STEM) courses in all U.S. institutions of higher education. Within DUE programs, particular emphasis is placed on improving access to STEM education for all segments of U.S. society, including persons with disabilities, populations underrepresented in STEM fields, and those in

technical or teaching careers. This presentation includes a brief description of the DUE programs that are most likely be of interest to chemists involved in undergraduate education, as well as an update on the new Course Curriculum, and Laboratory Improvement (CCLI) solicitation.

643. The Camille and Henry Dreyfus Foundation

Gerard L. Brandenstein III, The Camille and Henry Dreyfus Foundation, Inc., New York, NY

Programs of the Camille and Henry Dreyfus Foundation that support the chemical sciences at Primarily Undergraduate Institutions will be described. They include the Faculty Start-up Grant Program, the Henry Dreyfus Teacher-Scholar Program, and the Special Grant Program in the Chemical Sciences.

644. Funding opportunities for faculty at predominantly undergraduate institutions

Raymond Kellman, Research Corporation, Tucson, AZ

Research Corporation has been providing research support to individual faculty at predominantly undergraduate institutions since 1971, through our Cottrell College Science Award program. We support faculty in chemistry, physics and astronomy who are pursuing significant and fundamental research. While faculty at any stage of their careers may apply, our focus is on those faculty in the first three years of a tenure track appointment. Details of this and other programs available to this particular segment of the scientific community will be discussed.

Spectroscopy of Biomolecules, Interfaces and Materials IV

Organizer: Edward W. Castner Jr. Rutgers, The State University of New Jersey, Piscataway, NJ
Presider: Edward W. Castner Jr. Rutgers, The State University of New Jersey, Piscataway, NJ

645. Tracking Amyloid Formation by Single Molecule Spectroscopy

Troy C. Messina, Jason T. Giurleo, Hiyun Kim, Jongjin Jung and David S. Talaga, Rutgers University, Piscataway, NJ

We are investigating the mechanism for the initial stages of protein self-assembly leading to amyloid formation using single molecule spectroscopy (SMS). β-lactoglobulin (β-LG) has been shown to form amyloid under denaturing conditions and has been chosen as a model protein for this study. Initial bulk experiments have been performed utilizing dynamic light scattering (DLS) and steady state and time-resolved fluorescence of conformationally sensitive fluorophores. The measurements provide a preliminary theory for the mechanism leading to amyloid growth. However, SMS directly identifies critical intermediates that may only be hypothesized by bulk experiments. A single molecule imaging experiment utilizing incubated samples of mono-labeled TMR-(β-LG) has been designed to count number of precursor monomers per aggregate species by counting the number of photobleaching steps required to extinguish a single aggregate's fluorescence. The time evolution of the particle number distribution is fit to the preliminary kinetic model representing the mechanism of amyloid growth. We have developed Hidden Markov Model (HMM) algorithms for analyzing single molecule photon trajectories on a photon-by-photon basis. The algorithms are calibrated by applying them to single molecule measurements of 70 kD and 2000 kD dextran conjugated with 5.8 and 58 moles of TMR per mole of dextran, respectively. The models are then applied to aggregating β-LG. Global optimization of model parameters is obtained using multidimensional optimization algorithms, and one is able to extract kinetic parameters (fluorescent lifetimes, anisotropy, etc.), and the number of proteins per measured aggregate.

646. Molecules at Aqueous Interfaces

Kenneth B. Eisenthal, Columbia University, New York, NY

Studies using second harmonic spectroscopy to probe the equilibrium and dynamic processes of molecules at various aqueous and phospholipid/aqueous interfaces will be presented.

647. The Influence of Surface Charge on Interfacial Polarity: Does It Matter?

Robert A. Walker, Carmen Huffman, Milton Liu and Daniel Burden, University of Maryland, College Park, MD

Variable length surfactants can be used to examine the dipolar width of aqueous/organic interfaces. These surfactants consist of solvatochromic, hydrophobic probes attached to a charged headgroups by variable length alkyl chains. Using resonance enhanced second harmonic generation, we acquire effective excitation spectra of adsorbed surfactants. Results show that the response of the probe cares a great deal about the identity of the headgroup – cationic vs. anionic – and surfactant length, but that simple aqueous electrolytes, even at high concentrations, do not influence interfacial polarity. We have also studied the influence of charge on interfacial polarity in "uncoupled" systems where the adsorbed probe is a neutral solute. Again, neither the bulk phase ionic strength nor the identity of the electrolytes appear to influence the local dielenctric environment sampled by the probe at a liquid/liquid interface.

648. Intermediates in Light-driven DNA Repair by Photolyase

Robert J. Stanley, Zhanjia Hou, Madhavan Narayaran and Goutham Kodali, Temple University, Philadelphia, PA

DNA photolyase (PL) is a monomeric flavoprotein that binds cyclobutylpyrimidine dimers (CPDs) and repairs them *via* photoexcitation of the reduced flavin adenine dinucleotide cofactor (FADH). We have used femtosecond transient absorption spectroscopy to explore the electron transfer and repair kinetics of DNA photolyase with several substrates. An analysis using singular value decomposition shows that the flavin semiquinone (FADH□) is formed after photoexcitation of the protein:substrate complex, giving the first direct evidence that electron transfer occurs from the reduced flavin cofactor to an as yet unidentified initial acceptor. Interestingly, it also appears that excitation of the protein alone leads to a small degree of electron transfer. Other spectroscopic evidence for intermediates in the repair reaction will also be presented.

649. Single-molecule Polyproline Isomerization by Fluorescence Quenching due to Short-range Electron Transfer

Hiyun Kim, Youssef Issa, Troy Messina, Jongjin Jung, Jason T. Giurleo, Stephen S. Isied and David Talaga, Rutgers University, Piscataway, NJ

Single molecule polyproline isomerization is studied by fluorescence quenching, induced by short-range electron transfer between TMR (5-carboxytetramethylrhodamine) and DMPD (dimethyl-p-phenylenediamine). To do this, we have prepared a polyproline (n = 2,3) peptide with DMPD at its carboxylic end and TMR at its amino end. The electron transfer efficiency is measured by TCSPC (time-correlated single photon counting) in which the acceptor fluorescence lifetime is comparatively quenched according to the proximity of donor molecule. The change in the latter is the indication of the trans-to-cis (or vice versa) isomerization. The inducement of rapid isomerization by solvent polarity, ionic strength, or temperature allows us to monitor the conformational heterogeneity in a single molecule trajectories before the TMR gets photobleached. This experiment proves that PET (Photoinduced Electron Transfer) measurement can monitor local protein or peptide conformation at the level of a few residues (length <10 Å), which is very difficult in a FRET (Fluorescence Resonance Energy Transfer) measurement. It also allows us to investigate the role of conformation in biological electron transfer.

Thermochemistry and Chemical Kinetics II

Organizer: Joseph W. Bozzelli New Jersey Institute of Technology, Newark, NJ
Presider: Joseph W. Bozzelli New Jersey Institute of Technology, Newark, NJ

650. Assessing the impact of accuracy of ab initio calculations in describing chemically activated systems

Ioannis P. Androulakis, Rutgers University, Piscataway, NJ, Joseph Bozzelli, New Jersey Institute of Technology, Newark, NJ and Timothy A. Barckholtz, ExxonMobil Research and Engineering, Annandale, NJ

Chemically activated systems play an important role in combustion and atmospheric chemistry. The overall reaction paths exhibit complex pressure and temperature dependence because each intermediate involves a coupled system of competing multi-step isomerization, deactivation and dissociation paths. A number of estimation techniques exist for deriving the required thermo and elementary kinetic input parameters for rate estimation. The availability of high-level ab-initio methods promises to remove the inaccuracies associated with older empirical methods. The objective of this study is to evaluate the importance of the various thermochemical parameters entering the rate calculation. We describe and illustrate a computational framework to quantify the functional relationship between the thermochemical properties and the macroscopic observables through appropriate response surface methods. The approach is demonstrated by analyzing the impact of thermochemical properties in estimating autoignition delays in propane oxidation.

651. Complete particle nucleation and growth model: Comparison with the classical nucleation theory

Evgeni N. Chesnokov, Andrei V. Chernyshev and **Lev N. Krasnoperov**, New Jersey Institute of Technology, Newark, NJ

A complete elementary reaction model of particle nucleation and growth from supersaturated solutions was developed and evaluated. The model includes all possible forward reactions (i.e., of monomers, dimers, trimers, etc.) together with thermodynamically consistent reverse processes. The kinetic model was numerically evaluated using the surface tension approximation for the particle thermodynamics. The time evolution of the size distribution function was obtained. The results were compared with the predictions of the classical nucleation theory. The impact of the basic assumptions of the classical nucleation theory was assessed, and the applicability limits of the theory were outlined. Model calculations were performed for nano-particle formation by Rapid Expansion of Supercritical Solutions (RESS) and compared with the experimental observations.

652. Development of adaptive chemistry model for combustion simulation

Marianthi Ierapetritou and **Ipsita Banerjee**, Rutgers University, Piscataway, NJ

Detailed simulation of complex combustion systems involves the integration of a system of partial differential equations describing the evolution of mass, momentum, energy along with the chemical species. Extensive research in the modeling of combustion kinetics has led to the development of detailed kinetic networks, consisting of hundreds of species and thousands of reactions. However, solution of the detailed combustion system along with such large kinetic mechanism is a computationally demanding task. Hence the need for representing the complex chemical reactions by simple reduced models, which can retain considerable accuracy while rendering computational feasibility. A methodology is developed in this work to automatically construct reduced mechanisms by utilizing mathematical programming techniques, where the objective is to minimize the dimension of the system while retaining sufficient accuracy in the prediction of specific species profiles. The reduced mechanism thus obtained has the property of accurately predicting the system behavior over a range of conditions in and around the nominal point at which reduction is performed. Realistically, under different species conditions and at different points in time, different reactions become important, which has been exploited to develop an adaptive mechanism reduction scheme, such that the reduced reaction model adapts itself to the changing reactor conditions. The reduced models are then analyzed for the range of conditions over which they retain their predictive capacity. An algorithm is then developed to couple the adaptively reduced models with detailed reactive flow simulations. These ideas are demonstrated using the system of methane combustion in air.

653. An Experimental and Theoretical Study of the Gas-Phase Properties of the Natural Base Cytosine and the Damaged Base O-Methylguanine

F. Sedinam Amegayibor, Yunlin Fu and Jeehiun K. Lee, Rutgers University, Piscataway, NJ

Base pairing in DNA is important for replication, coding and expression. How nucleobases hydrogen bond is ultimately dependent on their acid-base properties. The intrinsic acidity and proton affinity of a nucleobase in a nonpolar environment is best assessed through gas phase calculations and experimentation. Using mass spectrometric methods, we have determined the gas-phase acidities and proton affinities of O-methylguanine (OmG) and cytosine. Using a novel gas-phase bracketing methodology we bracketed two acidic sites for OmG and find that the values compare favorably to those computed at the B3LYP/6-31+G* level of theory. Cytosine, however, is more complicated. Calculations predict that cytosine exists as a mixture of tautomers in the gas phase, with varying acidities. A particularly intriguing aspect is that the preferred tautomer in a polar aqueous environment is not preferred in the nonpolar gas phase. We present experiments aimed at resolving the issues associated with the presence of multiple tautomers.

654. Thermochemistry, Kinetics and Kinetic Modeling on Atmospheric Reactions of the Benzene-OH Adduct with O2

Chiung-Chu Chen and Joseph W. Bozzelli, New Jersey Institute of Technology, Newark, NJ

Thermochemistry, reaction paths, barriers and Arrhenius pre-exponential factors for atmospheric and thermal reactions of benzene-OH adduct (a hydroxy-cyclohexadienyl adduct, C•HD-OH) with O2 are important to benzene oxidation and reactions. The thermochemistry and kinetics have been evaluated using ab initio, density functional and composite methods in computational chemistry. Kinetics for chemical activation reactions are analyzed using quantum Rice-Ramsperger-Kassel (QRRK) theory for k(E) and master equation analysis for pressure falloff. The O2 addition to C•HD-OH adduct forms a number of hydroxyl-cyclohexadienyl peroxy (CHD-OH-OO•) isomers (cis-(Z) and trans-(E) othro- and para- hydroxy peroxyl adducts). The reaction energies (well depths, ΔHr, 298) of C HD-OH + O2 ↔ CHD-OH-OO isomers were determined to be -10.63 ~ -13.67 kcal mol-1 with ΔSr, 298 of -32.07 ~ -35.08cal mol-1 K-1 at G3(MP2)//B3LYP/6-31G(d,p) level. The CHD-OH-OO• isomers can stabilized, dissociate back to reactants, react via hydrogen transfer to hydroperoxy oxyl isomers, or cyclize to bicyclic peroxy adducts. The [(E)-o-CHD-OH-OO•]* adduct also can dissociate to phenol + HO2 via HO2-molecular elimination. A detailed mechanism with mass conservation and microscopic reversibility is assembled and used to identify the intermediates and products of the C•HD-OH + O2 reaction for comparison with experiment.

655. Comparison of the Ignition Quality of Propane and Dimethyl Ether

Timothy A. Barckholtz, ExxonMobil Research and Engineering, Annandale, NJ and Xiaoqing You, University of Southern California, Los Angeles, CA

The oxidation of hydrocarbons at low temperatures plays a critical role in the ignition quality of fuels. The "low temperature chemistry" is manifested as a "negative temperature coefficient" in the fuel ignition fuel. We focus on comparing the ignition of dimethyl ether (DME) and propane. These molecules have similar structures yet have a vastly different ignition quality, as indicated by the large difference in RON (0 vs. 109).

Propane is the smallest hydrocarbon that exhibits an NTC, which is derived from two reactions of the propylperoxy radicals. In one reaction, the CCCOO· radical isomerizes to C·CCOOH, which leads to chain branching, which accelerates oxidation. In opposition, the CCCOO· radical can eliminate the HO2· radical and propylene. The HO2· radical is stable at low temperatures, and undergoes a chain terminating self-reaction, which decelerates the oxidation. These two reactions give rise to the NTC in propane.

In contrast to propane, the DME peroxy radical, COCOO·, can only isomerize to C·OCOOH. Because the central CH2 is missing, there is no opportunity for chain termination. Thus, the only option for DME is chain branching, and the NTC is

lost. Furthermore, the lack of a single transition state for the peroxy radical is the reason why DME has a lower octane than propane. The the drop in ignition resistance is due to the lack of the concerted elimination transition state in COCOO·, with secondary roles played by thermodynamic and other minor changes.

656. Laminar flame speeds and kinetic mechanism predictions for C2 hydrocarbons

John T. Farrell, ExxonMobil Corporate Research, annandale, NJ

Text Not Available

Visions in Chemistry II

Organizer: Philip Wientraub sanofi aventis, Bridgewater, NJ
Organizer: Tahir N. Majid sanofi aventis, Bridgewater, NJ

657. Development of New Tools and Methods for Organic Synthesis

Steven V. Ley, University of Cambridge, Cambridge CB21EW, United Kingdom

The search for new ways to assemble molecules continues to be an important driver for organic synthesis. The biological activity and the exquisite structural diversity associated with many natural products stimulates invention by challenging the current state of the art synthetic methodology. Our research involves the discovery and development of new synthetic methods and their application to biologically active systems. Our group has published extensively on the synthesis of natural products and to date more than 100 target compounds have been synthesised. The group is also developing new ways of making complex carbohydrates and developing new strategies for combinatorial chemistry. This lecture will give some recent results from the group.

658. Carbanion-mediated Strategies for Synthetic Aromatic Chemistry

Victor Snieckus, Queen's University, Kingston, ON, Canada

The simple link between the Directed ortho Metalation (DoM) reactions and the rich cross coupling chemistry of B, Mg, and Zn and the enabling Directed remote Metalation chemistry has allowed the development of new regiospecific strategies in aromatic synthesis. Recent results from our laboratories will be described.

659. Calcium Channels as Drug Targets: Why Some ARE and Some Are NOT

David Triggle, State University of New York at Buffalo, Amherst, NY

The therapeutically available calcium channel antagonists are a chemically heterogeneous group of small molecules that are widely employed in a number of cardiovascular diseases, most notably hypertension, and have simultaneously been invaluable molecular tools with which to probe the structure and function of voltage-gated calcium channels. They owe their therapeutic success to a specific interaction with one subclass of channel–the L-type voltage-gated calcium channel.With the realization that the L-type channel is but one member of a widely distributed family that includes the CaV1.1-1.4 (L) types, the CaV2.1-2.3 (P/Q, N and R types) and the CaV3.1-3.3 (T-type) widely distributed in both the peripheral and central nervous systems and elsewhere an intensive search was initiated for molecules that were selectively effective at these channel types and that might offer therapeutic utility in neuronal disorders including pain, epilepsy, stroke, affective disorders etc as well as in cardiovascular disorders, notably arrhythmias. These efforts have not been successful and small molecule equivalents of diltiazem, nifedipine and verapamil with therapeutic utility have not yet been found. The underlying reasons for this are discussed and comments made on the virtues of selective vs non-selective agents and on whether all diseases are susceptible to “magic bullets.”

Nature/Nurture: Women in Academe

Organizer: Valerie J. Kuck Seton Hall University, South Orange, NJ
Organizer: Dr. Cecilia H. Marzabadi Seton Hall University, South Orange, NJ
Presider: Dr. Cecilia H. Marzabadi Seton Hall University, South Orange, NJ

660. A Comparison of the Doctoral Achievement Rates in STEM Fields: Does Gender Affect the Yields?

Valerie J. Kuck, Buckner Janine P., Marzabadi Cecilia H. and Nolan Susan A., Seton Hall University, South Orange, NJ

The doctoral attainment rates for female and male graduate students in chemistry shows that women are less likely than men to obtain a doctorate. Similarly, female graduate students in physics, electrical engineering, chemical engineering, and mathematics do more poorly than their male counterparts. Closer examination of the doctoral degrees granted by the top 25 ranked chemistry departments shows a wide variation in the doctoral attainment rates for women and men. At several schools women do as well as men in earning doctorates, whereas at other schools they obtain doctoral degrees at a significantly lower rate. These findings suggest that environment rather than innate talent may be playing a major role in

graduate school performance. Based on a survey of the female and male doctorates from the top ten ranked chemistry departments, factors that could contribute to the lower doctoral attainment rate for women will be discussed.

661. Gender patterns in training and career paths of doctoral students from top-ranked chemistry departments

Cecilia H. Marzabadi, Janine P. Buckner, Susan A. Nolan and Valerie J. Kuck, Seton Hall University, South Orange, NJ

Doctoral graduates from 11-top ranked chemistry programs were surveyed about their undergraduate, graduate and post-doctoral training, as well as, their first career choices. We compared the training experiences reported by men and women in this cohort to elucidate the factors that may be responsible for the under-employment of women, particularly in tenure track faculty positions at the top chemistry departments. Specifically, we looked at the numbers of applications submitted, the numbers of interviews received and the numbers of employment offers garnered for academic jobs for both men and women in this group. We also examined factors such as numbers and types of post-doctoral fellowships held, the criteria that were used to choose post-doctoral fellowships and first positions and the assistance provided by mentors to these individuals. Best practices to encourage and promote women in academic training and career settings will be proposed.

662. A Gender Analysis of Employment Trends in Academic Chemistry

Janel Kasper-Wolfe, American Chemical Society, Washington, DC

Women's representation in chemistry and related fields increased over the last four decades, yet parity has not arrived and gender differentials in both education and the chemical professional remain. One such area is the academic sector of the chemistry workforce. Numbers alone cannot explain the complex barriers women chemists in the academy face. The fact is, their lives are multifaceted and in order to know about women's careers in academic chemistry, information about the interacting factors that contribute to that career is necessary.

Through its employment and salary surveys, the American Chemical Society gathers a range of data that can shed light on gender issues relating to the chemistry workforce. Examining the annual Salary Survey and Survey of New Chemical Professionals through a gender lens allows for a comparison of men and women in a number of areas: perceptions of the relationship between academic training and employment, salary, trends in academic employment, employment status, and postdoctoral positions. This presentation will compare selected variables relating to employment trends in Academic Chemistry by gender.

663. Investigating the role of institution-specific training practices in shaping the early career perceptions and paths of graduates from top-ranked chemistry departments

Janine P. Buckner, Cecilia H. Marzabadi, Susan A. Nolan and Valerie J. Kuck, Seton Hall University, South Orange, NJ

Our presentation focuses on data drawn from a survey administered to doctoral graduates from 11 top-ranked Ph.D.-granting chemistry departments. In this talk we highlight respondents' perceptions of graduate and post-graduate training and early career experiences. Discussion will center upon the early mentoring and training that occur at baccalaureate instituions, which in turn appear to have some influence on future career outcomes for women and men--particularly careers as tenure track faculty in Ph.D.-granting departments. Best practices to encourage and promote women in these training and career settings will be proposed.

664. Leaving Science: Occupational Exit from Scientific Careers

Anne Preston, Haverford College, Haverford, PA

During the past thirty years there has been a dramatic decline in the number of U.S. students pursuing advanced degrees in STEM fields. Equally disturbing is the dramatic increase in the number of professionals leaving scientific careers. The major reasons for career change will be identified. Particular attention will be given to female faculty members who have left academe. In addition policies that would improve the retention of scientists will be addressed.

665. Coaching Women for Success

Sally Chapman, Barnard College, New York, NY

COACh, the committee for the advancement of women in chemistry, was established in 1998 by a small group of senior women academic chemists concerned about the slow increase in numbers of tenured women at major research universities. Funded originally by the Dreyfus Foundation, COACh now has support from the Department of Energy, the National Science Foundation, and the National Institutes of Health. A major COACh activity is the sponsorship of workshops at ACS and AIChE national meetings. These workshops have been adopted and adapted widely. The COACh website describes the workshops and other COACh activities, and provides resources for women in academic chemistry departments: http://coach.uoregon.edu/.

Becoming a Teacher at a College/Community College (Panel Discussion)

Official: Anita J. Brandolini William Paterson University, Wayne, NJ

666. Becoming a Teacher at a College/Community College Panel Discussion

Anita J. Brandolini, William Paterson University, Wayne, NJ

When faced with a career transition, many chemists consider the option of teaching in a non-PhD-granting college. For someone whose career has been spent primarily in industry, this change can be both rewarding and challenging. Four chemists who have switched from industry into smaller academic environments will discuss their experiences, and offer advice for those wanting to make the same transition. The panel participants are Dr. Anita Brandolini, Assistant Professor, William Paterson University, Wayne NJ; Dr. Steven Waller, Assistant Professor, Fairleigh-Dickinson University, Madison NJ; Ms. Helen Tanzini, Professor, Mercer County College, West Windsor NJ; and Dr. John Adamovics, Adjunct Associate Professor, Rider University, Lawrenceville NJ.

Catalyzing Student Excitement in Chemistry/Science

Organizer: Bettyann Howson Chatham HS, Madison, NJ

667. Using the *Journal* as a resource

Diana Mason, University of North Texas, Denton, TX

The *Journal of Chemical Education* offers teachers a “living textbook.” The *Journal* is continually updated and new features are added as needed. Our latest endeavor, Chemistry Teacher Connections, gives all subscribers easy access to our online collections of many useful resources for teachers. The resources presented at this symposium include the Classroom Activity series, Chemed Learning Information Center (CLIC), and special items from JCE:Software. JCE:Software offers exciting CD-ROMs such as Chemistry Comes Alive! with video clips that both dazzle and educate students. The JCE Classroom Activities are hands-on, ready-to-photcopy-and-use chemistry activities targeting high school students. Also, included will be examples of several novel uses of the *Journal* for professional development and outreach programs.

