


Opportunities

Undergraduate Research Program

2004 Summer Research Symposium Poster Abstracts

1
Synthesis and Thermal Analysis of Alkali and Transition Metal Monothiophosphates
Austin M. Savatt, Nathan J. Takas and Jennifer A. Aitken Department of Chemistry and Biochemistry, Duquesne University , Pittsburgh PA

Monothiophosphate, [PO 3 S] -3 , is a tribasic anion, whose sodium salt is currently known. Little research has been directed towards the field of monothiophosphates since 1885, when the sodium salt was first reported by Kubierschky, therefore only a small amount of data has been recorded regarding the physical properties and applications of these compounds. During my research period, we have synthesized lithium and sodium monothiophosphate, in an attempt to create crystals, or a crystalline powder. Following its synthesis, lithium monothiophosphate (Li 3 PO 3 S) was subjected to various characterization methods, such as differential thermal analysis (DTA), thermogravimetric analysis (TGA) and powder X-ray diffraction (PXRD). The materials were then used in metathesis reactions with various metal chlorides. Synthesis and physicochemical characterization of the resulting materials will be presented.

2
Rapid Microwave Synthesis of New Diluted Magnetic Semiconductors
Anna M. Pischera and Dr. Jennifer A. Aitken,Department of Chemistry and Biochemistry, Duquesne University Pittsburgh , PA

Dilute magnetic semiconductors with diamond-like structures are of interest because of their optical properties and their possible use in spintronic devices. The goal of our research is to produce a diluted magnetic semiconductor based on the chalcopyrite CuInSe 2 and study its magnetic properties. Multiple analysis methods indicate that we have been able to synthesize a relatively pure CuInSe 2 compound using microwave irradiation in less than 15 minutes. Doped samples with varying amounts of manganese have also been prepared, such as CuIn 0.95 Mn 0.05 Se 2 . The 2.5% sample has shown the greatest shift in the powder x-ray diffraction pattern. The volume of the refined unit cell obtained by using a silicon standard is 1.37% larger than the undoped compound. Attempts at producing other compounds in the microwave will also be reported. Thermal analysis and energy gaps of all compounds will be presented.

3
A Computational Study of Cadmium Sulfide Quantum Dots
Jacqueline Stoll 1 , Athena Spencer 1 , Stacie Nunes 2 , Jeffry D. Madura 1 , Duquesne University

We are studying different sized cadmium sulfide (CdS) clusters ranging from a few atoms to quantum dots to bulk clusters because of their potential applications in light emitting diodes, solar cells, and photoswitches. Specifically, our research focuses on CdS quantum dots, which have different optical and electrical properties compared to the bulk phase in their size, and shape. 1 To investigate the differences in their properties, PM3 semi-empirical quantum mechanical calculations were performed with the programs CAChe and

MOPAC2002 to identify the energies and molecular structures of CdS clusters with different sizes and ligation. The CdS clusters studied are [S 4 Cd 17 (SPh) 28] 2- , [S 4 Cd 17 (SCH 2 CH(OH)CH 3) 28] 2- , [Cd 32 S 14 (SPh) 36 •4H 2 O], and [Cd 32 S 14 (SCH 2 CH(OH)CH 3) 36 •4H 2 O]. Our computed band gaps were 4.78, 4.99, 5.01, and 5.12, respectively, and deviations from x-ray structures were measured in their RMSD values were 13.1, 13.1, 16.2, and 13.9, respectively. Using a method similar to Brändle, Calzaferri, and Lanz we have identified the surface states for these systems.

4

Computational Modeling of Acetonitrile

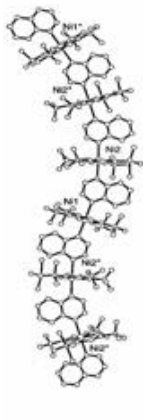
Kimberly J. Zanotti, Jeffry D. Madura, & Fraser F. Fleming, Duquesne University , Pittsburgh , PA

Carbanions act as strong nucelophiles in many important organic reactions. In reactions involving metallated carbanions, the product is stereoselective. The stereoselectivity is hypothesized to be dependent on the carbanion's geometry. Either linear or pyramidal geometry could potentially occur, dependent on the position of the metal's attachment to the carbanion. Computational modeling studies were undertaken in order to determine the carbanion geometry. Quantum mechanics calculations were conducted, with acetonitrile anion employed as a model carbanion. The effects caused by varying the metal, solvent, and level of theory were also examined. Initial results indicate that the carbon-metallated system in the gas phase has a lower energy than the nitrogen-metallated acetonitrile. The pyramidality of this carbon-metallated system could potentially provide an explanation for the carbanion's stereoselectivity.

5

Synthesis, Spectral and Computational Studies of Cobalt(II) and Nickel(II) Acetylacetonate-Quinoxline and 2,2,6,6-Tetramethyl-heptanedionato-Quinoxline Polymers

Metasebia T. Munie, Omar W. Steward, Jeffrey D. Evanseck, Department of Chemistry and Biochemistry, Duquesne University, Pittsburgh, PA



Homonuclear and heteronuclear coordination polymers of cobalt(II) and nickel (II) acetylacetonato and 2,2,6,6-tetramethylheptanedionato complexes with the nitrogenous base quinoxline have been synthesized. *trans* -[M(acac) 2 (qox) 2] (where M = Co, Ni) were reacted with M(acac) 2 or M(tmhd) 2 (where acac = acetylacetonate; tmhd = 2,2,6,6-tetramethylheptanedionate) to give the polymeric complexes. Infrared spectra of the polymeric complexes were determined and compared to the spectra of complexes of known crystal structures. Computational geometry optimization was also carried out on the S-shaped polymer, [Ni 3 (tmhd) 6 (qox) 3] n , see the Figure, and these results will be discussed

6

The Role of Periplasmic Nitrate Reductase (Nap) in Dissimilatory Nitrate Reduction and Cancer

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Nitrate Reductase is an enzyme that many nitrate respiring bacteria utilize to convert nitrate into nitrite. Epsilon Proteobacteria (e.g., *Campylobacter* sp., *Helicobacter* sp.) residing in the human GI tract and their free-living relatives (e.g., *Sulfurospirillum barnseii*) possess periplasmic nitrate reductase activity (NAP). In vivo nitrate respiration by the former may lead to production of reactive nitrogen compounds such as nitrous oxides and nitrosamines. Since these organisms share a similar nitrate reductase enzyme, it is of biological interest to purify and characterize the protein. The aim of this project is to amplify the *napA* from *S. barnseii* using a new primer set (F104, F204, R10, R20), clone this gene into the TOPO C7 vector, and express the NapA protein in *Escherichia coli* . Previous attempts to express active NapA from *S. barnseii* into *E. coli* were unsuccessful.