668. DigiDemos

Ed Vitz, Kutztown University, Kutztown, PA

The Journal of Chemical Education has published the Tested Demonstrations Feature since 1955, and demonstrations have become a centerpiece of good chemistry teaching. Our recent addition to the National Science Digital Library, called DigiDemos, provides many advantages over the print version of Tested Demonstrations. For example, it will be possible to search for demonstrations appropriate to any topic, and view multimedia presentations of the demonstrations. Perhaps more importantly, it will be possible to continually improve traditional demonstrations by adding new safety information, new presentation techniques, and connections with aspects of contemporary life that were unimagined when the demonstrations were first published. During this presentation we'll explore the DigiDemos library and invite suggestions on its contents and format.

669. Odyssey: DiscoveryBased learning with Molecular Simulations

Nathan Dacuycuy, Wavefunction, Irvine, CA

This session, for high school chemistry teachers, will showcase how to incorporate molecular modeling software into the curriculum. ODYSSEY addresses more than 70 core chemistry topics. The software allows for stunning molecular simulations that are carried out in real time by a fully-integrated computational engine. With on-the-fly user control of system parameters (temperature, volume, and system composition), compelling classroom demonstrations and innovative student assignments are within reach for every instructor.

670. New Ideas in Interactive Animations and Multimedia

Conrad N. Trumbore, University of Delaware, Kennett Square, PA

The Contemporary Chemistry Project consists of three parts: a book module available in Adobe Acrobat PDF format, an interactive multimedia module presented in Macromedia Flash, and a collection of Flash animations taken from the multimedia module for presentation in the classroom. In addition to containing interactive animations, exercises, and illustrations, each multimedia module page contains clickable links to: chapter principles, a chapter summary, a chapter or book glossary, additional reference material, a dedicated web site containing classified links to the Web, and interactive questions about the page content. These questions are of two types: essay-type questions with “hint” and “complete answer” links, and multiple-choice questions that provide extensive feedback for both right and wrong answers. A running score for students' answers to multiple-choice questions is also provided. Several formats are available for classroom use. Animations can be shown to the class, with or without essay-type questions, and used by the instructor for stimulating class discussion. Alternatively, small, in-class groups can use the animations in conjunction with essay-type questions as an organizing feature for the group sessions. The full multimedia module can be accessed by students on the Web or from a CD outside the classroom to reinforce classroom discussions and for review. Contemporary Chemistry covers

subjects that have been selected with the aid of extensive feedback from students, focusing on subjects that are important in their lives. Chemical principles are introduced on a need-to know basis. A version of this project containing only basic chemical principles is also being developed.

671. Using Peer Review and Competition to Motivate Learners

Diane, L. Marturano, Wayne Valley High School, Wayne, NJ

Most individuals covet peer recognition. In a high school setting many adolescents obtain this recognition through negative behaviors rather than positive behaviors. As educators, it is our challenge to channel this natural competitve drive to improve student learning. Many of the ideas presented are simple, low-tech, everyday activities to integrate peer review and competition into the classroom.

672. Young Science Achievers Program[SM]

Bobbi Gorman, North Brunswick Township High School, North Brunswick, NJ

Young Science Achievers Program[SM] is non-profit and receives financial and organizational support from the Lucent Technologies Foundation, the AT&T Foundation and the New Jersey Science Teachers Association. Under this program, all girls and African American, Hispanic and Native American students in all public and private high schools (grades 9 thru 12) throughout the state of New Jersey and in New York City may apply for up to $1,000 in funds toward the completion of a science project. Each project will have the support of a mentor from Bell Labs and AT&T Labs.

Young Science Achievers is helping high school students realize their potential for science and technology by providing them with the resources and technical support they need to succeed. We began this program because minorities and women continue to be significantly under-represented in the science and technology fields. Our program serves to encourage minorities and girls to pursue careers in the technical fields, and to further strengthen science education by providing high schools with laboratory equipment vital to student projects.

The research is conducted in schools during the school year and culminates with poster presentations and an Awards Banquet. A booklet with project ideas is available online.

673. Chemagination: Write a future feature article for ChemMatters Magazine

Marisa Burgener, American Chemical Society, Washington, DC, DC

The Content Standards of the National Science Education Standards support a multidisciplinary perspective and encourage teachers to provide opportunities for integrated approaches to science teaching. In particular, the History and Nature of Science Standards support the need of students to understand that “science reflects its history and is an ongoing, changing enterprise.” Engaging students in this project will give them the opportunity to see that science is a human endeavor which incorporates the ability to ask questions, think critically and logically, make decisions based on data, and communicate scientific arguments.

674. Chemistry Clubs and Special Activities

John Dantoni, Wayne Valley High School, Wayne, NJ

Chemistry Clubs are an excellent format to get students interested in the study of chemistry and keep the enthusiasm for the subject alive. Club activities occur throughout the year with special attention being paid to holidays, especially Mole Day. Come share in the ideas and activities of the Wayne Valley Chemistry Club.

Pedagogical Mnemonics: AP, POGIL, Etc

Organizer: Bettyann Howson Chatham HS, Madison, NJ

675. AP Chemistry Test Development Process

John Gelder, Oklahoma State University, Stillwater, OK

Developing the AP Chemistry Exam each year is a challenging task that involves the effort of the AP Chemistry Test Development Committee, the Chief Reader for AP Chemistry and Test Development Specialists from Educational Testing Service. During this presentation I will detail the process of developing an AP Chemistry exam from the Chief Reader's perspective, and then discuss what happens at the AP Chemistry Reading. This year the Reading occurs in early June in Clemson, South Carolina. It is estimated that approximately 79,000 AP Chemistry exams will be graded this summer.

676. AP Grader Remarks

Karen L. Galley, West Windsor-Plainsboro High School South, Princeton Junction, NJ

Did you ever wonder what happens to those exams after they are collected from your students? Are you concerned that the responses that your students poured their hearts into will not get the attention they deserve? And where do those "correct" answers come from anyway? Get the facts about how the grading of the free response questions on the AP Chemistry exam is done and wonder and worry no more!

677. POGIL: A Student-Centered Approach to Teaching Chemistry

Richard S. Moog, Franklin & Marshall College, Lancaster, PA

Process-Oriented Guided Inquiry Learning (POGIL) is a teaching strategy that involves students working in groups on specially designed classroom activities that guide them to the development of an important chemical concept. In addition, there is an emphasis on the development of important learning skills such as information processing, problem solving, critical thinking, and communication. In this workshop, participants will be introduced to the pedagogic basis of this approach, and will also experience a POGIL classroom from the student perspective. Data supporting the effectiveness of the approach will also be presented.

678. Laboratory Activities to Reinforce Concepts for Advanced Placement Chemistry

NJACS Teacher Affiliates, c/o Diane Krone, Dumont, NJ

Laboratory work plays an important part to the A.P. Chemistry Program. The laboratory program should challange every student to think analytically, understand problems, design and carry out experiments that answer questions, manipulate data, make conclusions and evaluate their validity, propose further questions, and communicate accurately and meaningfully about observations and conclusions. Examples of lab activities that meet these goals will be discussed.

679. POGIL: Guided Inquiry Laboratory Experiments for the General Chemistry Laboratory

Richard S. Moog, Franklin & Marshall College, Lancaster, PA

POGIL guided inquiry laboratory experiences are built around the learning cycle paradigm of exploration, concept invention, and application. The goal of this type of experience is the development of a new chemical concept or trend, not the confirmation of an idea that has already been presented to the students. This presentation will describe the pedagogic basis for this approach, and will include examples of the application of this approach to the general chemistry course.

680. Mathematics in Biology: Nothing to Fear and Much to Gain

L. Charles Biehl and Dr. Thomas C. Fleetwood, The Charter School of Wilmington, Wilmington, DE

This session will include an overview of selected topics in high school biology that embody the use of meaningful mathematics, such as aspects of evolution and related genetics. These topics will not be those thought of as part of the "traditional" use of mathematics, such as probability. It will also include a description of a recently-launched Rutgers University Institute for teachers that explores the linkages between mathematics and biology in the high schools. The presenters are a high school mathematics teacher and a high school biology teacher, both of whom are "lead teachers" in the Rutgers Institute.

PowerPoint in Education

Organizer: Bettyann Howson Chatham HS, Madison, NJ
Official: Patricia Duncan HIgh Point HS, Lakeville, PA

681. Powerpoint Presentations in Chemistry

Patricia Duncan, HIgh Point HS, Lakeville, PA

Learn how to develop PowerPoint presentations to enhance your chemistry classroom in this hands-on workshop. To participate, please email Bettyann Howson: chemphun@optonline.net.

ADMET Posters

Organizer: Anita J. Brandolini William Paterson University, Wayne, NJ
Organizer: Donglu Zhang Bristol-Myers Squibb, Princeton, NJ

682. Distribution of Periodontopathic Bacteria Among Asian Indians

Shari Smith, Elizabeth Pelaez, Raji Subramaniam and Patricia Schneider, Queensborough Community College, Bayside, NY

Anaerobic gram-negative bacteria, in particular Prophyromonas gingivalis, Treponema denticola, and Tanneiella forsythensis, are associated with severe forms of adult periodontal disease. Demographic characteristics, such as age, gender and race, have been shown to influence both the incidence of periodontal disease and the bacterial composition of subgingival plaque. However, the impact of these factors on Asian populations is largely unknown. This study investigated the prevalence of the three pathogens in Asian Indian periodontal patients at a private dental clinic. Periodontal bacteria were detected by enzyme assay (BANA hydrolysis) and PCR using specific 16s rRNA probes. We examined the relationship between bacterial distribution, BANA score, demographic factors (age and gender) and clinical parameters (pocket depth, dental history and bleeding on probing). Strong positive correlations were found between the severity of Periodontitis (pocket depth), BANA intensity and patient age. All three anaerobic pathogens were detected with equal

frequency, but mixed infections were only found in patients with moderate to severe Periodontitis. These results indicate that all three bacteria are significant pathogens in the Asian Indian Population, however disease progression appears to be associated with mixed infection. Shari Smith and Elizabeth Pelaez are participants in the NIH Bridges to the Baccalaureate Program at Queensborough Community College (grant 1 R25 GM65096-03).

683. Essential Fatty Acid Metabolizing Enzymes Expression in the Developing Rat Placenta and Trophoblastic Models

Yan Xu, Gregory T. Knipp and Thomas J. Cook, Rutgers, the State University of New Jersey, Piscataway, NJ

The placenta regulates the delivery of nutrients and xenobiotics to the fetus, thus nourishing and protecting the fetus during development. Metabolism and transport are the two primary processes that govern essential fatty acids (EFA) supply from mother to fetus, which are critical for fetal development. While the EFA metabolism pathways are described in many tissues, there is a dearth of information in placenta. In this study, we have determined the expression of several enzymes involved in EFA metabolism in the rat developing placenta and trophoblastic models: cytochrome P450 isoforms CYP4A1, 4A2, 4A3, and 4A8; cyclooxygenases COX-1 and –2; lipoxygenases 12/15- and 5-LOX. Placentas from rats on different gestation period were harvested. The junctional (JXN) and labyrinth (LAB) zones were separated. HRP-1 and Rcho-1 trophoblstic models were cultured. Gene expression was determined by RT-PCR using specific primers. Immunohistochemistry was utilized to determine the temporal and spatial protein expression. The relative expression of the CYP4As were: 4A1>4A2>4A3, 4A8, with greater expression in the JXN zone. COX-2 exhibited a greater expression than COX-1 after gestational day 11 with a shift in spatial expression from LAB to JXN as gestation progressed. 12/15-LOX was expressed throughout the gestation with 5-LOX undetected. The results demonstrate that the rat placenta expresses several enzymes involved in EFA metabolism. The differential expression suggests that there may be changes in placental EFA metabolism as a function of gestational age that can alter EFA supply to the fetus. Our work establishes a template for studying xenobiotics influence on placental EFA metabolism.

684. Preliminary Oral Pharmacokinetics of the Potential Chemopreventive Agents Farnesol and Geraniol

Joseph G. Desiderio, Harold Newmark and Thomas J. Cook, Rutgers, the State University of New Jersey, Piscataway, NJ

Introduction: The isoprenoids, farnesol [FOH] and geraniol [GOH], have previously demonstrated *in vitro* and preclinical *in vivo* activity as chemopreventive and chemotherapeutic agents, yet their disposition profiles have not been fully described. To this end, preliminary pharmacokinetic studies of FOH and GOH in the rat were performed. **Methods:** A single oral dose (1 g/kg) of either *trans-, trans*-[3-,^{14}C]-farnesol ([^{14}C]-FOH) or [3-^{14}C]-geraniol ([^{14}C]-GOH) was administered to male Sprague-Dawley rats. Blood was sampled over a 24-hr period, after which the animals were euthanized and tissues, total feces and urine were collected. Plasma and urine samples were analyzed by radiometric HPLC. Tissue and feces samples were dissolved or oxidized and analyzed by LSC. **Results:** Preliminary pharmacokinetic model analyses suggest [^{14}C]-FOH and [^{14}C]-GOH are rapidly absorbed after oral administration (T_{max}= 34 min and 3 hrs for [^{14}C]-GOH and [^{14}C]-FOH, respectively). Radiometric HPLC peaks corresponding to the respective parent compounds were absent in the plasma and urine samples. The maximal amount of radioactivity appeared in the liver of rats dosed with [^{14}C]-FOH (4.0%) and in the small intestine of rats dosed with [^{14}C]-GOH (3.2%). The majority of the radioactivity was excreted as metabolite in the urine (12.2% and 24.4% for [^{14}C]-FOH and [^{14}C]-GOH, respectively). **Conclusions:** The absence of parent compound in the plasma samples suggests FOH and GOH are subjected to extensive first pass metabolism in the liver and/or intestine. Their extensive metabolism has important implications on the chemopreventive potentials of FOH and GOH. Acknowledgement: Financial support from McKesson Bioservices through NCI subcontract N02-CN-95016.

College Education Posters

685. First-Year Organic Problems that Promote Student Reasoning

Ray A. Gross Jr., Prince George's Community College, Largo, MD

The structural features inherent in acyclic monoterpenes that follow the isoprene rule often lead to unique sets of ozonolysis products from which their structures, excluding stereochemistry, can be determined from molecular formulas only. Examples are provided to show how students may improve their reasoning skills by solving the structures of unknowns by a systematic analysis of the oxidative and reductive workup products. Data for 66 problems are provided. Fifty of them give a unique set of products from which a single structure can be elucidated by the techniques exemplified. The remaining 16 compounds give products that satisfy two structures. The problems vary in difficulty, and afford instructors of beginning organic or qualitative organic analysis courses a set of degradation problems that complement spectral and synthetic problems in engaging students to apply their knowledge to solve challenging problems.

686. Synthesis and Study of Silver Nanoparticles

Sally D. Solomon, adviser and principle author. Solomon Sally II, Aravindan V. Jeyarajasingam and **Mozhgan Bahadory**, Drexel University, Philadelphia, PA

A laboratory experiment on colloidal silver introduces students to a unique property of a nanomaterial,the intense yellow color exhibited by silver nanoparticles compared to ionic or bulk silver. Students synthesize colloidal silver, estimate particle size using visible spectroscopy and study the prevention of aggregation using a polymer stabilizer. An optimal set of conditions was determined for the synthesis of silver nanoparticles using borohydride reduction of silver nitrate. The method produces 12± 2 nm particles as determined by transmission electron microscopy. The plasmon absorbance is near 397 nm and the peak width at half maximum (PWHM) is 35-40 nm. This cost-effective experiment is a suitable laboratory activity for general chemistry. Details of the synthesis, determination of particle size by TEM and optical properties, as well as a discussion of aggregation and stabilizers are included.

687. Enhanced Learning through Group Problem Solving

Madhu Mahalingam, Fred Schaefer and Elisabeth Morlino, University of the Sciences in Philadelphia, Philadelphia, PA

We describe the implementation and impact of group work in recitation sections associated with the general chemistry course. To supplement the lecture portion of the course, recitation sections of approximately 45 students are used with the primary goal of having the student work on problem solving in small groups. Students are placed in groups of mixed ability based on math SAT scores in their first semester and regrouped based on their first semester grade for the second half of the course. The groups provide opportunity for students to interact in solving assigned problems that are designed to foster collaboration and discussion between group members. Student response to the implementation of group work in recitation has been positive. Exam averages have improved by about 8 points since the introduction of the group work. The effect of class composition on the outcome of the group work model will be discussed. The differences in the implementation of the group work by different faculty will also be presented. Ultimately, we show that student learning is enhanced through structured group-work in the course without changing faculty resources.

688. Development of laboratory experiments for the undergraduate forensic biochemistry laboratory

Francis Charles Mayville Jr., William Farina, Derick Siegel and Edward Fleming, DeSales University, Center Valley, PA

This investigation will involve the synthesis of several ionic liquids containing the 1-alkyl-3-methyl-imidazolium cation coupled to the chloride anion. These ionic liquids are added to tert-butyl alcohol and the freezing point depression can be obtained. The goal of this experiment is to develop a physical chemistry experiment that we could use in the undergraduate laboratory and to further understand the versatility of ionic liquids.

689. Development of laboratory experiments for the undergraduate forensic biochemistry laboratory

Francis Charles Mayville Jr. and Nicole Beyer, DeSales University, Center Valley, PA

In this study we are developing new experiments or revising existing experiments for the undergraduate biochemistry laboratory with a concentration in forensic analysis. These studies were prompted by our inability to find a suitable laboratory text to be used in our undergraduate biochemistry laboratory course. The laboratory experiments that are being explored involve: electrophoresis for fingerprinting of DNA and protein systems as well as polymer chain reaction technology. Our biochemistry course is a one-semester course taken by chemistry, biology and environmental science majors. Our goal is to modify or to create experiments to fit our current equipment and to accent the forensic applications of biochemistry.

690. A POGIL- and Project-Based Approach to Chemical Literacy for Non-Science Majors

A. Bryan Lees, Kean University, Union, NJ

Actively involving non-science majors in a one-semester chemical literacy course has posed a longstanding challenge for chemical educators, especially when a primary course objective is to apply rigorous chemical principles rather than descriptive discussion to chemical issues. Data-oriented POGIL classroom activities dealing with both chemical concepts and issues have been developed to engage students in actively reading, interpreting, and solving chemical problems in small groups. These classroom activities guide students to further literature research that may be applied to independent projects of their choice. Each project defines and illustrates a current chemical issue.

Student project reports are structured as possible POGIL activities. The project format includes (1) a summary of data illustrating the magnitude of the issue, (2) critical thinking questions that lead to cumulative understanding and (3) problems that apply stoichiometry to make qualitative and quantitative predictions related to the issue. Following the POGIL activity format and formulating their own critical thinking questions reduces students' tendency to simply summarize their references; instead, it focuses their efforts on communicating their results to others.

The self-knowledge and confidence students develop in solving classroom problems supports and directs independent research that was previously beyond their reach and makes them more comfortable with scientific information. Based upon exam grades, student performance has far exceeded that in a traditional lecture format.

691. The Use of Chiral Oxazolidinones in an Advanced Instructional Synthesis Lab

S. Shaun Murphree and Matthew P. Betush, Allegheny College, Meadville, PA

Chiral oxazolidinone chemistry is used as a framework for an advanced multi-step synthesis lab taught in the sophomore year. The cost-effective and robust preparation of chiral starting materials is presented, as well as the use of chiral auxiliaries in a synthesis scheme that is appropriate for students currently in the second semester of the sophomore organic sequence.

Electronic Structure Posters

Organizer: Anita J. Brandolini William Paterson University, Wayne, NJ

692. Rydberg excitation energies from LDA

Adam Wasserman and Kieron Burke, Rutgers University, Piscataway, NJ

The Local Density Approximation (LDA) yields accurate excitation energies for high-n Rydberg states. For the case of He and Ne, the asymptotic quantum defects predicted by LDA are in less than 5% error. These were found by analyzing *scattering* states of the LDA potentials, since the incorrect asymptotic behavior of such potentials unbinds the Rydberg series. The quantum defects of the lost Rydberg series, however, are determined by the potentials in the core and valence regions of the atoms, where the LDA description is excellent.

693. Negative ions on the verge of ionization

Kieron Burke and **Vazgen Shekoyan**, Rutgers University, Piscataway, NJ

The behaviour of negative ions on the verge of ionization is studied. Electron-electron correlation plays a significant role for negative ions, especially for the outermost electron. Answering questions such as what negative ions exist, what the behaviour of its electronic density is at the ionization threshold or why negative ions are particularly difficult to treat in DFT are important. A simple model of a 2-electron ion is introduced and its behaviour on the verge of ionization is studied in detail.

694. Double excitations in density functional theory

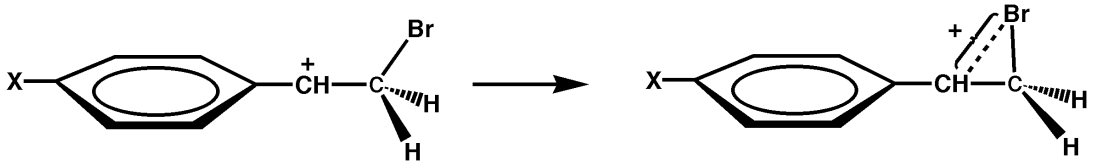
Fan Zhang[1], Neepa T. Maitra[2], Robert J. Cave[3] and Kieron Burke[1], (1)Rutgers University, Piscataway, NJ, (2)Hunter College of CUNY, New York, NY, (3)Harvey Mudd College, Claremont, CA

Excited state properties can be calculated in density functional theory (DFT) via different approaches. Time-dependent DFT (TDDFT) with linear response yields excitations, but only single excitations within the (standard) adiabatic approximation. A frequency-dependent exchange-correlation kernel is needed to capture double excitations. Second-order Goerling-Levy perturbation theory (GLPT) can be applied to both non-degenerate and nearly degenerate excited states. Some excitations are shown to be poorly described to first order (i.e. in exact exchange), no matter how weakly correlated the system is. Results are demonstrated on a simple model and short chain polyenes.

695. Computational Studies of Benzyl-Substituted Halonium Ions

Ronald R. Sauers, Rutgers University, Piscataway, NJ and Howard Haubenstock, The City University of New York, The College of Staten Island, Staten Island, NY

Experimental studies on additions of chlorine and bromine to styrenes have been rationalized in terms of bridged ions involving halogen lone pairs interacting with a positive center. An extensive series of ab initio and DFT computations were carried out with the objective of quantifying the interactions of bromine and chlorine atoms with neighboring cationic centers in a series of substituted 1-aryl-2-haloethyl cations. Analyses of structural changes and bonding interactions between the positive center and the halogens gave rise to linear correlations with σ+ values. The results are interpreted in terms of variations in the importance of halogen bridging. Electron-donating groups diminish bridging and electron-withdrawing groups enhance bridging.



696. Computational Machinery of Nuclear Shielding

Keith W. Wiitala, University of Minnesota, Minneapolis, MN

The quantum mechanic calculation of nuclear shieldings for molecules are presented in the context of Density Functional Theory (DFT). The mathematical constructs of the Ramsey formulation are succinctly reviewed allowing for appreciation of recent efforts to improve the accuracy of DFT methodology. Additionally, a historical perspective and review of relevant literature is made.