7

A Phenanthrene Scaffold as a new G-Quartet Binding Agent

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The Firestine Lab has recently synthesized a triazacyclopenta[b]phenanthrene compound **(1**) and they have shown that this agent has low affinity for double stranded DNA. Equilibrium dialysis studies were conducted to determine if **1** was selective for other types of DNA structures. This study revealed that **1** bound selectively to G-quartet structures.G quartet structures are found in human telomeres and compounds that can stabilize G-quadruplexes have exciting potential to be used in the treatment of cancer. Compound **1** readily promotes the formation and stabilization of G quadruplexes in conditions that do not favor its formation. Further studies indicate that **1** binds to the DNA molecule in a similar fashion to TmPyP4, which is a known G quadruplex-binding porphyrin molecule.

8

Pharmacophore Modeling and Computational Analysis of Potential Inhibitors of a Key Protein-Protein Interaction in Herpes Simplex Virus

Melanie J. Grubisha, S.M. Firestine*

The interaction between the DNA polymerase (UL30) and its processivity factor (UL42) is required for herpes simplex virus DNA replication. Inhibiting this interaction could lead to the development of new anti-HSV agents. To facilitate the design of inhibitors, molecular surface modeling was done to determine the binding site on UL42 where critical residues of UL30 make key interactions. Identification of 3 critical UL30 residues, coupled with the molecular surface model, allowed for the development of a pharmacophore model to screen compounds for potential inhibitory actions. Using a bicyclic scaffold with various substitution points and a library of functional groups, a virtual combinatorial library was generated and screened for potential inhibitors. Of the 1156 compounds screened through the pharmacophore model, 71 hits were obtained. These hits were evaluated with respect to the functional groups present and their alignment with the natural UL30 ligand. The best fitting compounds were then docked to confirm their possible actions as inhibitory compounds at the UL42 active site. Computational analysis of these compounds indicates they are good candidates for synthesis and testing, and may lead to the design and development of novel medicinal agents for treating the herpes simplex virus.

9

Optimization of the recognition reaction for a polymerized crystalline colloidal array ammonia sensor

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The polymerized crystalline colloidal arrays (PCCA) developed by the Asher group offer a wide range of possibilities as chemical sensors. Once the Bragg diffracting colloidal array is incorporated into a hydrophilic polymer mesh, changes in volume of the PCCA can be monitored by measuring the shifts in diffraction wavelength. In one approach to using a PCCA as a sensor, the PCCA is forced to change volume when the polymer forms new crosslinks in response to a certain analyte. The ammonia sensor uses the Berthelot reaction, which is a standard colorimetric ammonia assay in which ammonia, hypochlorite, and phenol form indophenol, a blue dye. There are numerous variables to be optimized to improve the efficiency of the ammonia sensor. Among these are the molecule used for ammonia recognition, the amount of the recognition

agent in the hydrogel, and the amount of catalyst.

10

Purification of the Periplasmic Nitrate Reductase from *Sulfurospirillum barnesii* strain SES-3

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The periplasmic nitrate reductases (Nap) from Epsilon Proteobacteria is involved in nitrate respiration (nitrate reduction to nitrite) in both free-living and pathogenic species. These enzymes form a unique clade among all nitrate reductases. Nap from the free-living bacterium *Sulfurospirillum barnesii* strain SES-3 was solubilized with CHAPS (2%) and purified by size exclusion chromatography (Sephacryl S-300 HR) and ion exchange chromatography (DEAE-Toyopearl). The enzyme was a heterodimer, NapAB. NapA is the catalytic subunit, which contains an iron sulfur cluster and a molybdenum cofactor. NapB is a diheme cyctochrome C. Visible spectra indicated the presence of cytochrome C. The large subunit (NapA) cross-reacted with polyclonal antibodies raised against Nap from *Ralstonia eutropha* . Studies of its substrate specificity, kinetics, and electron donors (e.g., quinones) are underway.

11

Electrochemistry of a Model Compound of Hydroxylamine from *Nitrosomonas europaea*

Christopher Yeisley , Jennifer DeCoskey, Danielle Sunseri# and Edward Zovinka* Department of Chemistry, Saint Francis University #Department of Chemistry, Pennsylvania State University , *Academic Research Advisor, Saint Francis University

Heme P-460 is the active site for the enzyme hydroxylamine oxidreductase (HAO) and converts ammonia into nitrite through a two-step reaction in which HAO is the second enzyme used to complete the reaction. This enzyme is found in the *Nitrosomonas europaea* , a soil living organism, which gains energy from the two-step reaction. A model compound, Cl-Fe III (meso-{2-hydroxyphenyl}-octaethylporphyrin, was synthesized and characterized by NMR, UV-Vis, and X-ray crystallography. We plan on finding out about the electrochemistry of this model compound, but desire a less electroactive complex for comparative purpose. The methanol group is not removed through the dematallaton leave the O-Methane group unreactive when the Iron is inserted. This comparison will allow the determination of E 'o of the metal and ligand. The final goal of this research is to help in the overall efficiency of ammonia base fertilizers by turning off this bacteria's enzyme.

12

Tetra(2',6'–dimethoxyphenyl)porphyrins as a Model for HAO

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#Department of Chemistry, Youngstown State University , *Academic Research Advisor, Saint Francis University

Hydroxylamine oxidoreductase (HAO), an enzyme in the bacteria *Nitrosomonas europaea* , found in soil, can transfer two electrons at a time during the oxidation of hydroxylamine into nitrite. By creating models of the HAO active site, we hope to better understand the behavior of the electron transfer. This may be beneficial agriculturally as the oxidation of ammonium to nitrite decreases the efficiency of fertilizers. Nickel and zinc tetra(2',6'-dimethoxyphenyl)porphyrins have been made as models of HAO. X-ray crystallography, nuclear magnetic resonance, and electronic spectroscopy have been used to experimentally characterize these porphyrins.

13

Coordination and Photophysical Properties of Luminescent Flavanoid-Lanthanide Complexes

Jeanette Cessarich, Demetra Chengelis, Stéphane Petoud*, Department of Chemistry, University of Pittsburgh , Pittsburgh , PA

While there is a substantial amount of research available on visible emitting lanthanide complexes, the amount of information for those emitting in the near infrared range (NIR) is limited. Flavanoids were investigated for their efficiency as antennae for NIR emitting lanthanides. They were chosen since they contain several oxygen donors (hard Lewis bases) and chromophore groups with fairly

low energy triplet states, making it likely that their donating energy levels will correspond to the NIR lanthanide cations' accepting levels. We investigated complexes formed between Neodymium and Ytterbium with the following flavanoids: Morin, Quercetin, Galangin (Figure1). Complexes were studied through UV/Vis absorption, emission, and excitation spectroscopy. Spectrophotmometric titrations were conducted to investigate the stoichiometry of the complexes formed in solution **.** Lifetime and quantum yield measurements were performed to help identify the properties of these complexes. The ligands' triplet state energies were investigated through time-resolved measurements while in complex with Lanthanum.

14

Adhesion and Proliferation of Murine 3T3 Fibroblasts on Stainless Steel Modified with Self-Assembled Monolayers of Varying Terminal Groups

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The fabrication of cell-resistant surfaces is crucial for the construction of biomaterials used as implants in tissue engineering. One approach used to increase the biocompatibility of these materials is the modification of surfaces by self-assembled monolayers (SAMs) that have cell-repellent properties. To analyze the *in vitro* adhesion and proliferation of murine 3T3-Swiss albino fibroblasts, stainless steel coated with different SAMs terminating in hydroxyl, methyl, carboxyl and amino functional groups, were seeded with fibroblasts in well-plates. Cell density on the coated pieces was determined using fluorescent LIVE/DEAD ® viability staining and CyQuant ® Cell Proliferation Assay. Samples that had amino, methyl, and carboxyl tail groups demonstrated the lowest 3T3 fibroblast adhesion and proliferation. Controls and hydroxyl terminated SAMs showed a high density of adherent cells. Results show that surfaces with amino, methyl, and carboxyl terminal groups may be useful as coatings of implants based on their biocompatibility and cell-repellent properties.

15

QM/MM Model of Water Dimer Hydrogen Bonding with ONIOM

Steve Arnstein and Jeffrey D. Evanseck, Department of Chemistry and Biochemistry, and Center for Computational Sciences, Duquesne University

Accurate modeling of the hydrogen bond in the water dimer is essential towards correct computational treatment of larger biological systems. We have investigated the effectiveness of the ONIOM method to model hydrogen bonding. ONIOM is a technique that allows the combination of high and low levels of theory from both quantum (QM) and molecular (MM) mechanics in one calculation (QM/MM). The technique is especially appealing when applied to large systems using high levels of theory to save resources and time. We have evaluated the accuracy of six different quantum chemical and molecular mechanical methods and 21 different basis sets in predicting several properties of the water molecule. We have found that commonly employed levels of theory may give correct structural and thermochemical properties, however for the wrong reasons. Cancellation of error is significant. We find that the 6-311+G (3d2f,2p) basis set with quantum chemical methods is necessary to describe properties of the hydrogen bond. In future experiments, we will apply our understanding of modeling hydrogen bonding with ONIOM to larger chemical and biological systems.

16

Effects of Single Dose Methylphenidate Treatment on Striatial Dopamine and Metabolite Levels

Meghan Andes – REU student, Amy Wagner- Professor Safar Center for Resuscitation Research, University of Pittsburgh

Methylphenidate (MPH) is currently used to treat patients with abnormal dopamine levels. Chemically, MPH works by blocking the dopamine neurotransmitter thus preventing dopamine reuptake, and ultimately increasing dopamine levels outside the cell. Currently, this drug is being used to treat patients suffering from a traumatic brain injury (TBI). It has been found that upon TBI dopamine levels are significantly decreased, thereby inhibiting motor and cognitive functions. The purpose of this study was to examine the effects of single dose MPH by measuring striatal dopamine levels after experimental TBI via microdialysis. Preliminary data shows that prior to MPH injection, the

average ipsilateral and contralateral dopamine concentrations were found to be 5.782nm and 0.4378nm, respectively for injured rats. Surprisingly, ipsilateral dopamine levels decreased after injection while contralateral levels increased. Results are based on only three subjects thus far. Research is still underway with plans to examine sham and injured rats injected with both MPH and saline.

17

The Diels-Alder Reaction of Coumalic Acid Derivatives

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The Diels-Alder reaction of coumalic acid and its derivatives has the potential to generate highly functionalized scaffolds, which may find utility in NMR analysis of racemic amines or as templates in peptidomimetic design. The synthesis of Diels-Alder adducts will be described, as well as progress toward the goal of their application.

18

A Novel Route to b -Carbolines and Related Heterocycles

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The Pictet-Spengler reaction of tryptophan derivatives with ninhydrin yields spirocyclic heterocycles that are readily converted to yohimbanones. The yohimbanone framework undergoes a novel oxidative ring opening to produce substituted b -carbolines. The preparation of analogues and efforts to expand the methodology will be described.

19

Structure and Reactivity of Nitrile Anions

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Nitrile anions possess unique structural and reactive properties that are not yet fully understood. In some nitriles the adjacent carbon exhibits a preference for a bond order of greater than four. To aid in the exploration of this anomaly, computational modeling at the HF/6-31+G* level was performed on two such nitriles: 2-lithio-2-methyl-3-phenylbutanenitrile and 1,2-dimethylcyclopentanecarbonitrile. Of particular interest in the butane nitrile is the hybridization and geometry of its top substituents. Both molecules were studied alone in the gas phase as well as their interaction with Li+. Additionally, the cyclopentane nitrile was modeled in its reaction with a chlorine ion, with an analysis of the behavior at the minima and transition state while solvated with DSMO and THF.

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A Comparison of CdS Quantum Dot Layers

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This study focused on bare, semiconductor quantum dots of CdS, particularly Cd17S32 and Cd32S50. Many properties, e.g. bond lengths, bad gap, for quantum dots differ from bulk properties. These properties were studied using the application of quantum mechanical (ab initio and DFT) methods. The electronic structure, band gaps, and density of states (DOS) for the various layers of the quantum dots were examined and compared to experimental properties. These properties will then be compared to capped CdS quantum dots as well as bulk CdS

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Machine Vision in Crystallography

Nicholas Nuar , Professor John Rosenberg Biology Department, University of Pittsburgh

Our Goal is to improve machine vision for crystal growth. Crystallography requires growing crystals from biological molecules in a trial and error process. A typical batch consists of 20 trays each with 96 samples. Using a computer to evaluate these trials will significantly improve productivity. We have already had some success sorting images to present the best for human inspection and in recognizing precipitate and micro-crystals, which can help to refine future experiments. Improvements will include lighting,

identifying 'big beautiful crystals', and detecting samples that have changed significantly over time. Machine vision can significantly improve a bottleneck

in the discovery process and improve throughput by an order of magnitude, but it is not a trivial task.