697. Charge Transfer Energies and Electronic Coupling across Peptides with Different Dihedral Angles: Ramachandran Electronic Coupling Surfaces for Different Peptides

Youssef Issa, Karsten Krogh-Jespersen and Stephan Isied, Rutgers University, Piscataway, NJ

Earlier work from this group investigated the charge transfer energy ΔE and the electronic coupling matrix element H_{DA} for electron transfer across polypeptides with different secondary structures. The results showed significant differences in ΔE and H_{DA} implying different electron transfer rates for different peptide secondary structures.(ref1) In this work we have studied the electron transfer reaction for the charge recombination of a modified tyrosine radical cation (Tyr^{+}) to a modified Tryptophan radical anion (Trp^{-}) across a diproline bridge (shown below), using Zerner ZINDO/S (ref2) and the Cave and Newton Methods(ref3).

The Psi and the Omega dihedral angles between the two proline peptides were systematically varied to cover a range of dihedral angles of peptide structures including conformations with less favorable angles and higher energies. An energy optimized relaxed geometry was generated at the AM1 level of theory for every structure prior to calculation of ΔE and HDA. The energy of the charge transfer process was found reasonably accessible (around 6 eV) and the electronic coupling element H_{DA} at different dihedral angles ranges from 200 to 800 cm-1. Similar calculations for the glycine and alanine dipeptides will also be presented and compared with the more structurally constrained proline dipeptides.

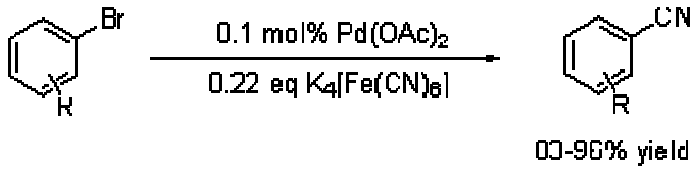
1. Y.-g. K. Shin, M. D. Newton and S. S. Isied J. Amer. Chem. Soc. 125, 3722 (2003). 2. ESPPAC, J.D. Westbrook and K. Krogh-Jespersen, Rutgers University 3. Cave, R. J.; Newton, M. D. Chem. Phys, Lett. 249, 15(1996).

Organic Posters II

Organizer: Anita J. Brandolini William Paterson University, Wayne, NJ
Organizer: Cecilia H. Marzabadi Seton Hall University, South Orange, NJ

698. Ligand-Free Palladium-Catalyzed Cyanation of Aryl Halides

Steven Weissman, **Daniel Zewge** and Cheng Chen, Merck, Rahway, NJ



A practical, *ligand-free* cyanation of aryl bromides that utilizes as little as 0.1 mol % $Pd(OAc)_2$ in combination with a nontoxic cyanide source, $M_4[Fe(CN)_6]$ (M = K, Na), is described. The reactions are performed in DMAC at 120 °C and provide the corresponding aryl nitrile in 83-96% yield, typically in less than 5 h. TON values of up to 7100 were attained.

699. Synthesis of a Merck NK-1 receptor antagonist

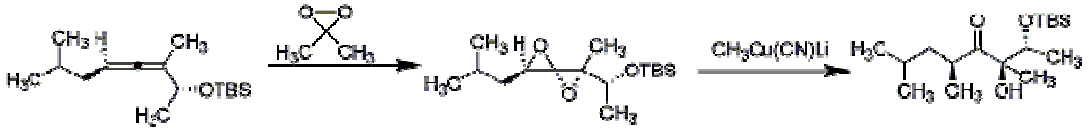
Jason J. Kowal, Merck & Co., Rahway, NJ

Substance P (NK-1) receptor antagonists have been shown to be potential therapeutic agents for a wide variety of important medical disorders. Among these, substance P has been shown to be effective in the treatment of chemotherapy-induced nausea and vomiting which led Merck to the identification of Aprepitant. Herein, we describe the synthesis of another Merck NK-1 receptor antagonist.

700. Addition Of Cuprates To Spirodiepoxides Derived From Allenes: A Concise Stereocontrolled Synthesis Of α-Hydroxyketones

Partha Ghosh, Rutgers University, Piscataway, NJ and Lawrence J. Williams, Rutgers University, Piscataway, NJ

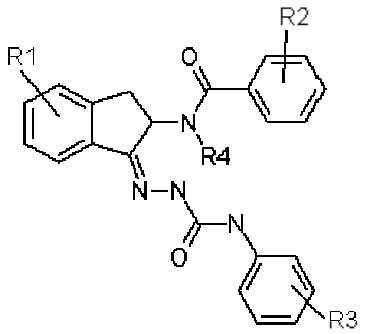
The substituted α-Hydroxyketone containing structural motif is prevalent among natural products like Erythromycins, Amphidinolides etc. We have developed a new methodology for the stereocontrolled synthesis of these classes of motifs by adding cuprates to the spirodiepoxides derived from allenes.



701. Preparation of 2-benzamidoindanone semicarbazone derivatives as insecticides

Elizabeth G. Rowley, Daniel H. Cohen, Ellen M. Crawford, Louis V. LaFrance, Ernest L. Plummer and David M. Roush, FMC Corporation, Princeton, NJ

N-aryl semicarbazones of 2-benzamidoindanone were prepared in order to investigate structures related to indoxacarb and the pyrazoline insecticides. The desired compounds were made from appropriately substituted indanones and found to be active against various Lepidoptera species. This poster will present the synthesis of these semicarbazone insecticides as well as their biological activity.



702. Preparation and reactions of chiral 2-oxazolinyloxy-substituted carbanions

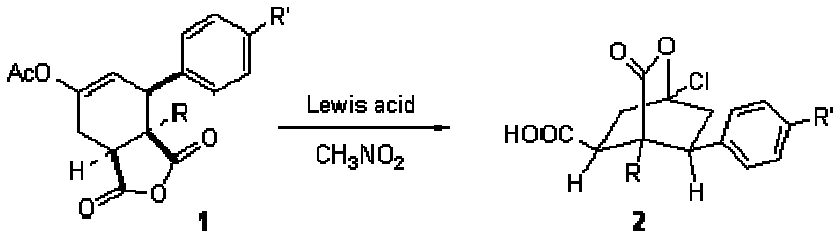
Lesley-Ann Nelson and Sasan Karimi, Queensborough C C, Bayside, NY

The aim of this research is to prepare chiral 2- oxzaolinyloxy -substituted carbanions, and study their enantioselective reaction with aldehydes. It is hypothesized that the anion will be formed by direct deprotonation of a chiral compound and will do so at a high degree of enantioselectivity. In obtaining such results, the carbanions will then react with achiral electrophiles such as aldehydes to produce a chiral alcohol. This protocol can provide an easy access to optically active alcohols in the middle of a long chain that are otherwise inaccessible.

703. A Geminal Chlorolactone Reaction

Andrew T. Bach[1], Raymond A. Baylouny[2], Edgar Leone[3] and Willis B. Hammond[3], (1)Novartis Pharmaceuticals, East Hanover, NJ, (2)Fairleigh Dickinson University (College at Florham), Madison, NJ, (3)Honeywell Corporation, Morristown, NJ

Geminal chlorolactones (2) having a bicyclo[2.2.2] octane ring system was formed when cis-anhydride (1) was treacted with $AlCl_3$, $MeAlCl_2$, or Me_2AlCl in nitromethane. The [2.2.2] ring system was unambiguously established by the display of an ABX pattern in the NMR of the reduced chlorolactone. In addition, several substituted cis-anhydrides formed analogous gem-chlorolactones by the same protocol.



Lewis acid = $AlCl_3$, $MeAlCl_2$, or Me_2AlCl
R = H, Me
R' = H, Me, OMe, Cl, Br

704. Synthesis and Biophysical Studies of c-di-GMP

Zhaoying Zhang, Barbara L. Gaffney and Roger A. Jones, Rutgers, The State University of New Jersey, Piscataway, NJ

A new and efficient method has been developed for the synthesis of c-di-GMP, which is an important signaling molecule involved in bacterial biofilm formation. UV, CD and NMR studies of this molecule in the presence of Li+, Na+, or K+ show a polymorphic behavior.

705. Preparation and reactions of 2-imidazolinyloxy-substituted carbanions

Shazim Mobin and Sasan Karimi, Queensborough Community College, Bayside, NY

The aim of this research is to prepare chiral 2-imidazolinyloxy –substituted carbanions, and study their enantioselective reaction with aldehydes. It is hypothesized that the anion will be formed by direct deprotonation of a chiral compound and will do so at a high degree of enantioselectivity. In obtaining such results, the carbanions will then react with achiral electrophiles such as aldehydes to produce a chiral alcohol. This protocol can provide an easy access to optically active alcohols in the middle of a long chain that are otherwise inaccessible.

706. A Practical One-Pot Preparation of 7-Hydroxyquinoline

R. Scott Hoerrner, Mark Cameron, Shawn Springfield, James McNamara and Ulf Dolling, Merck & Co., Rahway, NJ

An efficient, practical, one-pot preparation of 7-hydroxyquinoline, a key intermediate in a series of pharmaceutical drug candidates, is described. The procedure addresses safety concerns in handling highly toxic acrolein, as well as providing a high-yielding and direct isolation of crystalline 7-hydroxyquinoline from the crude reaction mixture.

707. Improved Method for Synthesis of DNA and RNA Containing a Thioalkyl Tether in the Minor Groove at Guanine for Crosslinking to Protein

Xiaorong Hou, Gang Wang, Barbara L. Gaffney and Roger A. Jones, Rutgers University, Piscataway, NJ

A guanosine analog containing a thioalkyl tether with the ability to crosslink can be used to constrain the folding of DNA/RNA-protein complexes and to facilitate their structural analysis and study. We have developed a new method in which guanosine is first derivatized with a thioalkyl tether protected as the tert-butyl disulfide, and then converted into a phosphoramidite for incorporation into either DNA or RNA. After synthesis, the thioalkyl tether can be reduced to the free thiol by DTT or converted to other disulfides of varying reactivity.

708. Major Differences in RNA Metal Biding Motifs Determined by ^{15}N NMR

Yupeng Fan, Barbara L. Gaffney and Roger A. Jones, Rutgers, the State University of New Jersey, Piscataway, NJ

Divalent metal ions play both structural and functional roles in RNA. A RNA hairpin from the group I intron P5b stem loop was synthesized with [8-^{13}C-7-^{15}N]-guanosine at a guanine in the tandem GG·UU pair (a known metal binding site) and [7-^{15}N]-guanosine outside the binding site for comparison. Its interactions with different metal ions in solution (Zn^{2+}, Cd^{2+}, Mg^{2+}, and $Co(NH_3)_6^{3+}$) were monitored using ^{15}N NMR. We observed very different metal binding effects compared to those we saw at a tandem GA·AG motif from the hammerhead ribozyme. (Wang, G.; Gaffney, B. L.; Jones, R. A. *J. Am. Chem. Soc.* **2004** *126*, 8908 -8909)

709. Substituent Effects for Two Series of Substituted N-Benzylideneanilines Using NMR Spectroscopy

John Tierney[1], Linda M. Mascavage[2] and Christopher Dieterick[2], (1)Pennsylvania State University, Media, PA, (2)Arcadia University, Glenside, PA

Two series of mono-substituted N-benzylideneanilines, 1 and 2, have been synthesized. The substituents were placed in the C-phenyl ring and the N-phenyl ring at either the 3 or 4 positions. This is a report of preliminary results for substituent effects on ^{13}C chemical shifts in both phenyl rings and at the benzylic carbon in deuterochloroform solution. The effects on the ^{1}H chemical shifts for the methine proton will also be shown.

1 2

710. Efficient Preparation of Acyclic Amidinium Salts by Orthoester Exchange and Amidinium Salt Transamination

Shahrokh Saba, Adeline Kojtari, **Marinda M. Rivera**, Peter D'Amico, Dana Canuso and Moses K. Kaloustian, Fordham University, Bronx, NY

A series of symmetrical and unsymmetrical acyclic amidinium hexafluorophosphates were prepared in good yields. Symmetrical *N,N′*-dialkyl-substituted formamidinium salts were produced by direct reaction of triethyl orthoformate with two equivalents of a 1^{o} amine in the presence of ammonium hexafluorophosphate. *N,N,N′*-Trialkyl- and *N,N,N′,N′*-tetraalkyl-substituted formamidinium salts were prepared by transamination of *N,N*-disubstituted formamidinium hexafluorophosphates using 1^{o} and 2^{o} amines, respectively.

711. An approach to syntheses of tetrahydroisoquinoline compounds

Bradley M. Hutnick[1], Lynn M. Bradley[1] and David A. Hunt[2], (1)The College of New Jersey, Ewing, NJ, (2)Albany Molecular Research, Albany, NY

Previous work in this research group had resulted in the synthesis of an aziridine intermediate from o-bromobenzaldehyde by way of imine formation and subsequent reduction with sodium borohydride. Creation of a nucleophilic carbon at the adjacent sp^2 arene carbon using bromine-lithium exchange should result in expansion of the three-membered aziridine ring, resulting in tetrahydroisoquinoline, a backbone for several natural products. This semester's research focuses on the duplication of previous work, as well as improving the efficiency of the aziridine formation process. Future work toward developing suitable conditions and reagents to effect ring-opening of the aziridine to create the desired tetrahydroisoquinoline will be reported in due course.

712. Synthesis and Reactions of Bicyclic Cyclopropylamines from Intramolecular Cylopropanation of Amino Acid Derivatives

Catherine A. Faler and Madeleine M. Joullie, University of Pennsylvania, Philadelphia, PA

Cyclopropylamines and substituted cycloproylamines are important structural element s in a variety of biologically active compounds. We have previously reported the Ti(II) mediated intramolecular coupling of a terminal olefin and the N,N-dimethyl carboxamide moiety of aromatic amino acid derivatives in the synthesis of novel and strained bicyclic structures. Here, we present the extension to other amino acids, [4.1.0] bicycles, and different amino substitutions. We also report the attempts of ring expansion to obtain novel piperidines and azepanes.

713. Synthesis of new cyclin dependent kinase 2 inhibitors

Ayana Moses and Kwesi Amoa, Medgar Evers College, Brooklyn, NY

CDKs is dependent upon a regulatory subunit called cyclin. Members of the cyclin family bind to and activate their CDK partners. For example, cyclins A and B activate CDK1, cyclins A and E regulate the activity of CDK2, and the D-type cyclins are associated with CDK4. While the concentration of the CDKs remains relatively constant throughout the cell cycle, cyclin expression and degradation occur in a periodic fashion. The rise and fall of cyclin concentrations are timed to provide specific CDK activities, as they are needed for progression through the various stages of the cell cycle.

The recognition of the importance of CDKs to the process of cell division has stimulated an interest in them as potential targets for proliferative diseases such as cancer, psoriasis, and restenosis, and for the prevention of chemotherapy-associated side effects such as alopecia. A number of small-molecules, which act as, inhibitors of CDKs have been identified and are described in recent reviews.

Thus, our interest is in developing new cyclin-dependent kinase 2 inhibitors. In particular, we want to study the effect of a phenylpentyl moeity at the 4th position.

714. Assignment of 13C Chemical Shifts to Ring Carbons of Acetophenones

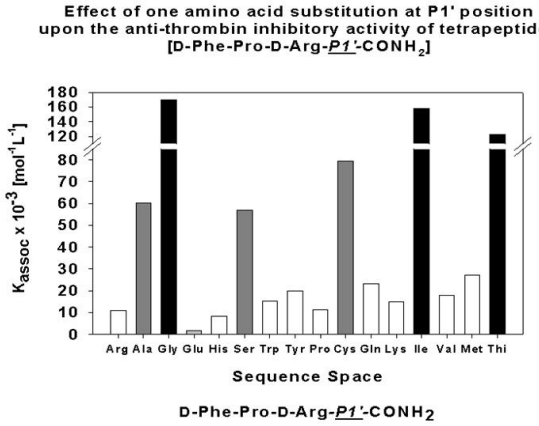
Donald D. Clarke, Fordham University, New York, NY

A substituent on a benzene ring alters delta at ring C atoms o- and p- to it depending on electronic sigma values, while the m- position is little affected. Nitrobenzene is an exception. There delta for the o- position is less than for m-; the opposite is predicted. The p- C behaves normally. In acetophenone the o- and m- C signals differ by 0.1-0.3 ppm. A JACS paper [94, 3089 (1972)] states that o- and m- assignments are unconfirmed, but suggested that o- signal has higher delta value. All databases copied this suggestion. We found by C-H COSY the opposite assignment is true. This seems to be a through space effect as invoked to explain the effect of the nitro group o- to itself. Phenacyl chloride and propiophenone behave similarly to acetophenone but &alpha,&alpha-dichloroacetophenone doesn't. Benzaldehyde, benzoic acid and methyl benzoate behave normally. Supported in part by NSF's Division of Undergraduate Education grant #9650684.

715. Structure-based design, synthesis and structure-activity relationship of peptide libraries containing Phe analogs as reversible inhibitors for thrombin

Cristina C. Clement and Manfred Philipp, Lehman College, City University of New York (CUNY), NYC, NY

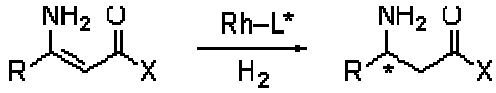
The major goal of this investigation was to perform a structure-based design and lead optimization of tetrapeptides that can reversibly inhibit thrombin. We were focusing on tetrapeptides with the sequence space (NH2)-DPhe (P3)–Pro (P2)–DArg (P1)-P1'-CONH2 which was shown previously to inhibit thrombin in vitro. F-moc manual synthesis of amide-tetrapeptide libraries was performed on a Rink-Amide resin incorporating phenylalanine (Phe) analogs in the P3 position such as trans/(cis) cinnamic, dihydrocinnamic acids, D-Naphthylalanine (DNal), Phe constrained analog 1,2,3,4- (D)-tetrahydroisoquinoline-3-carboxylic acid [(D) Tic], and 1,2,3,4-tetrahydronorharman-3-carboxylic acid. The libraries were obtained using the partition-mixing procedure coupled with parallel synthesis. Preliminary results showed that replacement of D-Phe in P3 position with D-Nal had a two fold increased inhibitory activity for thrombin in an in vitro assay competing with the chromogenic substrate S2238.



716. Highly Efficient Synthesis of b-Amino Acid Derivatives via Asymmetric Hydrogenation of Unprotected Enamines

Yi Hsiao[1], **Nelo R. Rivera**[1], Thorsten Rosner[1], Shane W. Krska[1], Eugenia Njolito[1], Fang Wang[1], Yongkui Sun[1], Joseph D. Armstrong III[1], Edward J. J. Grabowski[1], Richard D. Tillyer[1], Felix Spindler[2] and Christophe Malan[2], (1)Merck Research Laboratories, Rahway, NJ, (2)Solvias

A direct asymmetric hydrogenation of unprotected enamino esters and amides is described. Catalyzed by Rh complexes with Josiphos type chiral ligands, this method gives b-amino esters and amides in high yield and high ee (93–97 %ee). No acyl protection/deprotection is required.



X = OR, NR_1R_2

717. Reactivity Of Tris(Trimethylsilyl)Phosphite (TMSP): Attempt to prepare the N-mustard-bis Phosphonic acid of Bicine

Ji Suh, Queensborough Community College, St.John's University, Bayside, NY, Luis Vargas, Queensborough Community College, Bayside, NY and Ralph Stephani, St. John's University, Jamaica, NY

Steps in the conversion of bicine (bis-N,N-dihydroxyethyl- glycine) into the N-mustard-bis-phosphonic acid, using TMSP, are described. The object is to combine the alkylating action of the nitrogen-mustard group with the directing properties of the bis-phosphonic acid to develop a more efficient drug against bone cancer.

718. “Instant methylide" modification of the Corey-Chaykovsky cyclopropanation reaction

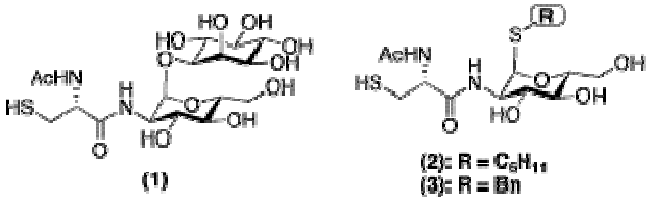
James A. Ciaccio, **Courtney E. Aman** and Shahrokh Saba, Fordham University, Bronx, NY

We recently reported that sulfoxonium and sulfonium methylides are generated upon treatment of storable, dry mixtures of $Me_3S(O)I$/ KO*t*-Bu and Me_3SI/NaH, respectively, with carbonyl compounds in DMSO to conveniently and rapidly afford the corresponding epoxides by the Corey-Chaykovsky reaction (Ciaccio et al., *Synth. Commun.* **2003**, *33*, 2135). Using mixtures of $Me_3S(O)I$/ KO*t*-Bu and $Me_3S(O)I$/ NaH under similar conditions, we now report that various □,□-unsaturated ketones afford the corresponding cyclopropyl ketones in good yields. This “instant methylide” modification of the Corey-Chaykovsky cyclopropanation reaction offers a convenient and experimentally simple preparation of cyclopropyl ketones, with advantages over conventional procedures: ease of handling (mixtures of sulfoxonium salt and base can be stored indefinitely under anhyd. conditions); in most cases, methylides are generated in the presence of the carbonyl substrate; reaction times are relatively short. Preliminary results suggest that aziridination of suitably substituted imines is possible.

719. S-Benzyl thioglycosidic mycothiol analogue

Michael Smerina and Spencer Knapp, Rutgers University, Piscataway, NJ

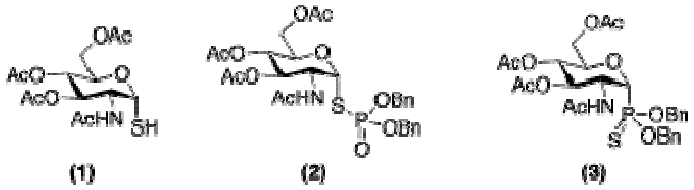
Most actinomycetes, including Mycobacterium tuberculosis, biosynthesize and maintain high levels of mycothiol (1) as protection against oxidative stress and electrophilic agents. Analogues such as (2) and (3), whose synthesis we describe, can be expected to participate in some of the same enzymatic pathways, and thus might serve as starting points for drug design.



720. P-Glycosyl-phosphonothiate O,O'-diesters

Kehinde A. Ajayi and Spencer Knapp, Rutgers University, Piscataway, NJ

Reaction of GlcNAc-alpha-mercaptan (1) with dialkyl N,N-diisopropylphosphoramidites gives the O,O'-dialkyl S-glycosylphosphothioate (2) or P-glycosyl-phosphonothioate (3) depending upon oxidation conditions. Mechanistic and other aspects of the rearrangement leading to (3) will be presented.



721. The Synthesis of a TMC-95 Intermediate from N-Boc-Tryptophan

Ahalya Ramanathan and Leslie, S. Jimenez, Rutgers, The State University of New Jersey, Piscataway, NJ

An intermediate of the TMC-95 class of natural products can be synthesized from N-Boc-tryptophan in 7 steps and further modification of this intermediate would lead to the total synthesis of TMC-95A-D.

722. Study of the Selectivity of the Lithiation of Secondary and Tertiary 3,5-Difluoro-Substituted Benzamides

Michael D. Green[1], **Francesca Khani**[1], Lynn M. Bradley[1] and David A. Hunt[2], (1)The College of New Jersey, Ewing, NJ, (2)Albany Molecular Research, Albany, NY

Substituted benzamides have been widely employed as valuable synthons for metalation reactions encompassing a wide variety of applications. Recently, research has lead to interest in dihalogenated benzamides for use as pest control agents. Previous studies of this laboratory group have revealed that metalation reactions with secondary 3,5-dichloro-substituted benzamides afford products resulting from ortho-metalation while metalation reactions with the corresponding tertiary dichloro-substituted benzamides afford only products resulting from para-metalation. To better understand the influence of halogens on the regioselectivity of these reactions, the corresponding 3,5-difluoro-substituted analogs were studied. Metalation studies with N-ethyl-3,5-difluorobenzamide indicate that products arising from both para- and ortho-metalation were produced, while initial results from the metalation of N,N-diethyl-3,5-difluorobenzamide indicate that products resulting from para-metalation were favored.