22

Further Characterization of the Respiratory Arsenate Reductase from *Bacillus selenitireducens*

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Duquesne University

The haloalkaliphilic low G+C gram positive bacterium *Bacillus selenitireducens* strain MLS-10 can grow by anaerobic respiration using arsenate as the electron acceptor. The respiratory arsenate reductase is a heterodimer with a catalytic subunit (ArrA, 110 kDa) and an electron transfer subunit (ArrB, 34 kDa) and belongs to the Dimethyl Sulfoxide (DMSO) reductase family of mononuclear molybdenum enzymes. The enzyme was purified using ion exchange (DEAE-Toyopearl) and size exclusion (Sephacryl S-300 HR) chromatography. Visible spectral analysis indicated the presence of an iron-sulfur cluster. Polyclonal antibodies were raised against a highly conserved region of ArrA (the catalytic subunit) and tested by ELISA and Western Blot analysis. Low levels of the enzyme were present when the cells were grown on nitrate, fumarate, selenite, and DMSO (as determined by activity assay and western blot analysis) suggesting regulation by arsenic. The molybdenum blue assay was adapted for detection of As (V) and As (III) in activity assays.

23

Transcranial Electrical Stimulation

Tyler Rath **,** Dr. Mingui Sun, University of Pittsburgh

Transcranial electrical stimulation, or TES, is an effective way to monitor the central nervous system while patients are under anesthetic. TES sends multipulse stimulation to the motor cortex, resulting in intraoperative patient muscular responses. In our research this summer, we want to develop a volume conductor model to describe the possible results of using TES. Poisson's equation will be evaluated according to boundary conditions determined from statistics of a real human head. The model will include the inhomogeneous aspects of a human head, which will impact the flow of current due to volume conductivity differences between the scalp, skull, cerebrospinal fluid, and the brain itself. We hope to

find a way to estimate the path of electric pulses through the different tissues of the head in order to determine the most effective placement of electrodes on the scalp, and the minimum threshold current and voltage values needed to achieve muscle stimulation.

24

Development of assay for cell specific splicing: analysis of expression from neuron and glial specific promoters

Theodora R. Bennett **,** Research Experience For Teachers (R.E.T) Paula Grabowski , Department of Biological Sciences, University of Pittsburgh

Alternative RNA splicing occurs in the nuclei of eukaryotic cells and is an essential and highly regulated process. The unknown portion of this experiment is the regulation of alternative splicing within the cell's nuclei and the splicing patterns associated with tissue specificity. Currently, verification of cell specific expression of promoters CAMKII(Calcium calmodulin Protein Kinase II) and Gfa2 (glial fibrillary acidic Protein) have been documented. The verification of expression of CMV(cytomegalovirus) will serve as a control and is the next portion to be documentation. We are using plasmids that have individual promoters driving the expression of either EYFP(green fluorescent protein) or

DsRed(Red fluorescent protein) and antibody staining of known molecular markers for neuron and glial cells. The data collected and analyzed from the control may support the observations documented for CAMKII and Gfa2 promoter expression.

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Self Assembled Monolayers on Molybdenum and Stainless Steel Substrates
Brian DiSalle, Dr. Ellen Gawalt, Duquesne University

Stainless Steel 316L (SS 316L) is used as a biomaterial for coronary stents. However, there have been problems in the past with blood clots at the stent site blocking the arteries. Our lab has been altering the surface properties stainless steel 316L to resist cell adhesion by forming self assembled monolayers on the surface. As part of this project, self assembled monolayers have been formed on molybdenum, a component of SS 316L, using octadecylphosphonic acid [CH 3 (CH 2) 17 PO(OH) 2] and stearic acid [CH 3 (CH 2) 16 COOH] in order to test whether the molybdenum in the steel affects monolayer formation on the steel's surface. Also, monolayers terminated with polyethylene glycol, a molecule known to resist cell adhesion, have been formed on SS 316L substrates by performing a coupling reaction to join polyethylene glycol to monolayers with reactive tail ends.

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Ab-Initio Studies of the Geometries and IR Spectra ofH 4 + (H 2 O) 4-6 Clusters
Glen Jenness , Kenneth Jordan, University of Pittsburgh

Abstract: Ab Initio calculations involving B3LYP exchanging-correlation functional with the 6-31+G(d) basis set was done on the clusters. Several local minima were optimized and the vibrational spectra calculated in the harmonic approximation. The calculated spectra were compared with those recently measured by the Johnson group. Based on this comparison, the isomers responsible for the observed spectra were identified.

27
Organometallics In Highly Regioselective S N 2' Reactions of Allyl Chlorides
Adam Robb , Theodore Cohen, Roman Ivanov,
University of Pittsburgh

Allyl phenyl sulfides are extremely versatile and widely used intermediates in organic synthesis. Simple ones are commercially available or easily prepared, as in eq. 1. One of the most widely used methods for preparing more complicated ones is to deprotonate the simple one with an alkyllithium and to treat the anion with an *electrophile* , such as an alkyl halide that attacks the allylic carbon atom attached to S. A new and hopefully even more general method, involving incorporation of a *nucleophile* , is being developed in this laboratory. It consists of chlorination of the allyl phenyl sulfide (eq. 2), and execution of an S N 2' displacement of the chloride ion by an organometallic, as in eq. 3. So, by varying the structure of the sulfur substituted allyl chloride and the organometallic group, we can determine the efficacy and generality of the reaction to form the S N 2' product.

28
Density functional explanation of C2-substituent substitution effects in bis(oxazoline) copper(II) catalyst complexes on the rate and selectivity of Diels-Alder reactions

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Bis(oxazoline) copper(II) complexes serve as important enatioselective acid catalysts for numerous organic reactions. However, how these catalysts change the rate and stereoselectivity of organic reactions is largely unknown. Density functional calculations have been carried out to determine the role that C 2 -substituent variation plays in such systems. Using Becke's three-parameter density functional theory with the nonlocal correlation of Lee, Yang, and Parr and the 6-31G(d) basis

set, the specific effects of *tert* -butyl, isopropyl, and phenyl substituent substitution are reported with regard to the Diels-Alder reaction of cyclopentadiene and acrylate imide. Consistent with experimental studies, the computed structures and rates of reaction are in good agreement. The importance of steric and electronic effects is discussed in rationalizing the observed rate and selectivity enhancements of the Diels-Alder reaction associated with these systems. Future work will involve modifying of the catalyst beyond the C 2 -substituents in order to optimize it for other important organic reactions.

29
Towards the Total Synthesis of Motuporin
Eddie Perry, Scott G. Nelson
University of Pittsburgh

Motuporin **(1)** is a marine oligopeptide isolated from the sponge *Theonella swinhoei* Gray found in Paupa New Guinea . Motuporin is one of the most potent inhibitors of protein phosphatase 1 known and shows strong in vitro cytotoxicity against a number of cancer cell lines. The natural product consists of a cyclic pentapeptide core with a pendant diene sidechain. Our retrosynthetic analysis forms motuporin from two main fragments, amino acid derivative **2** and polypeptide chain **3** . Synthon **2** will be prepared utilizing the AAC technology developed within these laboratories. Polypeptide **3** will be synthesized *via* coupling of amino acid derivatives of valine, glutamic acid, b -methyl-D-aspartate and serine. Current efforts are focused on preparing amino acid derivatives needed for the completion of polypeptide **3** .

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Catalytic Partial Oxidation of Methane in Extruded Monolith Reactors
Cynthia Snyder, Tengfei Liu, and Götz Veser

Department of Chemical Engineering, University of Pittsburgh
Catalytic partial oxidation of methane at high-temperature, millisecond contact-time conditions (T>900 o C????= 1-50 ms) is a technologically interesting novel reaction pathway for the production of synthesis gas or hydrogen. In order to distinguish different reaction zones in a typical monolithic catalyst, temperature profiles were measured inside the monolith channels and correlated with overall methane conversions and syngas selectivities. Supported platinum, rhodium, and nickel were studied as a function of catalyst lengths (2-10mm), total gas flow-rate (1slm - 4slm), and CH 4 /O 2 feed ratio (1.2 - 2.4). Temperature profiles differed markedly between different catalysts and catalyst lengths. The difference was attributed to changes in reaction mechanism (direct versus indirect oxidation). Rapid catalyst deactivation was also observed for Pt and Ni, and could be correlated with a shift in the location of the reaction front. Catalyst performance and temperature profiles will be compared and discussed in detail in the presentation.

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Determination of Ellagitannin Concentration and Permeability in White Oak Tree Samples
Kami R. Small, Paul Kolesar, Mitchel Fedak and Bruce Beaver, Department of Chemistry and Biochemistry Duquesne University

White oak trees are an essential part of the flavoring process of wine. Wine is stored in white oak wooden barrels. This is important to the wines taste because of the different chemicals that are extracted into the wine from the white oak. Of these chemicals, ellagitannins are among the most important. The ellagitannin concentration can be measured using the Folin-Ciocalteau method. The Folin-Ciocalteau Total Tannin Analysis method was used on select Western Pennsylvania white oak trees to determine the ellagitannin content for one hour versus that of multiple weeks. The measurements are recorded to determine how fast the ellagitannins are eluted (permeability of a tree). Ellagitannins are also known to oxidize over time. Further studies have examined the effect that oxygen has on the ellagitannin concentration over time, and how this affects the tree permeability. The results of this series of experiments are to help in the

ongoing investigation of oak aging on wine.

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Comparison of Implicit Solvation Methods of the Alanine Dipeptide over 100 Nanoseconds

Ryan A. Newton and Jeffrey D. Evanseck, Center for Computational Studies, Department of Chemistry and Biochemistry, Duquesne University , Pittsburgh

Molecular dynamics simulations typically involve explicit solvent molecules for accurate structure dynamics and property prediction. The use of explicit solvent is computationally expensive for large systems, restricting both system length and time scales. Different implicit solvent models have been developed over the past few years. This study compares the Generalized Born (GB), Analytical Continuum Electrostatics (ACE), and Generalized Born using Molecular Volume (GBMV) implicit models against a 519 explicit water simulation of the alanine dipeptide using the CHARMM program. This study compares the preference of the alanine dipeptide (*N* -acetyl- L -alanine- *N*'-methylamide) in each type of solvent environment for each of its seven conformations: C 7ax , C 7eq , a R, a L , C 5 , ß, and P II . Five 5 ns simulations have been conducted at 300 K using the NVE ensemble for each solvent model for a total of 100 ns. We discuss the ability of each model to sample conformational space and compare the findings against experimental results and explicit solvent simulations.

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Modeling the Failure of Surface Coatings

Benjamin A. Slavin, Steven P. Levitan
Location of Research: University of Pittsburgh

In recent years, a number of methods have been proposed for the self-healing of materials used in coatings and films (e.g. paint) that prolong the lifespan of surfaces and structures. Unfortunately, sufficiently detailed computer models do not exist to explore the behavior of these materials. Creating an accurate model of such materials would allow meaningful research into self-healing systems to be conducted. The purpose of this research is to build a model that meets these criteria through the use of a Lattice Spring Model (LSM); a model that represents the underlying structure as a three-dimensional network of harmonic elements. Fracture will be simulated by breaking the connections between these elements and investigating the dynamic response of the system. Through simulation of the natural contraction of surface coatings within this model, it will also be possible to investigate surface deformation.

34

Synthesis of Multinary Sulfides with Potentially Interesting Optical Properties

Katie L. McNerny and Jennifer A. Aitken Department of Chemistry and Biochemistry, Duquesne University , Pittsburgh , PA

Multinary sulfides exhibit several technologically useful optical properties such as second harmonic generation, extreme IR-transparency and photovoltaic effects. These properties lead to application such as frequency doubling of light, for example AgGaS 2 , long-wavelength IR-windows, for example KInS 2 and highly efficient solar cells, for example CuInS 2 . Therefore we were motivated to prepare new multinary sulfides and study their optical properties. We synthesized these materials via two routes: high temperatures solid state synthesis and molten flux synthesis. We succeeded in preparing a new diamond-like compound, Li 2 CdGeS 4 , from a stoichiometric mixture of Li 2 S, Cd, Ge and S heated to 800°C. Diamond-like semiconductors are of interest because they crystallize in a noncentosymmetric space group, thus leading to a nonzero second-order nonlinear optical susceptibility, ? (2) . Molten flux synthesis using polychalcogenide flux mixtures combined with metals at 500°C lead to the new compound K 1-x Na x InS 2 . Powder X-ray diffraction as well as thermal and optical characterization of these new materials will be presented.

35

Whole Blood Transformation of Lymphocytes

Derrick Cephas, Mikhil Bamne, Vishwajit Nimgoankar University of Pittsburgh Medical Center , Western Psychiatric Institute and Clinic

The purpose of this experiment was to determine a way to extract DNA from whole blood, via transformation of lymphocytes with the Epstein - Barr Virus (EBV). Current techniques involve separating lymphocytes from whole blood, transforming them, and incubating them for at least two weeks. However, those techniques are expensive - using Ficoll-Hypaque, which separates Lymphocytes from blood - and time consuming. Our technique is designed to cut the time needed to immortalize the cells, thereby cutting costs, provide a viable protocol for extracting DNA from whole blood, and allow our research group to utilize DNA from older, rarer samples of blood. There are several benefits when retaining whole blood. One advantage is the availability of serum for use in other experiments. Our technique saves money, as we do not use Ficoll-Hypaque. The cells are also subjected to less chemical interference, reducing complications such as hemolysis.