723. Sythesis and Characterization of a Naphthoquinone Derived Amino Acid

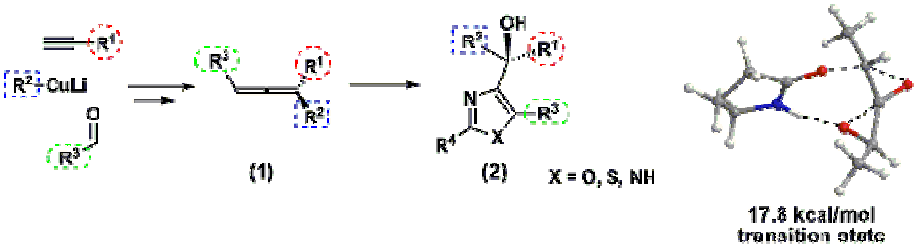
Bruce R. Lichtenstein[1], Ronald L. Koder[2] and P. Leslie Dutton[2], (1)University of Pennsylvania, Philadelphia, PA, (2)The Johnson Foundation and the University of Pennsylvania, Philadelphia, PA

Studies on quinone oxidoreduction have heretofore been almost exclusively performed within quinoproteins; thus limiting the experimental contexts to what nature designed. As an alternative to natural proteins, the use of an architecturally diverse synthetic-protein scaffold, or maquette, would allow for a much more tailored approach towards exploring quinone electron chemistry. Towards that end, we report the synthesis of a naphthoquinone-derived amino acid, its integration into a synthetic peptide, and initial explorations of its oxidoreduction properties.

724. Facile one pot synthesis of heterocycles from allenes and mechanistic insight on the opening of spirodiepoxides

Stephen D. Lotesta, Sreenivas Katukojvala, Sezgin Kiren, R. R. Sauers and Lawrence J. Williams, Rutgers University, Piscataway, NJ

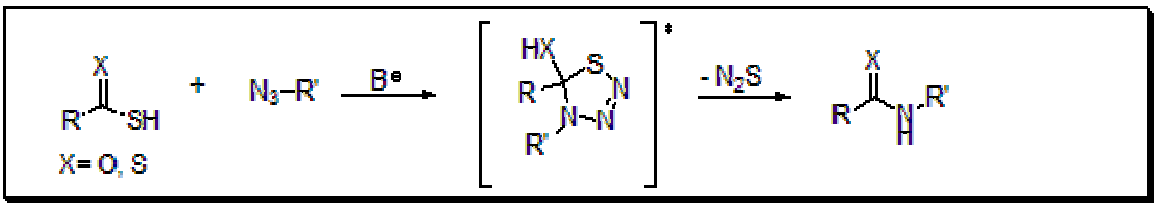
New routes to oxazoles, thiazoles, and imidazoles continue to be of interest to the synthetic community, as these moieties are common in pharmacologically active compounds and natural products. In the course of our studies on reactive heterocyclic intermediates, we discovered a direct approach to these heterocycles. Here we report a one pot procedure to heterocycles of type (2) from readily available allenes (1). Experimental and computational data support intramolecular general acid catalyzed spirodiepoxide opening.



725. Thioamides Via Thiatriazolines

Robert V. Kolakowski, Ning Shannggguan and Lawrence Williams, Rutgers University, Piscataway, NJ

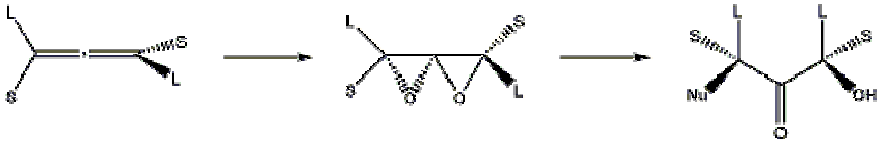
Herein we wish to report the facile synthesis of thioamides through the rearrangement of thiatriazolines. The azide and dithio acid precursors are coupled utilizing mild basic conditions and have been proven not to proceed through a complicating amine intermediate. Dithio acid/azide coupling efficiently generates thioamides where traditional thioacylation and isothiocyanate coupling techniques fail. This method uniquely provides a thioamidation at room temperature in water.



726. Stereoselective Synthesis of Alpha-hydroxy Ketones: Addition of Carbon Nucleophiles to Spirodiepoxides

Jennifer Inghrim and Lawrence J. Williams, Rutgers University, Piscataway, NJ

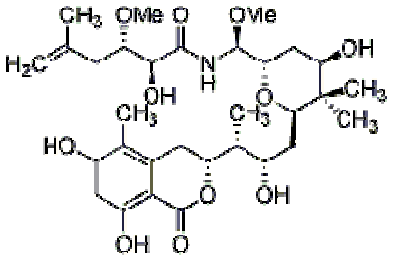
Spirodiepoxides derived from the oxidation of allenes offer a concise route to highly functionalized carbonyl motifs. In the course of our studies of the reactivity of spirodiepoxides, we have demonstrated that carbon nucleophiles can add stereoselectively to generate highly substituted alpha-hydroxy ketones. Herein we report a range of carbon nucleophiles found to successfully alkylate spirodiepoxides.



727. Studies Towards the Total Synthesis of Psymberin

Ning Shangguan, Sezgin Kiren and Lawrence Williams, Rutgers, The State University of New Jersey, Piscataway, NJ

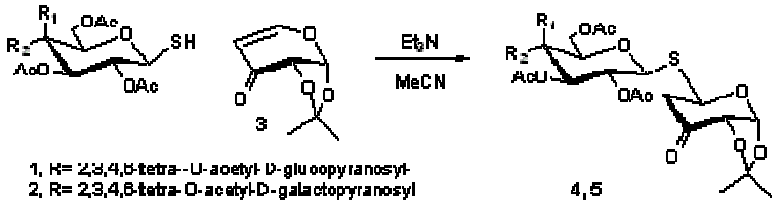
Psymberin is a pederin like natural product isolated from marine sponge by Crews and coworkers. It showed potent cytotoxicity and high selectivity against several solid tumor cell lines. A convergent and stereoselective synthesis of psymberin, which involves the use of a spirodiepoxide as a key intermediate, is underway. Progress toward the total synthesis of this interesting molecule will be presented.



728. Stereoselective Synthesis of 1, 5 S-thiodisaccharides from L-Arabinose Enones

Zbigniew J. Witczak and David Lorchak, Wilkes University, Nesbitt Schoolof Pharmacy, Wilkes-Barre, PA

As a part of a program to develop novel, versatile methods and strategies for S-thiodisaccharide synthesis, we have recently reported the synthesis and evaluation of differently functionalized S-1, 4-thiodisacharides and their sulfones. Here we describe further assessment of the stereoselective Michael addition of active 1-thiosugars to L-arabinose enones. In accordance with this new stereoselective concept, the synthesis of first novel 1, 5-thidisacharides is achieved. We demonstrated that activation of the conjugate Michael addition with various bases such as Et3N, and TMG allows the stereoselective synthesis of S-1-5 linked thiodisacahrides with no protecting group manipulation during and after functionalization.



729. The development of a reliable, highly sensitive technique to determine the metal ion concentration of cells using exciton-coupled circular dichroism

Samuel A. Simpson, New York University, New York, NY

This research is to develop a reliable, sensitive technique to determine the metal ion concentrations of cells by making various chromophores that have metal-binding pockets to produce exciton-coupled circular dichroism (ECCD) spectra. When two chromophores are close to each other, ECCD can be used to assign absolute configurations. The synthesis includes attaching two light absorbing compounds such as quinolines, to the nitrogens of biologically active compounds like chiral amines. The addition of metal ion salts like Cu(ClO4)2, fixes the geometries of the chromophores providing ECCD spectra. The ECCD method is non-empirical which eliminates the use of chiral reference compounds. Graphing the wavelength of absorbed light (λ) vs. the change in molar absorptivity of the polarized light (Δε) reveals positive couplets for the R-isomers and negative ones for the S-isomers. This method can use micromolar concentrations and enantiopurity can be assessed. X-ray crystals provide a second verification of chirality and structural conformation. Utilizing ECCD, chiral metal complexes show bisignate curves when the absorbance of left and right circularly polarized light is graphed vs. the wavelength of light. The development of several light-absorbing molecules such as quinolines, phthalocyanines, pyrenes, naphthalenes, and other fluorescent compounds expands the scope of the spectroscopy in the electromagnetic spectrum. This research is designed to lead to finding the concentrations of metal ions such as copper and zinc that build up in the cells of people with diseases such as Alzheimer's, ALS, and Parkinson's without requiring surgery.

730. Total Synthesis of Cyclopeptide Alkaloid Hymenocardine

Galina V. Kapustin, Rao N. Nallagancho, Weiying Yang and Madeleine M. Joullié, University of Pennsylvania, Philadelphia, PA

Hymenocardine, a 14-membered cyclic peptide alkaloid containing a p-ansa structure with 10-membered peptide-type bridge, was isolated from roots of Hymenocardia acida Tul. in 1968 and has not been synthesized. The leaves and root extracts of Hymenocardia acida showed numerous medical indications including malaria, anti-trypanosomal, antitumor activity and some of these may be related to hymenocardine. This biological activity led us to synthesize hymenocardine for testing. We now wish to report the synthesis of this compound. Hymenocardine contains two nonproteinogenic amino acids, a â-phenoxy amino acid with a tertiary alkyl-aryl ether linkage in the cyclic core and dimethyl amino allo-L-isoleucine on the N-terminus of the side chain. The key steps of the synthesis are the construction of the tertiary alkyl-aryl ether linkage and the macrocyclization. The synthesis was started from D-Ser-OMe which after protection was converted to a tertiary alcohol with methyl Grignard reagent. A SNAr reaction was used for installation of the alkyl-aryl ether bond. Different strategies have been tried for macrolactonization step. The details of the synthesis will be discussed.

Polymeric Biomaterials Posters

Organizer: Anita J. Brandolini William Paterson University, Wayne, NJ
Organizer: Kathryn E. Uhrich Rutgers University, Piscataway, NJ
Presider: Thomas J. Cook Rutgers, the State University of New Jersey, Piscataway, NJ

731. Mesoporous Silicate Materials as Carriers for Poorly Water-Soluble Drugs

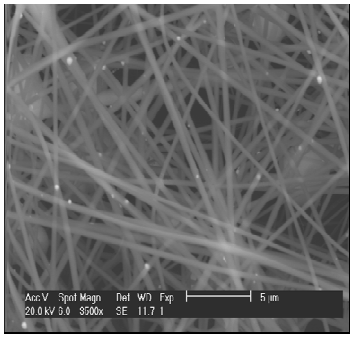
Rupali Shah[1], Shannon Dugan[2], Shannon Verissimo[2], Melissa Zastrow[2] and Isabelle Lagadic*[2], (1)University of Connecticut, Department of Chemistry, Storrs, CT, (2)University of Connecticut, Storrs, CT

Improving the solubility of poorly water-soluble drugs remains an important challenge for the pharmaceutical industry. Usually, these drugs are mechanically mixed with porous silicate substrates (e.g. calcium silicate or kaolin) to enhance their dissolution rates. Our objective was to investigate the loading of poorly water-soluble drugs (e.g. ibuprofen and naproxen) onto a mesoporous silicate material and its amino-functionalized derivative; and to study the kinetics of the drug release in simulated body (SBF, pH = 7.4) and simulated gastric (SGF, pH = 1.2) fluids. Interactions between the drug carboxylic acid groups and the amine functions of the carrier are expected to modulate the drug release. A loading up to 300 mg of drug per gram of solid was achieved. FT-IR, powder XRD and TGA/DSC characterizations indicate that the drugs are loaded in their more soluble amorphous forms. The drug release profiles in SBF and SGF at 37?C were determined by monitoring the concentration of the drug in the release medium by UV spectrophotometry. The release rates of the drugs in SBF were found to be dependent of the morphology of the drug-loaded solid (i.e. fine powder, coarse powder or pellet), while no release of the drugs was observed in SGF.

732. Electrospinning of porous silica micro/nanofibers containing silver nanoparticles

Alpa C. Patel, Drexel University, philadelphia, PA and Yen Wei, Drexel University, Philadelphia, PA

Porous silica micro/nanofibers containing catalytic silver and gold nanoparticles were synthesized by a sol-gel plus electrospinning method. Tetraethyl orthosilicate (TEOS), poly[3-(trimethoxysily)propyl methacrylate] (PMCM), silver nitrate (AgNO3) and Chloroauric Acid (HAuCl4-4H2O) were used as precursors for the production of silica-PMCM hybrid fibers and silver (Ag) & gold (Au) nanoparticles. Heat treatment of the fibers at high temperatures resulted in both the thermal decomposition of PMCM polymer, leading to the porosity, and the conversion of metal precursors to their respective metal nanoparticles. The color of the fiber mats can be changed from light yellow to dark golden brown and light pink to a dark purple due to the surface plasma resonance of the Ag and Au nanoparticles embedded in the fibers respectively. It is possible to tune the size and density of the metal particles in the silica fibers by varying the amount of metal precursor introduced and the thermal treatment conditions. The silica fibers containing the metal particles were then characterized by environmental scanning electron microscopy, transmission electron microscopy, X-ray diffraction, UV-Vis spectroscopy, and thermogravimetric analysis. The catalytic activity of the Ag containing fiber mats was assessed by reduction of methylene blue dye.



733. Methacrylate-silica nanocomposite dental materials with low volume shrinkage

Zhengfei Sun, Yen Wei, Praveen Solomon and Guoliang Yang, Drexel University, Philadelphia, PA

Polymerization shrinkage is the main disadvantage of dimethacrylate monomers used in dentistry. It compromises the adhesion of the restorative composite to the tooth structure and causes gap formation resulting in pulpal irritation, post-op sensitivity and recurrent decay. Our objective is to develop polymethacrylate-silica hybrid/nanocomposite dental materials with low volume shrinkage based on dense packing of vinyl modified silica nanoparticles. In this study, vinyl modified silica nanoparticles was assembled into thin film of densely packed particles. Upon photopolymerization of vinyl groups on the particles and vinyl monomers in the interstitial spaces, polymethacrylate-silica nanocomposite was obtained with low volume shrinkage. Further investigation is in progress to prepare bulk materials with dental monomers and visible light photoinitiators.

734. The use of carboxymethylcellulose as a drug carrier

Megan Nollenberger and Christine Martey-Ochola, Shippensburg University, Shippensburg, PA

The formation of peritoneal (intra-abdominal) adhesions is a common and dangerous side effect of general abdominal surgery, hernia repair, and radiation therapy, as well as many other invasive abdominal procedures. These adhesions may result in chronic pelvic pain, infertility and hemorrhaging. To reduce the occurrence of these internal adhesions, the use of barrier polymers is becoming a more frequent and very successful solution. One such polymer is Sodium Carboxymethylcellulose (SCMC) (fig. 1), which is a very attractive candidate for nucleophilic drug substitutions due to the presence of the carboxymethyl residues. In this study, we monitor the release of chemotherapy agents, specifically Mitoguazone and Eflornithine (fig. 1), from the polymer-drug conjugate previously synthesized.

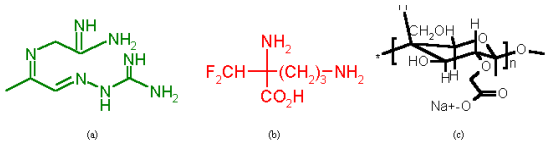


Figure 1. Structures of (a) Mitoguazone, (b) Eflornithine, and (c) SCMC

735. Synthesis and Characterization of Poly(vinyl acetate)-graft-PDMS Copolymers

Sarah E. Grieshaber and Yadunandan L. Dar, National Starch and Chemical Company, Bridgewater, NJ

Polymers with controlled architecture such as block, graft, and radical copolymers demonstrate unique features and significant utility in many fields. The unique interfacial properties of these materials as well as their ability to phase separate at a sub-micron scale have led to the ability to manipulate bulk and interface properties. Two notable examples are the compatibilization of material blends to lead to novel hybrid properties and materials with better bio-compatibility. In particular, materials with siloxane units have been used for their unique biocompatibility as well as the ability to form inorganic silica templates upon calcination. The latter can be used in a variety of applications including catalysis and structured inorganic films and coatings.

This poster describes the synthesis and characterization of graft copolymers with a vinyl acetate backbone with pendant poly(dimethyl siloxane) (PDMS) grafts. The aim of this work was to synthesize these materials and analyze for the amount of copolymerized PDMS. This is not trivial as the separation of the reacted PDMS from the unreacted PDMS macromonomer is not possible using traditional analytical techniques such as soxhlet extraction or precipitation.

The synthesis was conducted by solution polymerization. The analysis included verification of PDMS copolymerization with vinyl acetate and quantifying the level of PDMS macromonomer incorporation.

736. Amphiphilic-scoripion like macromolecules (AScMs): efficient carriers for intracellular drug delivery

Jelena Djordjevic and Kathryn E. Uhrich, Rutgers University, Piscataway, NJ

Amphiphilic scorpion-like macromolecules (AScMs) are biodegradable, non-toxic and non-immunogenic block copolymers that form micelles above their CMC (~ 10-7 M). The purpose of this study was to demonstrate and characterize uptake and intracellular retention of AScMs in vitro using human umbilical vein endothelial cells (HUVEC). Briefly, uptake studies were performed by monitoring cellular accumulation of the fluorescent dye-loaded AScMs (R110 and R123, respectively) as a function of time (15-240 min) and AScMs concentration (0.0001–1 mM); intracellular distribution and localization of dye-loaded AScMs in HUVEC was investigated using confocal microscope. In addition, intracellular localization of AScMs was confirmed using transmission electron microscopy studies. The uptake of R110- and R123-loaded AScMs was found to decrease with an increase in the AScMs concentration; the decreased accumulation of R110- and R123-loaded AScMs in HUVEC monolayers was inversely correlated with the extent of dyes partitioning into AScMs. In addition, uptake of R110- and R123-loaded micelles was found to be time-dependent; the uptake was seen as early as at 15 min and peaked within 60 min of experiment. Furthermore, confocal microscopy studies demonstrated increased fluorescence activity in the cells with increase in the incubation time, whereas TEM studies confirmed presence of AScMs within the cellular compartments. In conclusion, AScMs were shown to be rapidly internalized into the HUVEC; cellular uptake was shown to be time- and AScMs concentration-dependent, and the micelles were mainly localized in the cytoplasm. Thus, AScMs are useful for localizing therapeutic compounds or genes into endothelial cells to achieve a sustained therapeutic effect.

737. Long-circulating cylinder micelles demonstrate the strong effects of morphology on biological transport and interactions

Yan Geng, University of Pennsylvania, Philadelphia, PA, Paul Dalhaimer, Yale University, Peter Photos, Princeton University and Dennis Discher, Univ. Pennsylvania, Philadelphia, PA

Morphologies of natural vehicles such as viruses and pollen grains range from quasi-spherical to filamentous, and raise fundamental questions about the effects of vehicle shape on biological transport and interactions. With two series of copolymer-based assemblies, we synthetically decouple the effects of chemical variation from morphology and elucidate the biological impact of spherical versus cylindrical shape as well as length. Compared to spherical morphologies made from similar copolymers, microns-long cylindrical micelles, or flexicelles, exploit hydrodynamic interactions and mimimize capture by cells. These cylindrical vehicles are readily loaded with hydrophobic dyes or drugs and circulate through the microvasculature for more than a week after injection compared to tens of hours for viruses and carriers such as liposomes. While the protracted circulation and length-dependent interactions of flexicelles open up a myriad of applications, the results also provide generic insight into what is ‘nano' in biological systems.

738. Improved detection sensitivity in ELISAs by multi-labeled enzyme DNA dendrimers conjugated to anti-biotin antibodies

Johanna R. Mora and Robert C. Getts, Genisphere, Hatfield, PA

Enzyme-linked immunosorbent assays (ELISAs) are simple and inexpensive methods used to determine the presence of biomarkers for the diagnosis of multiple diseases and drug development. Output signal depends on the number of enzyme molecules that can be indirectly attached per analyte molecule. Improving the detection sensitivity of the assay would allow a better understanding of cellular mechanisms and decrease the amount of sample required per assay. To increase the assay's sensitivity other groups have tried successive incubations of enzyme labeled avidin and biotinylated anti-avidin antibodies. The main drawbacks of this approach are an increase in assay time and decrease in reproducibility due to the multiple incubations and washes. A better approach would be to deliver a higher number of labels. To this end, we have prepared DNA dendrimers conjugated to anti-biotin antibodies containing up to 300 molecules of horseradish

peroxidase (HRP), and compared these reagents to streptavidin-HRP (~2HRP/streptavidin). The assay format consisted of a standard microtiterplate ELISA in which the dendrimer conjugate is a “drop-in” reagent replacing the streptavidin, so that no extra steps are involved. Interleukin 1 alpha (IL-1&alpha) was selected as the model analyte. Upon optimization we were able to detect less than 2 pg/mL of IL-1&alpha, corresponding to greater than 20-fold signal amplification respect to streptavidin-HRP. The conjugate was also used to detect IL-6, TNF alpha, antibodies against beta 2 glycoprotein I (&beta2 GPI) and gastric pariental cell antibody (GPA). For these markers signal amplifications ranged from 5 to 200 fold compared to streptavidin-HRP detection.

739. Amphiphilic Star-like Macromolecules for targeted drug delivery

yichao Zhang, Rutgers University, Piscataway, NJ

Unimolecular micelles are multi-branched polymers that solubilize hydrophobic drug molecules in aqueous environment. These polymers were designed with multi-branched, hydrophobic interior (core) and hydrophilic exterior (shell) to maintain physical properties characteristic of conventional micelles, but with enhanced thermodynamic stability. In effort to utilize unimolecular micelles to transport and deliver anti-cancer drugs, we are developing a series of Amphiphilic Star-like Macromolecules (ASM) with improved drug loading efficiency. The hydrophobic core is prepared by acylation of tetra branched core initiator with various mucic acid derivatives. The hydrophilic shell is assembled by conjugating poly(ethylene glycol) (PEG) chains to the core. Targeting moieties, such as folic acid, are introduced at the PEG chain end to aid in selective delivery of encapsulated drugs.

740. Synthesis and Hydrolytic Stability of Poly(oxyethylene phosphonate)s with Different Macromolecular Architecture

Bogdana Goryanova[1], Kolio Troev[2] and Ivan Gitsov[1], (1)SUNY College of Environmental Science and Forestry, Syracuse, NY, (2)Bulgarian Academy of Sciences, Sofia, Bulgaria

The low toxicity, biocompatibility and structural similarity to naturally occurring biomacromolecules make phosphorus-containing polymers desired materials for biological and pharmaceutical applications. Poly(oxyethylene phosphonate)s with different macromolecular architecture were synthesized via polycondensation of commercially available dimethyl-H-phosphonates taken in excess to linear and branched poly(ethylene glycol)s. The number average molecular weight of the polymers was established by vapor pressure osmometry, size-exclusion chromatography (SEC) and NMR. The hydrolysis of poly(oxyethylene phosphonate)s at different conditions was studied independently by SEC and ^{31}P NMR. The results showed that at neutral pH the initial concentration of the polymer strongly affects the degree of ensuing hydrolysis (60% higher at 50 mg/mL than at 10 mg/mL). It might be assumed that the observed differences are caused by the concentration-driven changes in the solution behavior and aggregation mechanism of the poly(oxyethylene phosphonate)s. The influence of the poly(oxyethylene) segment length and architecture on the properties of the resulting polymers was studied, as well.

741. Effect of the Linker Structure on Salicylic Acid-Derived Poly(Anhydride-Esters)

Almudena Prudencio, Robert Schmeltzer and Kathryn Uhrich, Rutgers, The State University of New Jersey, Piscataway, NJ

A series of salicylic acid-derived poly(anhydride-esters) were synthesized by melt polymerization methods, in which the components linking the salicylic acids were varied. In this work, we define the "linker" as the structure that connects the two salicylate units. As the goal was to determine the relationship between the linker structure and the properties of the polymer, several linkers were evaluated for their inclusion into the polymeric backbone. The linkers were chosen based on their chemical structure and include linear aliphatic, aromatic and aliphatic branched structures. Polymer properties such as molecular weight, thermal decomposition temperature, glass transition temperature and contact angle were measured. For the linear aliphatic linkers, the molecular weight increased as the linker chain length (or number of methylenes) increased. Polymers with the most hindered linkers were more difficult to polymerize, yielding lower molecular weights. The thermal decomposition temperature also increased with the alkyl chain length but the glass transition temperature decreased, likely due to the enhanced flexibility of the polymer. The highest glass transition temperatures were displayed when using aromatic linkers due to the increased p-p interactions between the polymer chains. Drug loadings of 62-74 % by weight were obtained by modifying the linker structure. Water contact angles were measured to study the relative hydrophobicity of the polymers, which influences hydrolytic degradation rates. The ability to manipulate the physical properties of the polymers is relevant for tissue engineering, as well as drug delivery applications.

742. Microspheres Prepared from Salicylate-Based Poly(anhydride-esters)

Brian A. Yeagy, Robert Schmeltzer, Almudena Prudencio, Kathryn E. Uhrich and Thomas J. Cook, Rutgers, The State University of New Jersey, Piscataway, NJ

The aim of this work was to investigate how glass transition temperature (T_g) influenced polymer microsphere formation and degradation of three biodegradable salicylate-based poly(anhydride-esters) that differed by the linking group: poly (carboxyphenoxyhexanoate) (CPH), T_g = 57°C; poly (carboxyphenoxyoctanoate) (CPO), T_g = 30°C; and poly (carboxyphenoxydecanoate) (CPD), T_g = 27°C. These poly(anhydride-esters) are unique in that salicylic acid, an effective anti-inflammatory, is incorporated directly within the polymer backbone. Microsphere delivery systems prepared from these polymers would have a higher percentage of drug loading than standard biodegradable polymer systems. Microspheres of CPH, CPO and CPD were prepared using a oil-in-water solvent evaporation method and characterized

for particle size and morphology, in vitro release properties and residual poly(vinyl alcohol) (PVA) content. Spherical microspheres in the 1-10 μm size range were successfully prepared. The morphology of the microspheres determined by scanning electron microscopy (SEM) revealed that an extra washing step appears to increase aggregation as the T_g decreases; whereas only limited aggregation occurred in the polymer with the lowest T_g, CPD, in those not washed by centrifugation. An additional washing step also effectively removed residual PVA by >90%. The PVA content appeared to affect the drug release rates producing an 8 hr lag time and a 5% decrease in the amount of drug released over a 7 day period compared to microspheres washed free of PVA. Based on these results, poly(anhydride ester) microspheres can be prepared from several different polymers and have potential use as controlled drug delivery systems for anti-inflammatory conditions.

743. Antioxidant-Based Poly(anhydride-esters) : polymer properties and cytotoxicity results

Youngmi Kim and Kathryn E. Uhrich, Rutgers University, Piscataway, NJ

Phenolic derivatives present in olive oil have excellent antioxidant activity and play an important role in preventing cardiovascular disease and immune dysfunction. In addition, their antioxidant activity may be useful for regeneration of oxygen-damaged skin cells. Three phenolic compounds, vanillic acid, syringic acid, and 3-methoxysalicylic acid have been successfully incorporated into poly(anhydride-esters) using melt condensation polymerization methods. The advantages of a polymeric function are easy fabrication of films, fibers, and micropsheres for applications in various fields as additives in drugs or cosmetics. Moreover, toxicity or side effects will be minimized by reducing and controlling the antioxidant release. Polymer properties such as molecular weight, thermal transitions, solubility, hydrophobicity, and polymer erosion rates are attributed to the methoxy groups. For example, more methoxy-substituted polymers (i.e., syringic acid) have more hydrophilic values, based on contact angle measurements and diacid solubility in PBS than less methoxy-substituted polymers, which is also consistent with their slower erosion rates. Their biological activity will be evaluated for topical applications by cytotoxicity tests using fibroblast cells.

744. Differential Scanning Calorimetry of an Amorphous Phase Formed During Thermal Processing of PLA/PMMA Composites

Payal G. Patel, Kim-Phuong N. Le and Richard L. Lehman, AMIPP Advanced Polymer Center, Rutgers University, Piscataway, NJ

Mechanical blends prepared from granules [<600 μm]of poly(L-lactide) [PLA] and poly(methylmethacrylate) [PMMA] were annealed and quenched under various conditions of time and temperature to assess the degree and mechanisms of formation of a new intermediate amorphous phase first identified in extrusion experiments for this polymer system. The physical properties of these annealed and quenched blends were determined by modulated differential scanning calorimetry (DSC). Two isolated Tg's appeared in most of the blends, suggesting the immiscibility expected from solubility parameter calculations. However, at temperatures greater than 195^{o}C and at durations of 12 h, blends with 35 to 50 percent weight of PLA—the co-continuous range—exhibited a third Tg which occurred at approximately 80^{o}C, intermediate between the glass transition peaks of PLA and PMMA. The occurrence of this new phase suggests that PLA and PMMA may not be truly immiscible, but rather form an intermediate reaction phase, which we have termed PG80, under certain conditions. Subsequent to the initial study, which involved quiescent annealing and no shear, a modified version of this study was conducted in which particles and films were pressed at elevated temperatures to impart a combination of residence time at temperature with more intimate particle contact and a very modest level of shear. Results from both study segments will be presented and the effects of time, temperature, and shear on the formation of PG80 will be described.

745. Evidence of an Intermediate Amorphous Phase in PLA/PMMA Thermal Blends

Kim-Phuong N. Le, Richard L. Lehman and James D. Idol, AMIPP Advanced Polymer Center -- Rutgers University, Piscataway, NJ

Poly (L-lactide) (PLA) and Poly (methylmethacrylate) (PMMA) composites are of interest for in-vivo biomedical applications due to functional synergism between the bio-persistent load-bearing phase and the bioresorbable phase. When these polymers are processed to form an immiscible co-continuous blend, useful and interesting properties result. Recent studies in our laboratory have indicated the formation of a new amorphous phase in these blends when they are thermally processed. This phase, termed PG80, has a characteristic glass transition between that of PLA (59-61^{o}C) and PMMA (103-105 ^{o}C). The observation of this phase coincides with the synergistic mechanical and enhanced bio-compatibility of the composites. To exploit the positive impact of PG80 at the interface of a seemingly immiscible composite, the process conditions under which PG80 is formed, namely shear and reaction time, have been investigated. Combinations of shear levels and reaction times are achieved in a thermal extruder. Low shear, high reaction time experiments have been conducted by thermally pressing laminated structures of PLA and PMMA thin films where the thickness of each film were of the same magnitude as the domain size in extruded blends. The morphology of the blends was preserved via quenching. Assessment of results by DSC indicate that the PG80 phase forms under a range of shear/reaction time conditions. Possible chemical and physical interactions between the constituent polymers that lead to PG80 formation are discussed.

746. Using Supercritical CO_2 for polymer/drug formation into microspheres

Princy Varughese, Ke Wu and Jing Li, Rutgers,The State University of New Jersey, Piscataway, NJ

Supercritical CO_2 (sc-CO_2) has been used for extraction and separation (e.g decaffeination), as a reaction medium (for polymerization) and as a reprocessing fluid (in production of foams). Recent interest has sparked in using supercritical CO_2 as an anti-solvent for particle formulation. Here, drug-loaded polymers are dissolved in an organic solution and are introduced through a nozzle to the sc-CO_2. By an anti-solvent process, the sc-CO_2 extracts the solvent and the drug-loaded polymers saturate out, solvent free, into the desired shapes and sizes. These processed drug-loaded polymers would lead to improved drug delivery systems with enhanced therapeutic effects in terms of less dosage and controlled release of the drug. Here, we report some preliminary results on selected materials. The processed particles have been characterized by SEM and DSC for morphology and thermal properties, respectively

747. Biodegradable polymer with different morphologies formed by precipitation with super- and sub-critical antisolvent

Ke Wu, Jianjun Luo and Jing Li, Rutgers,The State University of New Jersey, Piscataway, NJ

Different morphologies of a model biodegradable polymer are achieved by precipitation with super- and sub-critical antisolvent CO_2 under a systematic manipulation of process variables. Spherical and/or fibrous products are produced with narrow particle size distribution. The effect of operation parameters on the size and morphology of the processed polymers is discussed herein. In addition, an effort to correlate chemical structure of the unprocessed polymer with physical characters of final product is made by qualitative comparison with literature. It turns out mass transfer, phase behavior, hydrodynamics are competing factors depending on chemical features of the target polymers. As a result, it is possible to better control the size and morphology of polymeric materials through this ″green″ processing technique.

748. Rheological Characterization of Hydrogels Assembled via Heparin-Peptide Interactions

Le Zhang, Nori Yamaguchi and Kristi L. Kiick, University of Delaware, Newark, DE

The design of materials in which assembly, mechanical response, and biological properties are controlled by protein-polysaccharide interactions could mimic the biological environment and find use in many biomedical applications. In the investigations reported here, the heparin binding affinity of a variety of heparin binding peptides has been monitored via heparin-sepharose chromatography and surface plasmon resonance (SPR) experiments. Results from these experiments indicate that a heparin-binding peptide that mimics the heparin-binding domain of human platelet factor 4 (PF4) demonstrates higher heparin-binding affinity and heparin association rate when compared to heparin-binding domains of antithrombin III and heparin-interacting protein. Rheological characterization indicates that hydrogels assembled via interactions of LMWH with PF4 exhibit the highest elastic modulus when compared to hydrogels assembled via other LMWH-peptide interactions, which correlates well with chromatography and SPR results. Manipulation of hydrogel physical properties and erosion profiles will provide novel materials for controlled drug delivery and other biomedical applications.

Computer Simulations (Workshop)

Organizer: Bettyann Howson Chatham HS, Madison, NJ

749. Interactive Web Based Inquiry Labs

John Gelder, Oklahoma State University, Stillwater, OK

Participants will learn how to use Java-based and Flash programs that are accessed using a web browser. Molecular Level Lab Experiments provide an interactive, molecular level view of an ideal gas,or an equilibrium reaction. The chemical kinetics of the equilibrium reaction can also be investigated. Each program includes several guided-inquiry activities for students. Both Java-based labs and Flash simulations, along with their accompanying inquiry activities have been classroom-tested in university and high school classrooms.

North Jersey American Chemistry Society Teacher Affiliates

Organizer: Bettyann Howson Chatham HS, Madison, NJ

750. Odyssey Workshop

Nathan Dacuycuy, Wavefunction, Irvine, CA

ODYSSEY is a new suite of instructional software for the initial chemistry classes in high schools, colleges, and universities. Featuring molecular simulation technology, ODYSSEY provides a highly interactive environment for learning and exploration. Rich content is included to accompany students and instructors throughout the introductory curriculum. Classroom demonstrations as well as student assignments are supported with ready-to-use materials. This hands-on

workshop will showcase how to incorporate molecular modeling software into the curriculum. Examples for the classroom, for homework assignments, and for the teaching laboratory will be highlighted.

Chemical Education At It's Best: Keynote Address and Teacher Awards

Organizer: Bettyann Howson Chatham HS, Madison, NJ

751. Weird Science: A Phenomenological Approach to Teaching

Lee Marek, University of Illinois at Chicago [Weird Science,], Chicago, IL

"Weird Science" is a series of short, easy and sometimes "weird" demonstrations and ideas on chemical and physical phenomena. The program uses the "phenomenological" approach to teaching science -- introducing a topic with a demonstration or lab so that students have something concrete on which to focus. It will highlight the use of demonstrations as exocharmic motivators to captivate student interest with novel demonstrations guaranteed to hook kids and adults into thinking about science concepts. Humor and audience participation are an integral part of "Weird Science". As Hubert Alyea said "Surprise, humor and truth are the servants of a good lecture." "Weird Science" entertains while it educates. It is our job to awaken our student's desire to learn--to keep the students mentally coming back. You cannot communicate with people who are not mentally present. If you want "presence" you have to capture attention. "Weird Science" provides tools to capture attention. A number of these demonstrations have been presented on the David Letterman Show and the WEIRD, WEIRD, SCIENCE kids show.

Advances in Organic Synthesis

Presider: Spencer Knapp Rutgers University, Piscataway, NJ

752. Spriodiepoxides: Mechanism, Methods and Applications

Lawrence J. Williams, Rutgers University, Piscataway, NJ

Spirodiepoxides, the oxidation products of allenes, serve as synthetically useful three-carbon units of bond formation and stereochemistry and provide direct access, via nucleophilic opening, to highly functionalized and highly enantioenriched ketones and ketone derivatives. Oxidation/nucleophilic opening installs three functional groups, nucleophile, ketone, and alcohol, with syn selectivity in the absence of other stereodirecting functionality. Indeed, this method effectively establishes specific stereochemical communication across a carbonyl. Issues such as the scope of compatible functional groups and nucleophiles, stereoselective oxidation of the allene precursors, elucidation of the mechanisms of spirodiepoxide opening, and applications of this method will be discussed.

753. Development and Application of New Synthetic Methods

Gary Molander, University of Pennsylvania, Philadelphia, PA

The synthesis of a variety of organotrifluoroborates and their application in selective organic synthesis will be outlined. Functionalized organotrifluoroborates are readily synthesized by several complementary pathways. The reagents thus generated are tractable solids that are stable to air and moisture. Additionally, they resist oxidation and attack by strong nucleophiles and bases. Consequently, functional groups incorporated within the trifluoroborates can be easily transformed, leaving the boron unit intact for subsequent processing. The organotrifluoroborates themselves are highly versatile partners for Suzuki-type cross-coupling reactions, as well as other palladium-catalyzed reactions. Some of the highlights of these processes will be revealed. The application of organotrifluoroborates in complex molecule synthesis will be showcased.

754. Syntheses of Complex, Bioactive Natural Products

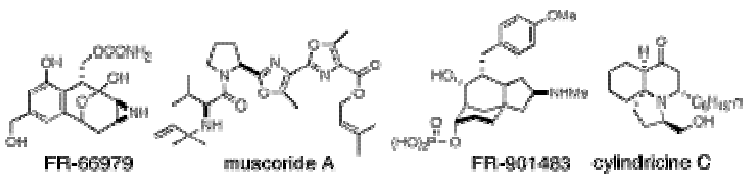
Erik Sorensen, Princeton University, Princeton, NJ

Text Not Available

755. Synthetic Studies on Heterocyclic Natural Products

Marco A. Ciufolini, University of British Columbia, Vancouver, BC, Canada

This presentation highlights recent efforts from the author's laboratory directed toward the total synthesis of biologically relevant nitrogenous natural products. Each target molecule poses chemical problems that serve as ideal vehicles for the development and application of new synthetic technology, as apparent from total syntheses of FR-66979, muscoride A, FR-901483 and cylindricine C. The methodology component of each project will be discussed in detail.



Applications of Vibrational Spectroscopy in Forensic Science I

Organizer: Gene Hall Rutgers University, Piscataway, NJ
Presider: Gene Hall Rutgers University, Piscataway, NJ

756. IR Microscopes in Forensic Science: Past, Present, and Future

John A. Reffner, Smiths Detection, Danbury, CT

In criminal and civil litigation, the forensic scientist is challenged to analyze a diverse array of materials, which forms the base for expressing an expert opinion. Often samples are microscopic and evidence samples must be maintained for adversarial examination. Infrared microanalysis has become a primary analytical technology for the forensic scientist. In the past two decades, instrumentation, techniques and applications have advanced. Every major crime lab has an infrared microprobe. These instruments are used for trace evidence and drug analysis. The bringing together of infrared spectroscopy and light microscopy has created a new technology for microanalysis. Infrared spectroscopy confirms and expands microscopical analysis. Synthetic fibers are often found as trace evidence. The infrared analysis of microscopic fibers adds information on their polymer composition, helping compare known and questioned fibers. Paint chips, either architectural paints or automobile finishes, are another common trace evidence material. These are analyzed, layer-by-layer to determine binders and pigments to determine their source. Chemists are drawn into litigation; either in the filing of, or defend patents. Currently, in the pharmaceutical industry, solid-state characterization of drugs is a major regulatory and patent issue. Infrared microprobe analysis plays a pivotal role in these forensic investigations.

757. Spectrochemical Analysis and Spectral Imaging of Latent Fingerprints and Trace Evidence Included within the Prints

Edward G. Bartick[1], Diane K. Williams[1], Heather L. Peters[1], Rebecca L. Schwartz[1], Nicole J. Crane[2], Rohit Bhargava[3], Daniel Fernandez[3], Scott W. Huffman[3] and Ira Levin[3], (1)FBI Laboratory, Quantico, VA, (2)Oak Ridge Institute for Science and Education (ORISE), Quantico, VA, (3)National Institutes of Health, Bethesda, MD

Fingerprints and trace evidence are critically integral to forensic investigations. Latent prints are comprised primarily of secretions from an individual in contrast to fingerprints imprinted in substances such as blood. They typically require invasive techniques using chemical reagents to develop the fingerprint ridges. Forensic trace evidence characterization traditionally involves the identification of the surrounding environment, determination of the material's identity, and the establishment of a possible source. Then, the material is circumstantially associated to prints in the vicinity. Trace evidence gathering often requires invasive and destructive approaches to latent fingerprints. For example, swabbing or taping techniques to remove trace materials for analysis are likely to destroy latent prints. At present, print containing areas are avoided in the removal of trace evidence, and consequently analysis of trace evidence within a print is not currently done. In this paper, we demonstrate a non-invasive infrared spectroscopic imaging approach to detect and record latent prints while simultaneously determining the presence and identity of contained trace evidence. We demonstrate the spectroscopic separation of overlapped prints and nanogram detection of an included explosive (RDX), - identifying a sensitivity sufficient to detect trace levels persisting after more than fifty prints have been made. Not requiring analyte transfer to an instrument, our non-optimized sensitivity arises from the spatial localization afforded by imaging and is amenable to detecting a number of different chemical species simultaneously. For the first time, probable correlations can be conducted between the individual identifiers of fingerprints and trace evidence.

758. Use of Drop Coated Deposition Raman (DCDR) for Detection of Explosives

Katia Rothhaar[1], Jimmy Oxley[2], Dor Ben-Amotz[3], Dongmao Zhang[3], Yong Xie[3], Corasi Ortiz[3] and Jo Davisson[3], (1)Tienta Sciences, Indianapolis, IN, (2)University of Rhode Island, Kingston, RI, (3)Purdue University, West Lafayette, IN

Raman spectroscopy has been previously shown to be useful in the study of explosives. However, one of the problems associated with the study of explosives by Raman spectroscopy is that samples are often too dilute for direct measurements. In our research, we demonstrated that this problem can be overcome by using a hydrophobic substrate and a technique called drop coated deposition Raman.

We will present you the impressive identification results obtained while studying about twenty explosives at a concentration of 1mg/ml in different solvents. Our results demonstrate that DCDR may be used to obtain high-quality normal (non-enhanced) Raman spectra from small quantities of explosives with high reproducibility.

759. Applications of Spectroscopy in a Museum

Janice H. Carlson and Jennifer L. Mass, Winterthur Museum, Winterthur, DE

For more than a century, artists, art historians, and art conservators and restorers have made use of numerous techniques that rely on the interaction of electromagnetic radiation with materials to study, examine and authenticate works of art. Light microscopy, x-radiography, and examination under infrared or ultraviolet light sources are perhaps the most common examples of these methods. A number of more sophisticated spectroscopic techniques, widely used in industry, have now become standard tools in many museums for the examination of artistic and historic objects. These

include non-destructive energy-dispersive x-ray fluorescence spectroscopy, Fourier transform infrared spectroscopy, Raman spectroscopy and scanning electron microscopy with energy dispersive x-ray microanalysis. This presentation will discuss the application of a number of spectroscopic methods to a variety of works of art including silver alloys, painted Pennsylvania German fraktur and furniture, Chinese pith paintings on rice paper and others.

760. Creation of an ATR-FT-IR Spectral Database of Nail Lacquer Enamel for Use in Forensic Science

Laurie E. Smith and Gene S. Hall, Rutgers University, Piscataway, NJ

Nail lacquer enamels (polish) have a basic blueprint that all manufacturers follow. However, the specifics vary for and within each company. Nail lacquer enamels compositions are typically composed of a large number of components with additional possible components. The combination and quantity differ for each individual lacquer enamel. The common ingredients make for similar spectral properties and difficulty in spectral identification hindering the distinction between lacquer enamels. The infrared spectrum is largely indicative of one of the main components, nitrocellulose. The direct assignment of the infrared bands cannot be used to conclusively distinguish between different nail lacquer enamels. Utilizing a digital spectral library composed of ATR-FT-IR spectra, however, one can correctly identify a particular nail lacquer enamel. Raman spectroscopy using a 785 nm excitation laser can also be used to identify nail lacquer enamels, more specifically the possible pigment components. ATR-FT-IR and Raman spectroscopy in combination with digital spectral libraries can successfully be used to positively identify the ingredients and distinguish between nail lacquer enamels. The database can be used to identify chipped nails with nail lacquer enamel from a crime scene.

Forensic Chemistry Education

Organizer: Laurence. J. Boucher Towson University, Towson, MD
Presider: Laurence. J. Boucher Towson University, Towson, MD

761. Forensic Science Education Program Accreditation Commission: Accreditation Standards

Peter R. De Forest, John Jay college of Criminal Justice / CUNY, New York, NY

Most of the scientists presently staffing forensic science laboratories worldwide entered the profession with degrees in biology or chemistry. This is due to the fact that until fairly recently the numbers of graduates of academic programs in forensic science have been relatively small. Thus, although a few programs have venerable histories, the small number of forensic science programs has rendered their collective contribution to laboratory staffing needs marginal. In addition, the quality of scientific preparation provided by some programs calling themselves forensic science programs was weak. From the perspective of students seeking an education in forensic science, or from that of laboratories recruiting scientists, *caveat emptor* applied. Because of the maturation of the field, and the recent explosive growth in the number of such programs, this situation is changing. It has become clear that standards are necessary.

The American Academy of Forensic Sciences established a standing committee which evolved into the Forensic Science Education Program Accreditation Commission (FEPAC). The commission is composed of ten scientists with extensive experience in the field. Half are forensic science practitioners, and half are forensic science educators. During the development of FEPAC and the accreditation standards, the services of experts in academic program accreditation were retained. The standards adopted by FEPAC are minimum standards. To date the commission has conducted two rounds of site visits and accredited the programs at about ten institutions.