36
Project Seed Program at Duquesne University
Jennifer Ann Aitken Duquesne University

Project seed is a program sponsored by the American Chemical Society that places economically disadvantaged high school students in a laboratory setting for 8 weeks during the summer. Funding to have this program take place at Duquesne University this summer was awarded by the American Chemical Society and several local donors, R. J. Lee Group Inc., Westinghouse, Duquesne University Bayer School of Natural and Environmental Science, PPG Industries and LabChem. Applications were solicited from area high schools and the best students were chosen based upon grade point average, teacher recommendations and a personal statement. These students were paired up with a Duquesne University faculty mentor and a graduate student supervisor. Each student conducted his or her own research project, interacted with other summer research students and participated is many enriching activities. A description of how to start a project seed program and the types of activities one can provide will be described in this poster.

37
Photodegration of Organics by Carbon Modified Titanium Dioxide Sample Under Visable Light Illumination
Kern B. Wilson, Jeffrey D. Evanseck and Shahed U.M. Khan, Department of Chemistry and Biochemistry, Center for Computational Sciences, Duquesne University

Cheaper and cleaner energy sources are absolutely necessary in the near future. At present, the accepted method used to harness energy from the sun produces an efficiency of about 2-3%. The problem is that only a small fraction of UV radiation is utilized from solar light. TiO 2 is known to be a promising photocatalyst, which can increase solar efficiency making it a viable and practical energy source. Carbon modified TiO 2 was prepared by adding 0.5M of tetrabutylammonium hydroxide drop wise to 50 ml 0.25M TiCl 4 solution at 0 o C.The precipitate obtained was aged for 7 days, dried and heated at 400 o C for 15 minutes. To investigate carbon modified TiO 2 as a solar catalysis, we mixed 10 ml of 2.5 x 10 -4 mol solution of phenol and a 0.01 g of modified TiO 2 . The mixture was illuminated at different intensities of light. By running UV-Visible light on the samples we determined whether TiO 2 generated better adsorption reading as compared to the modified TiO 2 . Ab inito calculations were used to model the geometry of the product obtained from the reaction of phenol with carbon modified TiO 2. Our results show that unwanted side reactions occur, and that a different organic substrate, 4-chlorophenol, is a better choice for testing the carbon modified TiO 2.

38
Synthesis of Thiolate-based Aza-bis(oxazoline) Catalyst SAMs on Gold and Theoretical Treatment of the Sulfur-Gold Surface Interaction
Osi Iyalomhe, Ellen S. Gawalt, Jeffrey D. Evanseck
Department of Chemistry and Biochemistry and Center for Computational Sciences, Duquesne University

An aza-bis(oxazoline) (Azabox) asymmetric pre-catalyst (bis[4,5-dihydro-(4 *S*)-(1-methylethyl)-1,3-oxazole-2-yl]-amine) has been synthesized. This catalyst, when coordinated with a Cu(II) center, is very useful in the asymmetric catalysis of important reactions such as the Diels-Alder and cyclopropanation of styrene. Diffuse Reflectance Infrared Spectroscopy (DRIFT) was used to examine gold substrates for adsorbates of 11-Mercaptoundecanoic acid (MUA). MUA has been coupled with the azabox structure to immobilize the catalyst on gold substrates.

Since the support possesses a sulfur headgroup, it is important to understand the nature of the sulfur-gold surface interaction. Density functional and second-order M Ø ller-Plesset perturbation theory calculations via ONIOM were carried out to investigate how SAMs of alkanethiols interact with gold substrates. Thiolates are preferred over thiols. Using Hartree-Fock and B3LYP (with the LANL2DZ basis set) methods, ethanethiol energy minimized to the bridge site, slightly off-centered towards the fcc/hcp site. Results from ONIOM calculations, edge-effect considerations, and multiple-layer effects are also used to describe the nature of the sulfur-gold surface interaction.

39
Adsorption rates for Ur lambda on Ymel
Patrick Grugan , Radu Moldovan
University of Pittsburgh

The dynamics of phage infection of bacteria are not well known. In order to infect a bacterium the phage must find a receptor on the surface of the bacterium cell and bind to it. The final step is the translocation of the phage DNA into the cell. Many factors can affect the binding, unbinding and DNA translocation of the phage. These factors include receptor density, temperature and concentration of polymers surrounding the bacteria and phages. In this study we look at the effects of temperature on the infection of Ur lambda on Ymel bacteria. In an earlier study it was seen that temperature did not affect the translocation rate for the wild type lambda on Ymel. In this study we suspect an effect of temperature since Ur lambda has extra appendages that help it to bind to the bacterium cell.

40

The Synthesis of Repeating Sequence Copolymers
Jeanita Pritchett ***,** Jim Copenhafer, and Dr. Tara Meyer. Chemistry Department of University of Pittsburgh , Pittsburgh PA

Inspired by Nature, we are preparing a series of polymers with a high degree of sequence control. These repeating sequence copolymers (RSC's) consist of alternating blocks of fluorene and methylene units. In contrast with classic block copolymers the blocks will be relatively short, n = 1-15, and monodisperse. The alkyl chains add flexibility to the rigid fluorene structure. The fluorene units add optical properties and a tendency to form liquid crystalline phases. These macromolecules are assembled using ADMET (acyclic diene metathesis), which has been proven to be useful in the synthesis of related polymers. Our primary interest is the investigation of the polymer properties as a function of both methylene and fluorene block lengths.

41
Investigation of the Potential Hybrid Origin of the "Sicklefin Redhorse"
Megan Ely, Christina Ventrice, Lisa Ludvico, and Brady Porter

The "sicklefin redhorse" (*Moxostoma sp.)* , a newly discovered fish from the Hiwassee and Little Tennessee River systems in SW North Carolina, is being considered for protected species status. The "sicklefin" has several intermediate morphological characteristics between *M. carinatum* and *M. breviceps* suggesting it may have been formed through hydrization between these two sympatric species. Taxonomic uncertainty has hindered the formal description of this species since its discovery in 1991. Previous experiments using mitochondrial gene sequences reject a recent hybrid origin for the "sicklefin redhorse" and suggest it either evolved cladogenically from *M. carinatum* or as a unidirectional reticulate species resulting from an ancestral hybridization event with *M. carinatum* as the maternal progenitor. The "sicklefin" could potentially be one of the first examples of a vertebrate reticulate species. The alternative hypotheses of its evolutionary origin are tested using nuclear DNA sequence data from an intron of Lactate Dehydrogenase (LDHA6).