This presentation will discuss forensic science education and the FEPAC standards for forensic science programs.

762. Challenges of an Undergraduate Forensic Chemistry Curriculum

Helen G. Reid, West Chester University, West Chester, PA

The major factors in establishing and maintaining an accredited undergraduate forensic chemistry curriculum are: knowledgeable faculty and appropriate facilities, forensic lab partnership(s), the required courses, recruitment of talented students, practical work experiences and/or field trips, research experiences, and maintenance of records for students and graduates. Chemistry, biology, and criminal justice faculty must coordinate efforts. The forensic budget competes within one of the departments for expenditures. Professional forensic laboratories and their personnel provide a variety of reality experiences for the students. Recruitment materials should be clear that the knowledge, skills, and abilities of forensic scientists include math skills and non-routine analytical thinking skills. Advisement of individual students throughout the curriculum, placement records, and surveys of graduates and employers complete the process. Graduates of forensic chemistry programs who choose to pursue a chemistry career other than forensic science should have the background to pursue graduate work in standard fields of chemistry, biochemistry, or toxicology.

763. Forensic Chemistry at a Community College

Ray A. Gross Jr., Prince George's Community College, Largo, MD

In 2000, Prince George's Community College (PGCC) initiated a program in forensic sciences for students who wish to begin their studies in a two-year college and later transfer to a four-year institution to complete a baccalaureate. As part of the program, a course in forensic chemistry was developed in AY 2002-2003 to train sophomores in the use of

instruments in forensic analyses. A 15-experiment lab manual was developed for the course, and students are guided by the manual in learning how to use five instruments that find extensive use by scientists in crime labs. An overview of the forensics program at PGCC will be presented, followed by a discussion on how the forensic chemistry course fits into the overall program and how the course is organized and presented to students.

764. Overview of the Forensic Chemistry and Forensic Science Programs

Sherry T. Brown, York College of Pennsylvania, York, PA

Long before the CSI and Forensic Files shows, there were many scientists engaged in forensic science and forensic chemistry work. Thirty years ago there were virtually no undergraduate programs in this area of science. Today many undergraduate programs in forensic science exist. A brief overview of the growth of this field at the undergraduate level will be presented.

765. Internships at the New Jersey State Police Crime Laboratory through Partnership

Thomas A. Brettell, New jersey State Police, Hamilton, NJ

A unique program has been established by the New Jersey State Police (NJSP) to provide internship opportunities and mentoring to students enrolled at The College of New Jersey (TCNJ) who are interested in exploring a career in forensic science. The program provides a maximum of 940 hours a year of paid internship opportunity. The program is divided into three phases. During the first phase of the program, eight weeks of full-time work at the NJSP crime laboratory during the summer is obligatory for program participants between their sophomore and junior year. The 2nd and 3rd summers follow with a similar format. The intent and goal of the program is to provide the student with a real-world educational environment and the knowledge as well as the hands on skills to perform actual evidential casework. Upon successful completion of the program, the student is equipped and fully prepared to take the experience into any crime laboratory in the country to perform DNA or other types of casework, including court testimony.

766. Experiences, Explorations and Research in a Forensic Chemistry Course: Forensic Chemistry at The College of New Jersey

John Allison, The College of New Jersey, Ewing, NJ

A Forensic Chemistry Concentration, for B.S. Chemistry Majors at TCNJ, has just been established. This presentation discusses the first Forensic Chemistry course, in which upper level students participate. A variety of activities are incorporated into the lecture time, including the collection and presentation of information on chemical compounds commonly found in household products, researched talking points, and chemical ‘scavenger hunts'. In the associated laboratory, students participate in: a) experience labs, b) discovery labs, and c) research. Much of the experimental design is the responsibility of the students; they work in small groups. One tool they use is a lab-in-a-laptop-bag. In this development, students design experiments using a variety of optical and electronic tools that can be easily interfaced to a laptop computer. Students communicate and share results through a wireless system. A common approach is used to introduce topics. First students work to understand what forensic scientists may do and how results are interpreted, then they approach the subject from a chemical perspective. For example, there are many references in the Forensic Science literature that discuss the use of luminol for the detection of blood. If one approaches the topic of luminol through the Chemistry literature, one finds that many chemical reactions involving luminol are used in studies of chemiluminescence and excited state formation. This leads to the design of experiments where luminol emission, following interaction with a variety of reactants, is measured and investigated. The goal of the program is not to create Forensic Scientists, but informed Chemists.

767. Forensic Science Education: More Programs, Lower Standards?

Lawrence Kobilinsky and Henrietta Margolis-Nunno, John Jay College of Criminal Justice, C.U.N.Y., New York, NY

Over the past few years public interest in the field of forensic science has grown dramatically. Programs like CSI and Cold Case Files have had a dramatic effect on the criminal justice system. Increasing numbers of students are seeking high school, undergraduate and graduate forensic science programs. There are now more than 90 undergraduate programs and approximately 45 graduate programs spanning the disciplines of chemistry, molecular biology, toxicology,and others. The American Academy of Forensic Sciences has established an accreditation body - FEPAC - to evaluate college level programs and to determine if standards are sufficiently high and if needed resources are available. Resource issues include personnel, laboratory and classroom facilities, equipment and expendable supplies, adequate library holdings, and curriculum. John Jay College has recently modified the curriculum of its undergraduate and graduate programs to include a track in molecular biology to complement the existing tracks in criminalistics and toxicology. All three tracks have capstone courses and outcomes assessment has been initiated for the overall program. A model curriculum at the undergraduate and graduate levels will be described.

768. Designing Forensic Science Curriculums to Meet Current and Furture Challenges

Brian J. Gestring, Pace University, NY, NY

In an era where forensic science programs are becoming more and more specialized, Pace is taking a more traditional approach. Its curriculum will attempt to educate the student from a generalist perspective. In most jurisdictions, forensic

questions are posed by non-scientists (i.e. prosecuting attorneys, case detectives). Pace hope to change this trend by teaching students to formulate their own questions based on their knowing the strengths and limitations of a broad range of analytical techniques.

Given the probable expansion of many forensic laboratory systems, the curriculum was devised so that students will be able to meet educational hiring guidelines for most entry-level positions in forensic laboratories regardless of specialty. Students will then begin learning basic concepts in forensic science using a crime scene focus. The guiding belief is that more mistakes are made in the recognition and collection of significant evidence at the crime scene than in the laboratory=s subsequent analysis, a view held strongly by Paul Kirk years ago. Graduates will be able to meet typical civil service requirements for employment as well as educational requirements mandated by such groups as the DNA Advisory Board.

Functional Proteomics, Cell Signaling and Disease Biomarkers

Official: Thomas A. Neubert New York University School of Medicine, New York, NY

769. Novel Multiplexed CSF Biomarkers for Antemortem Alzheimer's Diagnosis

Kelvin H. Lee, Erin Finehout, Zsofia Franck, Leila Choe and Norman Relkin, Cornell University, Ithaca, NY

We are applying a gel-based proteomics strategy to the analysis of antemortem cerebrospinal fluid from Alzheimer patients. Our goal is to identify antemortem biomarkers for AD diagnosis. Retrospective samples from definite Alzheimer patients as well as appropriate normal and neurological controls have been collected from a number of CSF banks in the United States. Prospective probable and possible AD samples are collected from a well-characterized clinical population in New York. Using protein two-dimensional electrophoresis, fluorescence staining and laser fluorescence scanning, we are able to visualize approximately 1200 protein spots from typical CSF samples. The Random Forest multivariate statistical analysis is applied to spot patterns to segregate AD and nonAD patient samples. A panel of protein spots is effective at segregating AD and nonAD patient samples. Matrix assisted laser desorption ionization tandem time of flight mass spectrometry has permitted us to characterize and sequence many of these proteins.

770. Serum peptide signatures of solid tumor cancers

Paul Tempst and Josep Villanueva, Memorial Sloan-Kettering Cancer Center, New York, NY

We have developed an automated platform, using magnetics-based sample processing and MALDI-TOF MS, to measure peptides in serum. The spectra appear to hold important information that may have direct clinical utility as a surrogate marker for detection and classification of cancer. Serum peptidome profiling provides a functional read-out of proteolytic activities degrading endogenous substrates, a process with vast combinatorial variability to generate peptides of different size and composition. The potential pool could exceed the number of gene transcripts and proteins, and may provide a more subtle correlate of biological events and disorders than regular expression genomics and proteomics. However, mass spectrometry, biostatistics, and environmental, dietary and psychological factors could all produce artifacts in the data. We believe that the influence of non-disease related elements can initially be evaluated by comparing sera from cohorts of patients with different cancers along with normal and cured control groups. Serum preparation, handling and storage are possibly even bigger problems, especially among archived samples. For example, two otherwise identical groups of control samples could be separated with 100% accuracy in class prediction analyses using peptide patterns, solely on the basis of the type of blood collection tube or the number of freeze/thaw cycles. Finally, adequate signal processing of the spectra (e.g. peak alignment, etc.) is more involved and rate limiting than the statistical analysis and currently the focus of intense developments

771. A Mass Spectrometry-Based Quantitative View of Protein Phosphorylation

Roland S. Annan, Francesca Zappacosta, Dean McNulty, Micheal Huddleston and Therese Sterner, GlaxoSmithKline Pharmaceuticals, King of Prussia, PA

Mutisite phosphorylation of individual proteins appears to be quite common, and may be more the rule than the exception. While mapping multiple phospho- acceptor sites is now fairly reliable, understanding which phosphorylation sites modulate protein function or are active in a given biological pathway is still a difficult problem. Adding to the complexity of this problem is the fact that phosphorylation-dependent function may not depend on activity at a single site, but rather be dependent upon serial activation of several sites. We are developing and using mass spectrometry-based tools to provide a quantitative view of phosphorylation dependent structure-function relationships. With or without stable isotope tagging we are able to define a subset of the total in vivo phosphorylation sites which are functionally significant. Following this, one or multiple, specific epitopes can be monitored in a highly sensitive assay using mass spectrometry.

772. The identification of possible blood proteins as biomarkers for atherosclerotic plaque

Stanley A. Hefta, Bristol Myers Squibb Co., Princeton, NJ

Putative biomarkers for atherosclerotic plaque were found by proteomics analysis. The initial studies involved treatments of tissue culture cell lines with LDL and oxidized-LDL. Comparisons of treatment groups lead to the identification of candidate markers. These putative markers include proteins involved in tissue remodeling (Matrix Melletalloproteinase 9, urokinase–type plasminogen activator receptor [UPAR], and cathepsin L), coagulation factors (thrombin-anti-thrombin

[TAT]) and proteins known to be up-regulated in people with lipid storage diseases (chitotriosidase, and chitinase-3 like protein). Subsequent immunoassays in human plasma from patients undergoing angioplasty procedures, and the publications from other groups, confirmed the in vitro experiments.

773. Functional Proteomics of Ephrin Signaling

Thomas A. Neubert, Daniel S. Spellman and Guoan Zhang, New York University School of Medicine, New York, NY

Ephrin receptors (Ephs) are a large family of receptor tyrosine kinases involved in vascular development, tissue border formation, cell migration, axon guidance, and synaptic plasticity. While many of the signals downstream of these receptors converge to regulate the cytoskeleton, many of the molecular details of ephrin-mediated signal transduction remain unclear. We have used Stable Isotope Labeling by Amino Acids in Cell culture (SILAC) in combination with nanoflow HPCL coupled directly to a Micromass Q-TOF Micro tandem mass spectrometer to characterize anti-phosphotyrosine immunoprecipitates following EphB receptor stimulation by ephrinB1 ligand in NG-108 cell cultures. We identified 120 unique proteins, 35 of which demonstrated increased abundance in phosphotyrosine immunoprecipitations upon ephrinB1 stimulation as compared with unstimulated cells. Four proteins demonstrated decreased abundance, and 81 did not change relative abundance but were present in phosphotyrosine immunoprecipitations of NG108 cells in both stimulation states. We confirmed and extended the results by specific immunoprecipitation and Western blot experiments. The results confirmed previously reported interactions, as well as provided additional insights into ephrin-mediated signal transduction.

NanoScience and Technology

Organizer: Yves J. Chabal Rutgers University, Piscataway, NJ
Organizer: Eric Garfunkel Rutgers University, Piscataway, NJ
Presider: Yves J. Chabal Rutgers University, Piscataway, NJ
Presider: Eric Garfunkel Rutgers University, Piscataway, NJ

774. Self-Organization of Nanoscaled Photonic Materials

Charles Michael Drain, Hunter College - CUNY, New York, NY

Some applications of nanoscaled, supramolecular porphyrinic systems, such as molecular sieves and photonics, depend on the exact nanoarchitecture of the molecules and/or atoms; therefore require self-assembled systems of discrete arrays and highly ordered crystals. Other applications, such as oxidation catalysts for simple substrates, may be effected by the use of self-organized materials with less molecular order. Porphyrin nanoparticles can be considered self-organized supramolecular systems that are governed by the principles of supramolecular chemistry. The formation, properties, and potential applications of nanoparticles of these chromophores are discussed with special emphasis on the variables in the methods used to make these materials, and in terms of the supramolecular chemistry. These nanoscaled colloidal materials exhibit properties obtainable neither by the chromophore nor by the bulk materials. Additionally, stability and deposition on surfaces will be discussed.

775. A Unique Approach towards the Design of Nano-Materials: Hybrid Inorganic-Organic Semiconductors with Tunable Structures and Properties

Jing Li, Rutgers,The State University of New Jersey, Piscataway, NJ

An exciting and promising area of materials research that concerns chemistry and physics of inorganic-organic hybrid materials is rapidly emerging. Hybrid materials that combine the superior electronic, magnetic, optical properties and thermal stability of inorganic frameworks with the structural diversity, flexibility, high processability, and light-weight of organic molecules may reveal new phenomena and new properties, and enhance/strengthen the existing functionality and performance of materials. Thus, they are of both fundamental and technological importance. We have recently designed and developed a unique class of hybrid nanostructured semiconductor materials that possess interesting properties of colloidal quantum dots but have perfectly ordered crystal structures. These hybrid nanostructures are assembled as single-atomic chains or slabs of II-VI semiconductor MQ (M = Zn, Cd; Q = S, Se, Te) that are interconnected by mono- or bi-functional organic molecules via chemical bonds. They possess numerous improved properties over conventional II-VI semiconductor bulk materials, including broad band-gap tenability and high absorption coefficients. More significantly, they exhibit extremely strong quantum size effect that results in very large blue shifts in their optical absorption edges (1.0-2.0 eV), and their structures and properties can be tuned systematically.

776. Time Resolved Decay Dynamics and Mechanism of Energy Transfer in Undoped and Mn2+ Doped ZnSe Nanoparticles

Christian D. Grant[1], Edward M. Olano[2], Thaddeus J. Norman Jr.[3], Edward W. Castner Jr.[1] and Jin Z. Zhang[2], (1)Rutgers, The State University of New Jersey, Piscataway, NJ, (2)University of California Santa Cruz, Santa Cruz, CA, (3)Lawrence Livermore National Laboratory, Livermore, CA

Energy transfer dynamics in Mn^{2+}-doped ZnSe nanoparticles have been studied via time-integrated and time-resolved spectroscopic techniques. Steady state photoluminescence (PL) shows bandedge excitonic emission that is quenched on doping with the characteristic broad Mn^{2+} emission centered at 584 nm. Time-resolved picosecond PL and femtosecond transient absorption studies show that the Mn^{2+} doping substantially shortens the lifetimes of both the bandedge excitonic states and the shallow trap states. Energy transfer from ZnSe to Mn^{2+} likely follows two mechanisms: one that involves mediation through trap states and another without.

777. Nanocrystals and Nanocrystal Assemblies: Building with Artificial Atoms

Christopher B. Murray, E. Shevchenko and D. Talapin, IBM Corp, T. J. Watson Research Center, Yorktown Heights, NY

Collodial nanocrystals with controlled crystal shape, structure and surface passivation are now increasingly available. The tunability of the electronic properties of these structures and the development of discrete energy levels has lead some of these nanocrystals or quantum dots to be compared with a new artificial set of atoms. This talk will focus on nanowires and nanocrystal superlattice that can be built by 1D and 3D assembly of these "artificial atoms". We combine a high temperature solution phase synthesis with size selective processing techniques to produce organically passivated semiconducting and magnetic nanocrystals with size distributions less than 5%. The monodisperse semiconductor nanocrystals can be induced to self-organize through oriented attachement to from single crystal nanowires while boboth semiconducting and magnetic nanocrystals can assemble to produce 2D and 3D superlattices (colloidal crystals, opals) during drop casting. Our goal is to study the properties of both the dispersed nanocrystals and assemblies as all major structural parameters are varied (composition, size, and spacing). Procedures have been developed for model semiconductors including CdSe, PbSe, PbS, PbTe semiconductor quantum dots and Co, Ni, FePt, and Fe2O3 magnetic nanocrystals. Assemblies are not limited to a single repeat unit but now the formation of complex materials by controlled binary assembly is now possible. Preliminary examples of superlattices with AB13, AB2 and AB5 structures will be discussed.

778. Supramolecular Extension of pi-Conjugation in Conjugated Oligomers

Tsunehiro Sai, Polytechnic University, Brooklyn, NY

In this abstract, we hereby propose a supramolecular extension of p-conjugation in aniline oligomers, assisted by excess amount of dopants present in the system. Self-organization in organic conjugated materials provides us with the probability to optimize the desired optoelectrical functional properties, usually in the form of solid thin film. Usually, the final solid-state morphology is well dependent on these non-covalent interactions which work in a synergistic fashion. Thus manipulation of these non-covalent interactions at the molecular level enables us a better understanding of the self-organizational processes involved, leading to a supramolecular structure. Oligomer approach to tackle the intractable fundamental issues regarding conjugated polymers, such as aggregation phenomenon and the impact of interchain interactions on the resulting charge properties, has been a useful way to understanding the problems regarding the parental polymer. Also, oligomers by themselves are of great interest since precise architectural control over their chemical and physical properties permits us to work with a well-defined “building blocks” at the molecular scale. This in turn, provides us with a better understanding of the self-organizational processes involved in supramolecular formation from the nano-, mirco- to the macroscopic level. In this paper, we propose that excess amount of dopants promote supramolecular network of the TANi : dopant complexes, leading to a linear psuedo-polymeric structure with extended p-conjugation length.

779. Integration of Semiconductor Nanowire Array onto Si Chips Using Highly Aligned DNA Strands as Scaffolds

Yufeng Ma[1], Jianming Zhang[2] and **Huixin He**[1], (1)Rutgers University, Newark, NJ, (2)Rutgers University, Newark Campus, Newark, NJ

Nanometer-size inorganic dots, tubes, wires and belts exhibit a wide range of electrical and optical properties that depend sensitively on both size and shape, and are of both fundamental and technical interest. Recently, one-dimensional semiconductor nanostructures have attracted considerable attention due to their superior properties, such as linear polarized photoluminescence (PL), increased global Stokes shift, and more efficient electrical transport. These new properties enhance the existing performance and also open up new opportunities, such as miniaturized polarized photodetector and phototransistors. Proof-of-concept nanodevices from individual semiconductor nanowires have been fabricated. However, mass production of these nanodevices has been thwarted by the difficulties in assembling the millions of nanostructures required with precise control over the density, position, and orientation. Taking advantage of facile manipulation of DNA molecules, in this presentation, we will report that semiconductor nanowire array will be

integrated onto Si chips using highly aligned DNA strands as growing scaffolds, which hold a great potential for mass production of polarized optoelectronic nanodevices.

780. Formation of nano-particles by rapid expansion of supercritical solutions: In situ characterization by laser scattering

Takuya Matsunaga, Andrei V. Chernyshev and Lev N. Krasnoperov, New Jersey Institute of Technology, Newark, NJ

A technique for in situ characterization of the RESS process (Rapid Expansion of Supercritical Solutions) was developed and applied to RDX nano-particles formation. The technique is based on the combination of laser scattering and time resolved imaging. An excimer laser (248 nm) was used in combination with a fast gated ICCD camera. Particle size distribution functions downstream the RESS jet were obtained for neat CO2 as well as for supercritical solutions of RDX in CO2. Plausible particle growth mechanisms are discussed.

781. The Effect of Polyelectrolytes on the Aggregation of Cyanine Dyes in Langmuir-Blodgett Films and in Aqueous Solution; Some Kinetic Aspects of J-Aggregates

Hussein Samha, Southern Utah University, Cedar City, UT

The tendency of the cyanine dye, 1,1'-diethyl-2,2'-cyanine (PIC) to form aggregates in the bulk of aqueous solutions of polyvineylsalfate (PVS) and on the surface in Langmuir Blodgett (LB) films is compared using ultraviolet-visible (uv-vis) spectroscopy. PVS is used to provide charged surfaces where aggregates of the dye can be formed. J-aggregates, characterized by a sharp and intense “red-shifted” (~ 572 nm) absorption (compared to the monomer), are formed upon adding an aqueous solution of the PVC to the dye monomers in aqueous solutions. However, the use of PVC in the subphase produces only monomeric monolayers of the dye in LB films. Data analysis indicates that the cyanine dye cations are embedded on 50% of the repeating units of the polymer in solution. A lifetime of 40 pico-seconds for the excited state of the J-aggregate adsorbed on PVS is observed. An 85% quenching of the excited state is achieved in solution when methyl viologen is used as an electron acceptor. We calculate the quenching constant from the Stern-Volmer relation to be 1.8x107 mL.mol-1 with an electron transfer rate of 7.5x10-7 mL.molecule-1.s-1.

Tissue Engineering and Cell-Material Interactions

Organizer: Treena Livingston Arinzeh New Jersey Institute of Technology, Newark, NJ
Organizer: Michael Jaffe New Jersey Institute of Technology, Newark, NJ

782. Protein Biomaterial Communication with Stem Cells to Control Tissue Outcomes

David Kaplan, Tufts University, Medford, MA

Text Not Available

783. Substrate Elasticity Directs Adult Mesenchymal Stem Cell Differentiation

Adam J. Engler, Mark F. Berry, H. Lee Sweeney and Dennis E. Discher, University of Pennsylvania, Philadelphia, PA

Substrate stiffness is critically important for anchorage-dependent cells. Here we demonstrate that full pluripotent mesenchymal stem cell (MSCs) lineage commitment requires not only growth factor stimulus but also proper matrix elasticity. Indeed, MSCs adopt neuronal-like branched morphologies and express neurofilament heavy chain (NFH) only on substrates with a Young's modulus (E) near E_{Nerve}. Myoblast-like elongation and expression of Myogenic Differentiation Factor 1 (MyoD1), a myogenic marker, is seen in cells on substrates only near $E_{Skeletal\ Muscle}$. Incomplete expression relative to C2C12 myoblasts is augmented by stimulation with hydrocortisone thus inducing full differentiation; chemical or physical stimulus alone cannot. MSCs on substrates near $E_{Osteoblast}$ have a polygonal morphology and express Core Binding Factor □1 (RunX2/CBF□1), an osteogenic marker. Again, expression is incomplete compared with hFOB osteoblasts unless stimulated by L-acetate-2-phosphate and proper matrix elasticity. Mechanosenstive signaling for such differentiation pathways proves to be tension-based, involving myosin II contractility. However, similar myosin levels in MyoD1- and CBF□1-expressing MSCs indicate two different tension-generative pathways involving mDia and ROCK, respectively. Overall, this data implies that, in addition to chemical stimulus, tissue and/or matrix stiffness is critical for development and cell therapies in fibrotic tissue.

784. Conformational Behavior of Alanine-Rich Protein Polymers with Varying Functional Group Placement

Robin S. Farmer, Lindsey M. Argust, Jared A. Sharp and Kristi L. Kiick, University of Delaware, Newark, DE

The synthesis of protein-based polymers with controlled conformational properties and functional group placement offers many opportunities for the design of advanced materials. In this work, protein engineering methods have been used to produce three new classes of repetitive alanine-rich proteins with the general sequence $[AAAQAAAEAAAQ]_x$. These sequences were designed on the basis of the high helical propensity of alanine, and they may mimic architectural features

of certain alanine-rich helical sequences found in natural proteins such as the antifreeze proteins. Modifications to the general sequence allow for variations in both the spacing and the number of chemically reactive glutamic acid residues along the protein backbone. The three families of alanine-rich proteins have been designed to display glutamic acid residues at nominal distances of 17Å, 35Å, and 65Å, and members of each family can be easily expressed from *E. coli*. Circular dichroism spectroscopy (CD) characterization of these proteins demonstrates that purified proteins of all three families are highly helical. The helical character of the three proteins can be altered by increasing temperature and protein concentration as monitored via CD and infrared spectroscopic methods. Circular dichroism studies indicate that the conformational behavior of the proteins from the three families differs at elevated temperatures and can be manipulated depending on solution conditions, results which were confirmed through thermal analysis via differential scanning calorimetry (DSC). The demonstrated control of the conformational properties of these artificial proteins suggests that they may be excellent candidates for use in nanotechnology and biological applications.

785. Reversible Binding of Collagen Mimetic Peptide Derivatives to Collagen Films Effects Cell Adhesion and Spreading Behaviors

Allen Y. Wang, Jared S. Hierman, Chang-Soo Yun and Michael S. Yu, The Johns Hopkins University, Baltimore, MD

Collagen has been utilized in the development of engineered tissue and organ replacement therapies in the past decades. For such applications, conjugation of exogenous functionalities to collagen is often desired. To date, most of such conjugation process has been carried out by chemical means; however, the problems in controlling the chemical reactions and minimizing chemical toxicity have not been solved. As an alternative to the conventional "covalent" modification method, we recently reported a novel "physical" technique to functionalize collagen scaffolds using collagen mimetic peptides (CMPs) of sequence -(Pro-Hyp-Gly)x-. Here we show the reversible binding of CMP to the collagen film at near-physiological temperature as well as the practical use of CMP and poly(ethyleneglycol)-CMP conjugates in controlling cell organization in 2D collagen substrates. Our cell adhesion studies suggest that under certain conditions (e.g. high incubation temperature, small CMP size), the bound CMP derivatives can be released from the collagen matrix. Although such reversible binding may present problems for applications that require a permanent modification, it may provide new opportunities for manipulating cell behavior especially by dynamically controlling the amount of signaling molecules in collagen matrix.

786. Withdrawn

787. Neuronal cell guidance and protein adsorption on a melt-crystallized binary polymer blend

Andrea Tuckett and Kalle Levon, Polytechnic University, Brooklyn, NY

Cell-biomaterial interactions are very important in nerve regeneration applications. An important feature of any synthetic biomaterial is its surface chemistry which will determine protein adsorption and subsequent cellular behavior. Nerve guidance materials should be biocompatible, biodegradable, and mechanically strong to support cell attachment. Micro patterning of proteins has been used widely to provide cellular direction on substrates. However, in this work, cellular guidance is achieved by controlling the crystallization kinetics in a binary polymer blend of poly (e-caprolactone) (PCL) and poly (styrene-co-hydroxystyrene) (PSH) containing 7wt% hydroxystyrene. By precise control of the thermal environment of the blend system via manipulation of the competing velocities of the crystalline polymer (PCL) and the diffusing impurity (PSH), spherulitic crystals are architectured with differing morphology and surface chemistries. Polymer blend compositions of 20/80 PSH/PCL and 40/60 PSH/PCL were annealed at various temperatures and times, above and below the blend lower critical solution temperature (LCST). The annealed substrates were coated with collagen IV and collagen I, seeded with PC12 pheochromocytoma cells and cultured in vitro for 2 weeks. Substrate adhesion preference by collagen IV over collagen I influenced the cells' capacity for proliferation. PC12 cells guidance and morphology were found to be inherently dependent on the crystalline architecture. Spherulitic interfaces with dense impurity environments were favorable as neuronal channels.

ACS Waksman Landmark: Celebrating Waksman

Presider: Arnold Demain Drew University, Madison, NJ
Presider: Douglas Eveleigh Rutgers University, New Brunswick, NJ

788. Natural product antibiotics from actinomycetes - past, present and (hopefully) future

William Strohl, Merck and Company, West Point, PA

The historical role of actinomycetes in natural product antibiotic discovery will be discussed, and placed in context with the current reality and projected natural product antibody discovery efforts of the future.

789. Why aren't we finding antibiotics as easily as we used to?

Julian Davies, University of British Columbia, Vancouver, BC, Canada

Why aren't we finding antibiotics as easily as we used to?

Most of the antibiotics used today were discovered between 1940-1970; the search for new anti-infectives since that time has had limited success in finding new chemical entities with the required activity. Many reasons for this failure have been suggested, among them, that most types of antibiotic have already been found or that the number of targets in the microbial cell is limited. It is known that 99% of the bacterial kingdom with the potential to make millions of novel, bioactive small molecules is inaccessible to laboratory research. How can we access these treasures to produce new therapeutics?

790. Soil as a source of genes encoding the production of novel anti-microbials

Gerben Zylstra, Boris Wawrik and Jerome J. Kukor, Cook College, Rutgers University, New Brunswick, NJ

Many bacteria, particularly actinomycetes, are known to produce secondary metabolites synthesized by polyketide synthases (PKS). Bacterial polyketides are a particularly rich source of bioactive molecules many of which are of potential pharmaceutical relevance. In order to directly access PKS gene diversity in soil, we developed degenerate PCR primers for actinomycete type II ketosynthase genes. Various New Jersey soil samples were examined for their total bacterial diversity, actinomycete species diversity, and PKS gene diversity by terminal restriction fragment length polymorphism (TRFLP) of PCR products generated from DNA extracted directly from the soil samples. Based on the TRFLP patterns, two samples contained a particularly rich and unique actinomycete community and had a correspondingly high PKS gene diversity. PCR products from these and three additional samples with interesting TRFLP patterns were cloned and seven novel clades of PKS genes identified. The nucleotide sequences were between 74 and 81% identical to known sequences in GenBank, indicating a wealth of new PKS genes waiting to be discovered in nature.

791. Small-molecule inhibitors of bacterial RNA polymerase

J. Mukhopadhyay[1], E. Sineva[2], Y.W. Ebright[1], V. Mekler[1], A. Volkov[1], A. Srivastava[1], A. Kravets[1], D. Wang[1], X. Wang[1], S. Ismail[1], S. Sarafianos[3], S. Tuske[3], B. Hudson[3], A. Clarke[3], J. Birktoft[3], C. Dharia[3], M. Bayro[3], G.V.T. Swapna[3], J. Huang[3], L.C. Ma[3], J. Knight[3], O. Laptenko[4], J. Lee[4], S. Borukhov[4], H. Berman[3], E. Arnold[3], G. Montelione[3], R. Levy[3] and **R.H. Ebright**[1], (1)Howard Hughes Medical Institute, Rutgers University, Piscataway, NJ, (2)Rutgers University, Piscataway, NJ, (3)Rutgers University, (4)UMDNJ-Stratford

Bacterial transcription is a validated target for antibacterial therapy. Rifampicin, rifapentine, and other ansamycin antibiotics function by binding to, and inhibiting, bacterial RNA polymerase. The ansamycin antibiotics are of major clinical importance in the treatment of bacterial infection, particularly in the treatment of tuberculosis. Due to the public-health threat posed by multi-antibiotic-resistant bacterial infection, there is an urgent need for novel classes of antibacterial agents that target bacterial RNA polymerase (and thus have the same biochemical effects as ansamycin antibiotics) but that target different, non-overlapping structural elements within bacterial RNA polymerase (and thus do not exhibit cross-resistance with ansamycin antibiotics).

We are using integrated crystallographic, biophysical, biochemical, genetic, and combinatorial-chemistry approaches to identify and characterize novel small-molecule inhibitors of bacterial RNA polymerase.

Representative results will be presented.

792. TB: Global Time bomb

Lee Reichman, University of Medicine and Dentistry of New Jersey, Newark, NJ

Globally, TB infects 2 billion people – one third of the world's population, newly afflicts 8.6 million annually with active TB and kills 2 million, according toWHO who has termed it “A Global Health Emergency”.The reasons for the continued epidemic include: Deterioration of infrastructure, HIV infection, foreign born individuals, neglect and inattention. Any recent decline is almost certainly due to the major infusion of support and most importantly, the directly observed therapy short course (DOTS). All cases of TB disease are curable and the disease usually becomes non-infectious within a few days from the start of treatment, but only if patients.take their medication properly. In developing nations there are , limited to almost non-existent resources, failure to adhere to international standards, availability of less efficacious, less expensive TB drugs and lack of attention to good TB practices in the private sector. With the recognition of the danger of Multidrug Resistant Tuberculosis (MDRTB), an increased level of awareness, has been engendered in the health care worker community. Balanced, rational approaches have been few and far between, but MDRTB is prevented by appropriate DOTS! The WHO/IUATLD DOTS five strategy elements receive focus.New strategies in developing new TB drugs, diagnostics, and efforts to find a new TB vaccine are wonderful advances but the global epidemic will only turn around when all basic tenants of TB control are met. Focus must be the control measures. Finally, the most important aspect of control of TB is political will to ensure proper attention, care and resources globally.

793. Actinomycete secondary metabolites: gifts from the soil

Arnold Demain, Drew University, Madison, NJ

Microbial secondary metabolites are extremely important to our health and to the environment in which we live. As a group that includes antibiotics, immunosuppressants, hypocholesterolemic agents, antitumor compounds, antiparasitic agents, bioherbicides and many other types of compound, they have tremendous economic importance. Antibiotics are the best known secondary metabolites. Of all the antibiotics known, 66% are produced by the actinomycetes, 55% from

the genus Streptomyces alone. This amazing contribution by the soil inhabiting filamentous bacteria began in the laboratory of Selman Waksman with his students Boyd Woodruff, Hubert Lechevalier, Albert Schatz and others. Here at Rutgers university, the antibiotics streptomycin, neomycin and actinomycin D were discovered. The work that started here in the 1940's led to an amazing group of medically and agriculturally useful natural compounds produced by actinomycetes. Of special mention are antibiotics such as streptomycin, gentamicin, kanamycin, cephamycins, tetracyclines, tylosin, thienamycin, rifamycins, and the new antibiotic, daptomycin, an anti-resistance enzyme inhibitor, e.g., clavulanic acid, immunosuppressants such as sirolimus and tacrolimus, antiparasitics such as avermectin, antitumor agents such as doxorubicin and bleomycin, anticoccidial agents and animal growth promotants such as monensin and salinomycin, and insecticides such as spinosyn. The world owes much to these gifts from the soil and the gift-giving all started here in a small laboratory at Cook College, Rutgers University.

Electrostatic Hazards and the Control Of Dust Explosions (Workshop)

794. Electrostatic Hazards and the Control Of Dust Explosions

Vahid Ebadat, Chilworth Technology, Inc., Plainsboro, NJ

Part 1 – Electrostatic Hazards

One ignition source that is not usually well understood is electrostatic discharge. This part of the presentation will take a look at electrostatic hazards including: - Electrostatic Charge Generation - Electrostatic Charge Accumulation - Electrostatic Discharges - General Precautions for eliminating/controlling electrostatic hazards

Part 2 – Control of Dust Explosions

Part 2 of this presentation will discuss the conditions that are required for dust cloud explosions to occur, and presents a well-tried approach to identify, assess, and eliminate/control potential dust explosion hazards in facilities.

The majority of powders that are used in the processing industries are combustible (also referred to as flammable, explosible). An explosion will occur if the concentration of the combustible dust that is suspended in air is sufficient to propagate flame when ignited by a sufficiently energetic ignition source.

Enantioselective Reactions and Syntheses

Organizer: David A. Conlon Merck & Co., Inc., Rahway, NJ

795. Biocatalysis: Synthesis of Chiral Intermediates for Drugs

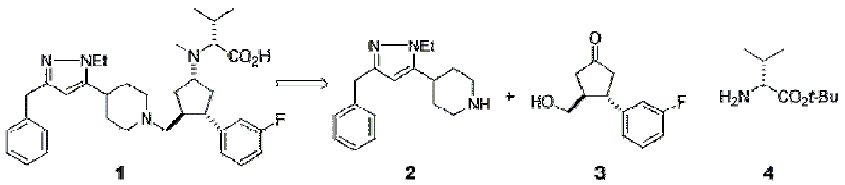
Ramesh N. Patel, Bristol-Myers Squibb, New Brunswick, NJ

There has been an increasing awareness of the enormous potential of microorganisms and enzymes for the transformation of synthetic chemicals with high chemo-, regio- and enatioselective manner. Chiral intermediates are in high demand from pharmaceutical industries for the preparation bulk drug substances. Single enantiomers can be produced by chemical or chemo-enzymatic synthesis. The advantages of biocatalysis over chemical synthesis are that enzyme-catalyzed reactions are often highly enantio- and regioselective. They can be carried out at ambient temperature and atmospheric pressure, thus avoiding the use of more extreme conditions which could cause problems with isomerization, racemization, epimerization, and rearrangement. Microbial cells and enzymes derived therefrom can be immobilized and reused for many cycles. In addition, enzymes can be overexpressed to make biocatalytic processes economically efficient. This presentation will provides examples of the use of enzymes for the synthesis of single enantiomers of key intermediates for drugs.

796. Stereoselective Synthesis of a Merck Anti-HIV Drug Candidate and Studies in the Development of the Mo-Catalyzed Asymmetric Alkylation Reaction

Michael Palucki, Merck and Co., Rahway, NJ

Stereoselective synthesis of the Merck anti-HIV drug candidate **1** is accomplished from 3 components: substituted pyrazole **2**, chiral cyclopentanone **3**, and commercially available t-butyl valine **4**. The chemistry used in the preparation of intermediates **2** and **3** is described along with the final end game. In addition, development work on the Mo-catalyzed asymmetric alkylation reaction, including synthetic and mechanistic aspects of this reaction will be described.



797. Strained Silacycles: A Powerful Platform for Asymmetric Reaction Design

James L. Leighton, Columbia University, New York, NY

When constrained in a five-membered ring with 1,2-diols, aminoalcohols and diamines, silicon exhibits significant Lewis acidity leading to unusual reactivity patterns. For example, uncatalyzed aldol and allylation reactions based on this concept have been demonstrated in which no external Lewis acid catalyst/promoter is required. Various strategies for exploiting this phenomenon will be described. Asymmetric allylation and crotylation reactions of aldehydes and ketones and N-acyl hydrazones derived from both aldehydes and ketones have been achieved. More recently this phenomenon has been exploited in the development of an extraordinarily simple and general chiral silane Lewis acid that mediates several carbon-carbon bond forming reactions with excellent levels of enantioselectivity.

798. Asymmetric Catalysis in the Synthesis of Stereochemically Complex Targets

Eric N. Jacobsen, Harvard University, Cambridge, MA

This lecture will describe the different strategies by which stereochemically complex molecules are synthesized, and the ways asymmetric catalysis can impact on all of them. The development of general methods to prepare synthetically useful building blocks leads to an expanded “chiral pool” of potential starting materials for asymmetric synthesis. The possibility of discovering new reactions to access new types of building blocks is particularly attractive, and serves to help define the frontiers of the field. Asymmetric catalysis can also be applied to diastereoselective synthesis such that the stereochemistry of the catalyst – and not that of the substrate – determines the relative configuration of the product. Finally, in reactions where multiple stereocenters are generated simultaneously or in tandem, catalyst- and substrate-control can operate in a complementary manner to achieve one of many possible stereochemical outcomes selectively. Our group has developed several new catalyst systems that effect highly enantioselective nucleophile-electrophile addition reactions with broad substrate scope. The synthetic scope and utility, and the mechanistic underpinnings of these catalysts will be discussed. Applications to natural product synthesis will be emphasized.

Microreactors and Microreaction Systems for Development and Production (Workshop)

799. Microreactors and Micro-reaction Systems for Development and Production

Craig Wurzel, Invenios, Inc, Hawthorne, NY and Thomas Dietrich, mikroglas Chemtec GmbH, Mainz, Germany

For several years now, microreaction technology has been discussed by experts in industry and universities. The advantages of this technology are well known. Many modules (e.g. reaction chambers, mixing units and heat exchangers) have been developed and tested, mainly by research institutes. This presentation will describe the processes to manufacture microreaction modules from the photostructurable glass FOTURAN, and the combination with different pumps, valves, sensors, safety features, process control units, etc., which are necessary to run a microreactor for fast exothermic reactions with aggressive chemicals. The "mikrosyn" microreaction device will be available for the presentation.

Applications of Vibrational Spectroscopy in Forensic Science II

Organizer: Gene Hall Rutgers University, Piscataway, NJ
Presider: Gene Hall Rutgers University, Piscataway, NJ

800. Novel Method for ATR Microanalysis of Multilayer Paint Chips

Thomas J. Tague Jr., Bruker Optics, Billerica, MA

A new reflecting objective for attenuated total reflection (ATR) infrared microanalysis has been designed to provide excellent sample viewing, high infrared sensitivity, and increased ease-of-use. The ATR objective incorporates a unique vertical sliding mechanism, which allows the internal reflection element (IRE) to be positioned out of the field of view (FOV) for viewing of the sample and in the FOV for high throughput infrared analysis. When the IRE is out of the FOV, contrast enhancement methods can be readily employed, such as visible polarization, fluorescence illumination, darkfield illumination, etc. The IRE is an anvil design with an 80-micron tip providing access to small areas within the sample of interest.

There are five contact pressure levels to choose from, where the contact pressure can be optimized for the sample hardness and tractability. Optimal pressure is indicated by an LED indicator and an audible beep. The germanium IRE functions as an immersion lens yielding a 4x magnification of the IR field aperture. This increases the spatial resolution to significantly better than the wavelength of light.

Multilayer paint chips from ancient works of art, aircraft, and automobiles, were visualized utilizing crossed polarized light and fluorescence illumination. The IR aperture was visually adjusted to mask each area of interest followed by infrared ATR data collection. Pure spectra were obtained for each component of the chip without contamination from adjacent areas.

801. Applications of Raman Spectroscopy in Forensics Science

Fran Adar[1], Sergey Mamedov[1], Andrew Whitley[1] and Luc Brazeau[2], (1)Horiba Jobin Yvon, Edison, NJ, (2)Canada Border Service Agency, Ottawa, ON, Canada

A combination of vibrational and Xray fluorescence spectroscopies is being successfully applied to trace analysis. Forensic analysis of documents can involve identification of the composition of the inks, dyes and papers used. The combination of Raman, Infrared and Xray microscopy enables identification of both inorganic and organic materials with 1-10um spatial resolution (depending on the technique used). Examples of successful identification of document forgeries such as checks and passports will be presented. The same analytical techniques can also be used to identify forged and illicit drugs. Raman spectra of drugs can be examined directly in their packaging (if it is transparent) and small amounts of material extracted even at low concentrations can be identified when deposited on Tienta hydrophobic substrates. Finally Raman spectra of polymers will also indicate the potential usefulness for forensic matching of fibers collected from crime scenes and suspects' environments.

802. Deployment and Use of Infrared Microspectroscopy in Mobile Laboratories: Forensic and Homeland Defense Applications

John A. Seelenbinder, Kenneth J., Fredeen and Mark L. Norman, Smiths Detection, Danbury, CT

The recent emphasis on Homeland Security is forcing many police and forensic teams to increase their capabilities, identifying and prosecuting cases of terrorism or terrorist hoaxes, potentially involving chemical or biological weapons. In order to respond to these cases in a more timely fashion and to dissolve potentially dangerous hysterical responses, many forensic teams are investigating the use of mobile laboratories which can be taken directly to the scene of the incident. Infrared microspectrometers are a natural choice for mobile laboratories; identification of many chemicals can be accomplished quickly by searching the obtained data against large spectral libraries. Microspectroscopy gives the added advantages of spatially separating species within a mixture, greatly extending the number of real world samples which can be identified. Pairing infrared microspectroscopy with Polarized Light Microscopy (PLM) further enhances the utility by providing a technique to choose unique species to measure as well as providing a confirmatory identification technique. Implementation and use of infrared microscopes in mobile labs deployed by the National Guard Bureau will be discussed. The talk will focus on factors required for fielding of infrared microspectrometers in mobile labs as well as the use of instruments in these labs. Size, durability, and compatibility with existing equipment will be discussed in addition to sample preparation, spectral searching and decision methodology for identification of unknown samples. Examples of samples which have been analyzed using infrared microspectroscopy and PLM will be given to demonstrate where this combination of techniques fits into the overall scheme of sample identification.

803. Utilization of FT-IR and Raman Spectroscopy in a Crime Laboratory

Phil Antoci, NYPD Crime Lab, Jamaica, NY

This presentation will discuss the implementation of FT-IR and Raman spectroscopy in a Crime Laboratory. Actual cases using the complimentary techniques of FT-IR and Raman will be presented. Detailed sample handling, data interpretation, and conclusion will also be presented.

804. What Can Raman Spectroscopy Do For the Forensic Scientist?

Diane Allen, Renishaw Inc., Hoffman Estates, IL

Text Not Available

805. Use of Vibrational Spectroscopy to Characterize Counterfeit Banknotes and Postage Stamps

Gene S. Hall, Rutgers University, Piscataway, NJ

The modern-day counterfeiter has a number of sophisticated tools such as high resolution scanners, high-resolution inkjet and laser printers, and image analysis software to literally “make money”. Therefore, the modern-day spectroscopist has to stay one-step ahead of the counterfeiter to use sophisticated analytical tools to characterize these counterfeit ephemera. With this in mind, our laboratory has been using micro Raman and micro ATR-FTIR to characterize these counterfeit items non-destructively. Our goal has been not only to determine if the banknote or postage is a counterfeit, but to determine the sources of raw materials i.e. paper, inks, and security stripes that were used in the counterfeiting operation. This presentation will cover actual uses of Raman and ATR-FTIR to characterize the inks, paper, and security stripes from counterfeit US and British banknotes and Hawaiian Missionary postal stamps. Creation of Raman and FTIR spectral databases of the raw materials used in counterfeiting and their use in solving the sources of the counterfeiting will also be presented. Raman and FTIR are complimentary vibrational techniques that offer the forensic scientist analytical methods to solve counterfeiting crimes.

COPE Scholar Symposium

Organizer: Cecilia H. Marzabadi Seton Hall University, South Orange, NJ
Organizer: R. David Crouch Dickinson College, Carlisle, PA
Presider: R. David Crouch Dickinson College, Carlisle, PA

806. Hydrocarbon Oxidation Methods for Synthesis

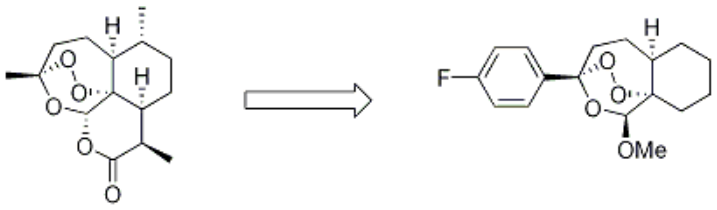
M.-Christina White, Harvard University, Cambridge, MA

We have discovered a new class of sulfoxide-based palladium C-H oxidation catalysts that provide access to either (E)-allylic acetates or branched allylic acetates with excellent selectivities and good yields. The distinctive features of our systems are that they require no heteroatom-directing group on the substrate to achieve high reactivity and regioselectivity and are extraordinarily functional group tolerant. As a result of these features, the potential for improving the efficiency of small molecule synthesis with these reactions is significant.