42
Melatonin—The Drug to Suppress the Estrogen-Activated Tumors in Females?
Aksana Vasilyeva , Dr. Paula A. Witt-Enderby, Dr. Vicki Davis, and Byron Kohut, Division of Pharmaceutical Sciences, Duquesne University, Pittsburgh, PA

Estrogen is a known risk factor for breast cancer. It has been shown that in vivo

melatonin treatment downregulates estrogen receptor levels in breast cancer cells and blocks ER DNA binding. We hypothesize that melatonin may prevent breast cancer development by counteracting estrogen stimulation of breast tissue. Our study employed four groups of 2-month-old MMTV- *neu* mice treated with vehicle, estrogen, melatonin, and estrogen+melatonin. For 30 days, females were smeared daily to determine their estrous cycle stage; then, they were sacrificed in estrus. Melatonin receptor levels will be assessed in the dissected tissues by radioligand-binding assay to determine if the treatments modified melatonin receptor expression. Whole mounts will be prepared to examine the treatment effects on mammary gland structure. Other markers of tumor development will be investigated such as serum estradiol and progesterone levels and expression of ER, PR, and *neu* in the mammary gland. As expected, melatonin altered cycling. This suggests other hormone-responsive markers will be modified.

43

Molecular Dynamic Simulations of Carbonmonoxy myoglobin using the Generalized Born Continuum Model for Solvation

Leonardo I. J. Rabathaly , Patrice Pique and Jeffrey D. Evanseck, Center for Computational Sciences and Department of Chemistry and Biochemistry Duquesne University

Molecular dynamics of carbonmonoxy myoglobin (MbCO) is of particular interest because of its integral role in biochemical processes such as oxygen transport and storage. The fundamental goal of this study is to determine if MbCO dynamics can be replicated in a dielectric continuum. For this purpose, the CHARMM force field is used to explore the different MbCO conformational changes that occur in an aqueous environment, whether it be explicit or implicit. Generally, explicit water simulations are costly due to the number of solvent molecules. By contrast the Generalized Born model (GB) simulates effectively the electrostatic interactions of a polar solvent by use of an implicit continuum model that can replicate the dielectric properties of the solvent. Multiple 1ns trajectories of MbCO have been carried out using the Generalized Born Solvation model. A comparison of the captured dynamics with known experimental mutation, spectroscopic and kinetic data will be discussed.

44

Absorption Line Systems in Quasar Spectra

Nicholas Allen, Dr. David Turnshek University of Pittsburgh

Quasars are believed to be super massive black holes surrounded by accretion disks. Although they are the farthest objects in the known universe, they can illuminate foreground objects for further study via the absorption signature the objects leave behind in quasar spectra. Using various programs written by senior graduate student, Dan Nestor, we will process approximately 45,000 quasar spectra from the Sloan Digital Sky Survey. We will then use our clean sample to measure absorption line doublets caused by Mg II. These absorption line systems are caused by galaxies between observer and the quasar and can be used to derive gas properties within the galaxies, their distance, and give us a picture of the universe as it was billions of years ago. Our focus this summer is to study these lines to help better understand the formation and evolution of these intervening galaxies.

45

"Quasi-Elastic Neutrino Interaction Study"

Nichelle Madison, Dr. Donna Maples University of Pittsburgh

The Minerva Experiment is designed to study the scattering of neutrinos of energies less than 50 GeV. This experiment will be particularly useful for understanding the measurements of neutrino oscillation experiments, since there is little data available in this energy range. This summer, I will use a simulation of the Minerva detector to study the efficiency of reconstructing quasi-elastic neutrino interactions: muon neutrinos interacting weakly with neutrons inside of the detector, producing protons and muons. The efficiency is a measure of how well the detector can track and reconstruct the interactions which occur inside it. Several algorithms must be developed to use the geometry of the detector to reconstruct the paths, energies, momenta, etc of the outgoing particles. The efficiency of the detector will be measured by taking the ratio of the observed momenta of the reconstructed outgoing protons to the actual momenta of the outgoing protons of quasi-elastic interactions.

46

PAT Case Study: Effusivity and NIR of Tablets and Compacts

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Effusivity (Ws 1/2 /m 2 K) is a thermal property which dictates the interfacial temperature when two semi-infinite bodies meet 1 . All materials have specific effusivity values. This non-destructive analysis is used frequently on-line to determine the end point in blending analyses, where the end is characterized by minimal variation in an effusivity reading of several components. Here, we use this off-line testing method to analyze tablets and compacts. Theophylline tablets were manufactured using direct compaction and wet-granulation methods. They were evaluated with respect to hardness, concentration of API, and analysis of polymer coating. Results were compared with near-infrared data. Reflectance spectra and crushing strength were collected on a FOSS NIRSystems 5000 spectrometer and an Elizabeth-Hata, respectively. Results show a strong correlation between percent API and effusivity; however, the range of effusivity values of both tablets and compacts did not correspond to the range in the reference or NIR method values for hardness or theophylline content.

47

Effects of melatonin on the sub-cellular location of the proteins MEK, ERK, MEK-P, and ERK-P in human adult mesenchymal stem cells

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Department of Biological Sciences, Bayer School of Natural & Environmental Sciences 1
Division of Pharmaceutical Sciences, Mylan School of Pharmacy 2 Duquesne University

Previous experiments demonstrate that melatonin in an osteogenic medium enhances human Adult Mesenchymal Stem Cell (hAMSC) differentiation into osteoblasts when compared to osteogenic medium without melatonin. Differentiation occurs through a signal transduction pathway involving the two MAP kinases, MEK and ERK. The goal of these experiments was to determine the sub-cellular location of MEK, ERK, MEK-P, and ERK-P in hAMSC following a ten-day treatment with combinations of control medium, osteogenic medium, or melatonin (50nM). This was accomplished through immunohistochemical staining with antibodies specific to MEK, ERK, MEK-P, and ERK-P. Thus far, the different treatments show MEK to be found predominantly in the nucleus, ERK in the nucleus and cytosol, and ERK-P in the nucleus. The MEK-P immunostain is not detected. The experiment is being repeated and will complement Western blot experiments of fractioned cells.

48

Cellular Assessment of Calcium Aluminate Materials for Bone Tissue Engineering

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We are evaluating calcium aluminate-based (CA) materials for applications in bone tissue engineering. Results indicate that calcium aluminates are biocompatible with human MG-63 osteoblast-like cells, and human adult mesenchymal stem cells (hAMSC) in both dynamic and static culture conditions. Attachment, proliferation, and viability of MG-63 cells and hAMSC were assessed using the MTT assay and fluorescent stains including Live/Dead viability stain and DAPI nuclear stain. The viability of cells when attached to CA is above 90%, and cells readily proliferate when attached to the CA surface. We are also assessing differentiation of hAMSC on CA. Over the course of 14 days in an osteogenic supplement, differentiation is visible as indicated by alkaline phosphatase histochemical stain, a marker for osteoblast differentiation. Based on these studies, calcium aluminate-based materials may be an effective material for use in bone tissue engineering.