807. Artemisinin Antimalarials: Mode of Action and Potent Analogs

Jared Cumming, Schering-Plough Research Institute, Kenilworth, NJ and Gary H. Posner, The Johns Hopkins University, Baltimore, MD

The antimalarial natural product artemisinin (**1**), and its many semi- and fully-synthetic analogs, offer hope of chemotherapy for millions of people infected with malaria. Our work in the last decade has focused on understanding the mode of action of these endoperoxides, and we have elucidated the molecular cascade that is initiated by complexation of the endoperoxide core with free heme. Harnessing this information for mechanism-based design has lead to our development of structurally simplified analogs (*e.g.* **2**) that show excellent potency *in vitro* as well as in mouse models of malaria.



Artemisinin (**1**) **2**

808. Regiocontrolled Synthesis of substituted 2-pyrones and Their Synthetic Applications

Cheon-Gyu Cho, Hanyang University, Seoul, South Korea

Prepared in single step from coumalic acid, 3,5-dibromo-2-pyrone undergoes both normal and inverse electron demand Diels-Alder cycloadditions, similar to mono-brominated 2-pyrones, but with higher reactivity, to provide a variety of functionally rich and stereochemically defined bicyclolactones. It also undergoes Pd-catalyzed coupling reactions with terminal alkynes, amines, stannanes as well as boronic acids to furnish various 3- or 5-substituted 2-pyrones in highly regioselective manner. A brief summary on the mechanisms of the regioselectivity in the Pd-catalyzed coupling reactions will be presented as well as the synthetic applications of the coupling products.

809. Synthetic Approaches Towards a Preclinical Target Molecule

Todd D. Nelson, Merck Research Laboratories, Wayne, PA

Text Not Available

810. Multicomponent, Sequential Ring-Forming Reactions

Gary H. Posner, The Johns Hopkins University, Baltimore, MD

Our success with 2+2+2 construction of 6-membered carbocycles will be reviewed. Sequential connection of four different components in one flask will be shown for 4-atom expansion of 5-7 membered lactones and ketones into more complex and more valuable medium ring macrolides. Recent progress will be described for 3-atom expansion of 5-7 membered conjugated cycloalkenones into homoallylic macrolides, including total synthesis of some macroloide natural products.

Catalytic Routes to Novel Biomaterials

Organizer: Richard A. Gross Polytechnic University, Brooklyn, NY

811. Lipase Catalysis: Monomer, Macromer and Polymer Synthesis

Richard A. Gross, Polytechnic University, Brooklyn, NY

This lecture provides an overview of recent progress by our Center on the use of lipases and esterases for the synthesis of monomers, macromers and polymers. Promising strategies have been developed for ring-opening polymerization as well as bulk step-condensation copolymerizations between polyols, diols, diacids, and molecules of mixed functionality (e.g. bis-hydroxybutyric acid). Regioselectivity during lipase-catalyzed polycondensations circumvented the need for protection-deprotection steps that are traditionally required for chemical catalysis to avoid forming highly branched structures and/or crosslinked gels. Furthermore, low temperatures and mild reaction conditions of lipase-catalyzed condensation reactions allowed the polymerization of functional silicone building blocks without unwanted side reactions. Regioselective acylations of carbohydrates is another way in which lipases can be used by polymer chemists. By this approach, mono-aryl multifunctional monomers can be formed without protection-deprotection steps. Also, fermentative synthesis of glycolipids was used as a short-cut to generate complex building blocks for polymer synthesis. A perspective on future opportunities will be presented.

812. Enzymatic Catalysis in Supersaturated Solutions

Evgeny N. Vulfson, Akzo Nobel Chemicals, Dobbs Ferry, NY

Biotransformations are now well established as a means of manufacturing fine chemicals and pharmaceuticals. The major attractions of using biocatalytic processes are the high stereo- and regio-selectivity of enzymes and mild processing conditions. However, a large number of elegant enzyme-based developments have not made it to the market place largely due to insufficient productivity achieved in the reactor. The introduction of new approaches and reaction systems that would enable efficient transformations at very high substrate concentrations is therefore of great industrial importance.

In this talk, I will briefly review biocatalytic systems where the selection of common reaction solvent is problematic (e.g. biotransformations involving both hydrophilic and hydrophobic substrates), and then focus specifically on two systems developed in my laboratory: eutectic mixtures and supersaturated solutions. It was found that various amino acid derivatives (which are solids as individual compounds) readily form liquid and semi-solid eutectics on mixing at ambient temperatures. Such eutectics can be used as reaction media for a wide range of proteolytic enzymes in the preparative synthesis of short peptides and their derivatives. I will also describe some of our results on enzymatic (trans)glycosylation in supersaturated solutions using a range of crude commercially available glycosidases. The practical utility of the latter system will be demonstrated by several examples, including the regioselective synthesis of polymerizable sugar derivatives and other biotransformations.

813. Enzyme Immobilization onto Polymeric Supports

M. Elizabeth Miller, James C. Bohling, Marlin K. Kinzey, James F. Tate, Jr., Mark J. VanderHoff and William J. Zabrodski, Rohm and Haas Company, Spring House, PA

The growth in ‘green chemistry' research on the use of enzymes to carry out chemical processes has sparked a renewed interest in methods of enzyme utilization that maintain high levels of enzymatic activity. Biocatalytic processes become more cost-effective as a result of multiple cycles of biocatalyst re-use, made possible through enzyme immobilization onto solid supports. Immobilization yield and subsequent on-bead activity can be affected by enzyme loading conditions such as incubation time, buffer strength, and temperature. Immobilized Penicillin G Acylase was studied using porous acrylic support media (Amberzyme^{TM} resin) containing oxirane functionality for covalent attachment.

814. Biosynthesis of Sophorolipids by Candida Bombicola Using Industrial Fatty Acid Residues and Its Anti-HIV/Spermicidal Activity

Vishal Shah[1], Arthur Felse[1], Gustavo F. Doncel[2] and Richard A. Gross[1], (1)Polytechnic University, Brooklyn, NY, (2)CONRAD, Norfolk, VA

Text Not Available

815. Fermentative Production of Sophorolipids by Candida bombicola Using Industrial Fatty Acid Residues and its Anti-HIV/Spermicidal Activity

Vishal Shah[1], P. Arthur Felse[1], Gustavo F. Doncel[2] and Richard Gross[1], (1)Polytechnic University, Brooklyn, NY, (2)CONRAD, Norfolk, VA

Sophorolipids are extracellular glycolipids produced by Candida species when grown on mixtures of carbohydrates and fatty acids. Typically, sophorolipids consist of a dimeric sophorose connected by a glycosidic bond to the penultimate hydroxyl group of an 18-carbon fatty acid. Nickel contaminated industrial fatty acid residual wastes derived from tallow, stearate and coconut oil combined with glucose were evaluated both in batch and fed-batch processes for the production of sophorolipids using Candida bombicola ATCC 22214. Maximum sophorolipid yields of 120 g L-1 and productivity of

12.0 g L-1 d-1 was obtained by fed batch fermentation using tallow fatty acid residue. Feed of coconut fatty acid residues increases the cell production. The presence of nickel in the fermentation medium did not alter the production levels of sophorolipids and cells. The sophorolipid produced and its structural analogues have been studied for its spermicidal and anti-HIV activities. Sophorolipid di-acetate ethyl ester derivative is the most potent spermicidal and virucidal agent of the series of SLs studied. Its virucidal activity against HIV and sperm-immobilizing activity against human semen are similar to those of commercial spermicide Nonoxynol-9.

816. Regioselective Modification of Starch Nanoparticles by CAL-B

Soma Chakraborty, Columbia University, New York, NY and Richard Gross, Polytechnic University, Brooklyn, NY

A one-pot selective esterification of starch nanoparticles using Candida antartica Lipase B (CAL-B) in its immobilized (Novozym 435) and free (SP-525) forms has been reported. The starch nanoparticles were made accessible for acylation reactions by formation of Aerosol-OT (AOT, bis(2- ethylhexyl)sodium sulfosuccinate) stabilized microemulsions. These reverse micelles acted as nanoreactors. Starch nanoparticles in microemulsions were reacted with vinyl stearate, ε-caprolactone, and maleic anhydride at 40 °C for 48 h to give starch esters with degrees of substitution (DS) of 0.8, 0.6, and 0.4, respectively. Substitution occurred regioselectively at the C-6 position of the glucose repeat units. Infrared microspectroscopy (IRMS) revealed that AOT coated starch nanoparticles diffuse into the outer shell of catalyst beads. Thus, even though CAL-B is immobilized within a macroporous resin, CAL-B is sufficiently accessible to the starch nanoparticles. Free CAL-B could also regioselectively catalyze the acylation of starch nanoparticles within AOT-coated reversed micelles. Dynamic light scattering analysis revealed that the starch nanoparticles retain their nanostructure even after hydrophobic modification.

817. Crosslinking/Branching Studies for Polymers Synthesized By Chemical Versus Enzyme-Catalyzed Synthetic Methods

Wei Gao, Jun Hu, Ankur S. Kulshrestha, Wenchun Xie and Richard A. Gross, Polytechnic University, Brooklyn, NY

Lipase-catalyzed polymerizations have attracted much attention in recent years because they can provide high efficiency, good enantio- and regio-selectivity, proceed in the absence of solvents, and circumvent potentially toxic catalysts. Our laboratory has developed a simple but versatile synthetic strategy to synthesize polyol-containing polyesters. Examples are copolymers of octanediol adipate with sorbitol adipate and copolymers of octanediol adipate with glycerol adipate. To ascertain potential benefits that may be derived by using enzyme-catalysis instead of traditional chemical methods to prepare functional polyesters, work was performed to compare the crosslink/branching of poly(octanoyladipate-co-glycerol adipate) synthesized using Novozyme 435 and dibutyltinoxide as catalyst by direct condensation of adipic acid (A2) with octanediol (B2) and glycerol (B3). Size-exclusion chromatography (SEC) combined with online multi-angle light scattering (MALS) was employed for analysis of molecular weight averages, molecular weight distributions and branching. The degree of branching obtained by SEC-MALS was compared to that from NMR. The topological factor G, instead of branching factor g, was used to distinguish branching characteristics of functional polyesters prepared by chemical and enzyme-catalyzed condensation polymerizations.

818. Self-Assembly of Fermentative products from Candida bombicola

Shuiqin Zhou[1], Chang Xu[1], Jun Wang[1], Wei Gao[2], Rena Akhverdiyeva[2], Vishal Shah[2] and Richard Gross[2], (1)CUNY College of Staten Islande, Staten Island, NY, (2)Polytechnic University, Brooklyn, NY

Sophorolipids are produced by culturing the yeast Candida bombicola on mixtures of carbohydrates and lipids. These glycolipids have great potential as therapeutics for the treatment of cancer and severe immune disorders, enhanced oil recovery, germicidal preparations, and cosmetics. Here, we report the self-assembly of an acidic sophorolipid (SL-COOH). The complex and unique structure of SL-COOH provides an intriguing asymmetric bolaamphiphiles, including an asymmetrical polar head size (disaccharide vs. COOH), kink hydrophobic core (cis-9-octadecenoic chain), and a non-amide polar-nonpolar linkage. Light microscope, small and wide angle X-ray scattering, FT-IR spectroscopy, and dynamic laser light scattering were used to investigate the supramolecular structures of the self-assembled aggregates of SL molecules at different pH values. In acidic conditions (pH < 5.5), giant twisted and helical ribbons of 5-11mm width and several hundreds micrometers length were observed. Increase in solution pH values slowed ribbon formation, decreased ribbon yield, and increased the helicity and entanglements of the giant ribbons. An interdigitated lamellar packing model of acidic SL-COOH molecules with long period of 2.78 nm, stabilized by both the strong hydrophobic association between the cis-9-octadecenoic chains and strong disaccharide-disaccharide hydrogen bonding is proposed. The neutralization of SL-COOH in water to SL-COONa produced clear solutions with the formation of short-range ordered aggregates. At concentrations below 1.0 mg/mL, the size of self-assembled aggregates increased as the concentration increased. At concentrations above 1.0 mg/mL, narrowly distributed micellar aggregates with a constant hydrodynamic radius (Rh) of about 100 nm are formed.

Celebrating Chemists and Chemistry, NJ and Beyond!

Organizer: Jeannette E. Brown 2004 Société Fellow Chemical Heritage Foundation, Hillsborough, NJ

Presider: Jeannette E. Brown 2004 Société Fellow Chemical Heritage Foundation, Hillsborough, NJ

819. Plumbago, Bamboo, and Goldenrod - Thomas Edison and God's Almighty Warehouse

Kevin Olsen, Montclair State University, Montclair, NJ

Thomas Edison (1847-1931) has long been recognized as America's most famous inventor. His 1,093 patents ranged from stock tickers to cement houses. Historians generally agree that his greatest single invention was the modern research laboratory where multidisciplinary teams worked on complex technological problems.

Edison believed that when using a substance, it was important to be fully cognizant of its chemical and physical properties. His experimental approach often included testing thousands of different substances to find the one best suited for an application. In order to have a diverse stock of materials, he created stockrooms that were the precursor of modern compound libraries. Although it seemed a random process, Edison's knowledge of chemistry and extensive library research often provided a valid starting point.

As famous as this approach became, it seems to have exerted little influence on twentieth century drug discovery which itself uses a very similar trial and error methodology. Paul Ehrlich is rightfully recognized as the father of compound screening for medical research.

Edison's absence from pharmacological history seems largely to have been the result of the perception that he lacked a theoretical understanding of the systems he was studying. The word “Edisonian” is used to describe trail and error research undertaken without theoretical understanding. Edison's Myth of the down to earth, practical inventor who had little time for academic theory has denied Edison his rightful place in the history of modern science.

820. Thomas Edison, Chemist

Jeannette E. Brown, 2004 Société Fellow Chemical Heritage Foundation, Hillsborough, NJ

This will be a review of an ACS monograph entitled “Thomas Edison, Chemist” written by a North Jersey Chemist Byron M. Vanderbilt. We will review the book and show photos of Edison's chemistry laboratory in West Orange New Jersey. “Thomas Edison – inventor, innovator, electrical and mechanical wizard- was first and foremost a remarkably versatile chemist. He was deeply involved in chemical work before the American Chemical Society was founded and had been applying his chemical knowledge to intensely practical ends for more than 40 years before the Society's first journal on applied chemistry appeared. We will review each chapter in the book that discusses the state of the art at the time Edison worked, the chemistry behind the problems and the way Edison solved the problems. Edison's many successes can best be explained by his own words when he sad: “I never did anything worth doing by accident, nor did any of my inventions come by accident: they came by work.”” (From the back of the book).

821. Seven Twists of Fate That Propelled the Explosive 1918-1940 Growth of the U.S. Chemical Enterprise

Donald G. Hicks, Georgia State University, Atlanta, GA

Right after 1900, chemists knew little about atoms, chemical bonds, or polymers. Much like today, chemists then had the image problem that their contributions to society were mostly credited to engineers and others. The fledgling U.S. chemical enterprise was a narrowly focused chemical industry with little government or private support for research, and the pharmaceutical and organic chemical industries were non-existent. After World War I a great debate raged among both chemists and the public about whether the U.S. chemical industry should, or was even capable of expanding to produce organic materials. Many Americans thought that only German chemists could make quality organic and pharmaceutical chemicals! But a fiercely patriotic chemist fought the "global economy" ideas of that era, and the protected U.S. chemical industries experienced an explosive 1918-40 expansion to become Wall Street's recession proof darling! The image of chemists and chemistry was at its peak by 1940! All this might never have occurred except for SEVEN UNFORESEEN TWISTS OF FATE, described in this paper, which profoundly influenced both the career of that patriotic chemist as well as the development of the U.S. chemical industries that employ almost a million workers. Although this two-time ACS President was arguably the most important 20th century American born chemist, his name is not among the 250 in the ACS Luminaries of the Chemical Sciences. At the end of the presentation one might say, like famous radio commentator Paul Harvey, "Now you know the rest of the story!"

822. The History of African American Women Chemist Project

Jeannette E. Brown, 2004 Société Fellow Chemical Heritage Foundation, Hillsborough, NJ

African American women in science have always labored under the "double bind" of being a woman and a minority in science. To date, limited knowledge exists on the educational experiences of African American Women Chemists We will discuss the establishment of a project to extend the current knowledge base about African American women in chemistry.

Dr. Marie Daly was the first African American woman to receive a PhD in chemistry in 1948. She is noted for her research that preceded the discovery of DNA. It takes true diligence to come up with other African American women who pursued careers in chemistry before Dr. Daly and also other women contemporaries of Dr. Daly and beyond. This is the motivation for establishing this History of African American Women Chemists Project. We will be developing curriculum materials for teachers of students aged 9-14. We realize that this information should be available in forms other than a book because students at this age are best reached through use of multiple media. We are developing a multimedia program, web site, links to chemistry sites, activities geared toward the science of women chemists and workshops where students, especially girls, can interact with contemporary African American women chemists either in person or via the web by e-mail and chat rooms. This paper will detail our progress to date.

Process Oriented Guided Inquiry Learning POGIL

Organizer: Richard S. Moog Franklin & Marshall College, Lancaster, PA

823. Process Oriented Guided Inquiry Learning and the POGIL Project

Richard S. Moog, Franklin & Marshall College, Lancaster, PA

Process Oriented Guided Inquiry Learning (POGIL) is a student-centered instructional approach that combines a guided inquiry pedagogy with group learning. In addition, an emphasis is placed on the development of important process skills to improve higher order thinking skills and enhance the mastery of content. This presentation will introduce the principles of the POGIL approach, and will also describe the various efforts of the POGIL project, funded by the National Science Foundation, to disseminate this pedagogic approach throughout the country.

824. POGIL and PLTL: Contrast and Comparison

Thomas H. Eberlein, Penn State Schuylkill, The Capital College, Schuylkill Haven, PA

We have used a wide variety of student-centered, active learning techniques in connection with chemistry instruction at Penn State Schuylkill. Many of these approaches have received support from the National Science Foundation through its Multi-Initiative Dissemination Project. This talk will highlight, compare, and contrast two of these techniques, Processes Oriented Guided Inquiry Learning (POGIL) and Peer-Led Team Learning (PLTL). We believe each of these methods helps students develop their problem solving skills and facilitates their intellectual maturation. Qualitative and quantitative data will be provided supporting these claims.

825. POGIL in a Graduate Molecular Spectroscopy Course for High School Chemistry Teachers

Susan R. Phillips, University of Pennsylvania, Philadelphia, PA

POGIL physical chemistry materials have been incorporated into a graduate molecular spectroscopy course for high school chemistry teachers at the University of Pennsylvania. This course is part of a unique masters' program developed by chemistry department faculty. Courses within the Master of Chemistry Education Program (MCEP) are taught using the “Penn Inquiry Model” (PIM), which features a research-based cycle of inquiry. In addition to improving the teachers' content knowledge, a major goal of the MCEP program is to change the teaching and learning methodologies used by the teachers in their classrooms to a more research-based pedagogy. Parallels between the PIM and POGIL models, use of the POGIL materials within the context of the PIM, and feedback from high school teachers about the course and the use of the POGIL materials will be presented.

826. Teaching reasoning process in organic chemistry using electron energies

R. Daniel Libby and Carl Salter, Moravian College, Bethlehem, PA

POGIL, Process Oriented Guided Inquiry Learning, uses carefully constructed activities in small group discussions to help students work together to learn both the content of chemistry and the reasoning processes required to understand chemical concepts. We believe that content and reasoning processes are best learned when chemical phenomena are linked to a unifying scientific principle: energy. We want students to connect the consumption or release of energy in chemical reactions to changes in electron energies resulting from structural changes in those reactions. We have developed Electron Energy Analysis (EEA), a simple yet theoretically rigorous method for predicting both thermodynamic and kinetic reactivity of molecules. EEA is a simplification of Frontier Orbital Theory that uses the changes in energies of the highest energy electrons (HOMOs) of reactants, transition states and products to judge both kinetic and thermodynamic reactivity. EEA provides students with a conceptually simple way to identify the most reactive sites even in complex reactions. By connecting changes in molecular structures to changes in electronic energies, EEA provides students with a theoretical basis for understanding and predicting reaction thermodynamics, reaction mechanisms and relative rates of reactions. EEA has two advantages over more traditional approaches: 1 It helps students focus on what is important for analyzing reactions, and 2 It provides a process for assessing the effects of structural changes on electron energies of molecules, ions and transition states leading to an understanding of energy consumption or release in chemical reactions in terms of changes in electron energies.

827. Student Resistance to POGIL Implementation in an Organic Chemistry Course

Kelly E. Butler, Chestnut Hill College, Phila., PA

Students' reactions to the implementation of POGIL in a two-semester Organic Chemistry course will be discussed. This was the first experience of POGIL for all of the students, and the majority of initial responses were quite negative. However, with a structured process for students to air their grievances as well as minor modifications of classroom practices, the students began to accept this new approach. Course evaluations indicate that by the end of the semester many students appreciated the benefits of the POGIL method. Results of course evaluations for the second semester and an analysis of students' experiences over both semesters of the course will be presented.

828. The POGIL (Process-Oriented Guided-Inquiry Learning) Laboratory

Frank J. Creegan, Washington College, Chestertown, MD

A POGIL (Process-Oriented Guided-Inquiry Learning) laboratory (http://www.pogil.org) is one in which students, in advance of any classroom work on underlying principles, work in teams to conduct experiments rather than exercises that verify previously taught principles. In a pre-lab session, which may be real or virtual, the instructor poses a focus question (Can Alcohols React as a Base? What Role Might Substituents Play?) and students propose a set of tentative answers. To test these hypotheses, students run reactions and collect data, which are pooled and then analyzed with the aid of post-laboratory guided-inquiry questions. This learning cycle approach not only guides students to construct their own understanding of important chemical concepts but also helps them to develop valuable learning process skills. In this presentation, the application of the POGIL approach to courses in General and Organic chemistry as well as the criteria for a POGIL experiment will be described.

Regional Industrial Innovation Award Symposium

Organizer: Vanessa Johnson-Evans American Chemical Society, Washington DC, DC
Presider: Vanessa Johnson-Evans American Chemical Society, Washington DC, DC

829. Recognizing scientists behind research & development

Vanessa Johnson-Evans, American Chemical Society, Washington DC, DC

Come and hear about the outstanding developments of these scientists.

Willie Lau Rohm & Haas Company, Spring House, PA Development of the transport catalyst, cyclodextrin, that allows polymerization of hydrophobic monomers

Andrew Daly, Richard Haley, Paul Horinka, Casmir Ilenda, Joseph Kozlowski, Greg Mill, Edward Nicholl, John Petro, Eugene Reinheimer, Grant Schlegel, Navin Shah, Michael Spera, and Gordon Tullos Rohm & Haas Powder Coatings, Reading, PA Development of Lamineer®, the first low-temperature cure powder coating technology for coating medium density fiberboard

Donald Nuzzio Analytical Instrument Systems, Inc., Ringoes, NJ Development and successful commercialization of instrumentation for in situ voltammetic analysis which has been used for study of chemical processes from lakes to the deep-ocean hydrothermal vents