49

The Effects of PEG on the Absorption of Lamda by Ymel

Bernadette Douglas **,** Dr. Wu
University of Pittsburgh

Phages are viruses which only infect bacteria. This summer I am working with

lambda phages and the bacteria E. coli to determine how adding linear polymers affect the absorption of phages onto bacteria. The polymer which is used is Polyethylene Glycol (PEG). We found that PEG hinders the absorption of lambda phages. PEG may hinder absorption by causing the head of lambda to be attracted to the bacteria instead of the tail due to the depletion force. Another possibility for why it hinders absorption is that it causes the phage to bend, not allowing the phage to insert its DNA into the bacteria. PEG stops having a noticeable affect on absorption at approximately 0.1% weight/ volume.

50
Study of PDE Inpainting and Denoising Models
Monica Rothhaar, Dr. Stacey Levine
Duquesne University

In the rapidly evolving world of wireless communication and medical imaging, new technology is constantly being created and implemented to improve the accuracy of transmitted data. The restoration of such data is one of the many motivations for digital image inpainting, the filling in of missing information in an image, as well as denoising, the removal of unwanted static. Art restoration has been done for centuries, and though many of the same ideas are used, the human- eye subjective approach to image processing is not suitable for the precision and accuracy needed in the wireless and medical fields. Partial differential equations (PDEs) provide an automated, accurate, and objective analog to the ancient subjective approach. Suing PDEs to model the physical processes of diffusion and transport, regions of images can be recreated or denoised based on the surrounding information. A comparison and analysis of several such models will be completed, and will focus on factors such as CPU time and accuracy.

51
Behavioral Effects of Alarm Pheromone on Terrestrial Salamanders
Jessica Furnier, Dawn Foehr, Sarah Woodley Duquesne University , Department of Biological Sciences

Pheromones, detected by the vomeronasal organ of the nose, are chemical signals used by conspecifics to relay a wide spectrum of information ultimately influencing behavior and physiology. Many animals under stress emit defense secretions. Other studies have shown that these secretions can act as alarm pheromones, signaling a dangerous environment to conspecifics. *Plethodon shermani* , a terrestrial salamander, emits a white sticky substance when stressed. We hypothesized this secretion was acting as an alarm pheromone and tested the prediction that the salamanders would avoid a substrate saturated with alarm secretions. We tested animals' avoidance of substrates moistened with alarm secretion vs. distilled water. It was found that *P. shermani* avoided the alarm substrate. Additional trials will be done to further investigate causes of avoidance of alarm substrate.

52
Determination of Methyl mercury and Inorganic Mercury in Fish Tissue by Modified EPA Draft Method 3200
Stephen McHenry, G. M. Mizanur Rahman, Theodor G. Towns and, H. M. 'Skip' Kingston , Department of Chemistry and Biochemistry, Duquesne University

Mercury speciation analysis from environmental samples has been a field of growing interest. Such interest is mainly due to the toxicological impact, ecological problems, and biogeochemical cycling of mercury involving distribution, accumulation, transformation, and transport pathways in the natural environment. According to the United States Environmental Protection Agency (US EPA), the US Food and Drug Administration (US FDA), and the National Academy of Science (NAS), the consumption of mercury contaminated food poses serious health effects to people. Therefore, the purpose of this summer study was to determine the total mercury concentration as well as mercury species concentration from canned and raw fish tissue purchased from local fish markets (Pittsburgh , PA). In this study, fish tissues were extracted with modified EPA draft Method 3200 and analyzed with three different instruments: direct mercury analyzer-80 (DMA-80), inductively coupled plasma mass spectrometry (ICP-MS), and high performance liquid chromatography (HPLC) coupled with ICP-MS.

53
Detection of Courtship Pheromones by Terrestrial Salamanders
Dawn Foehr, Jessica Furnier, Sarah Woodley Duquesne University , Department

of Biological Sciences

During courtship, male salamanders (*Plethodon shermani*) apply secretions produced by a gland located under the chin to the nose of females. Purified gland extract as well as a major component of the gland extract, Plethodontid Receptivity Factor (PRF), increase female receptivity through detection by the vomeronasal organ (VNO) (Rollmann, et. al., 1999). We hypothesize that reproductive condition affects female sensitivity and response to courtship pheromones as well as PRF. An initial step was to adapt a method (Wirsig-Wiechmann, et. al., 2002) using agmatine, a small cation channel permeable molecule to identify and quantify sensory neurons of the VNO with receptors for courtship pheromone. Agmatine molecules permeate through opened non-selective cation channels in pheromone stimulated sensory neurons and can be detected through immunocytochemistry for agmatine. PRF is one of the few pheromones to be characterized in vertebrates, and this method should help in the understanding of pheromone processing in all vertebrates

54

A *DE NOVO* Engineered Antimicrobial Peptide Penetrates the Cytoplasmic Membrane of *P. aeruginosa*

Raynard Washington, Berthony Deslouches, Kazi Islam, Timothy A. Mietzner, and Ronald C. Montelaro
The University of Pittsburgh School of Medicine , Pittsburgh , Pennsylvania

Antimicrobial peptides are selective host-derived agents that have been intensely investigated as a potential source of new antimicrobials. However, because t here are several models explaining how antimicrobial peptides kill bacterial cells, the mechanism of action of a peptide can hardly be predicted. Our previous studies showed that WLBU-2, a lead antibacterial compound from *de novo* engineered multimers of a 12–residue peptide, has high antibacterial activity and the ability to perforate the cytoplasmic membrane of *P. aeruginosa.* To determine whether WLBU-2 penetrates bacterial cells and disrupts critical intracellular processes, we established by circular dichroism that physiological concentrations of NaCl and MgCl 2 have no effect on the propensity of WLBU-2 to form an a -helix. However, CaCl 2 decreased peptide helicity by 25%. Using confocal microscopy, we further demonstrated that Cy5-labeled WLBU-2 co-localized with GFP in *Pseudomonas* . We are currently investigating the interaction of WLBU-2 with bacterial DNA and its influence on replication.

55

Simulating Artificial Muscles

Brandon Redding, Dr. Steven P. Levitan University of Pittsburgh

Electroactive Polymers (EAPs) function as actuators and sensors and are attractive due to their low actuation voltage, fast response time, and durability. One of the most promising types of EAP is the Ionic Polymer Metal Composite (IPMC). Before this technology can be used in applications, a complete system model must be developed. This model will increase understanding of the system and accelerate the design process by reducing the need for prototyping. The goal of my research is to develop a dynamic model which accurately predicts the behavior of IPMCs under varying physical and chemical parameters. The model will lead to the development of a time-dependent simulation focusing on the relationship between deformation and force. A finite element analysis tool called FEMLab will be used for simulation. Simulation results will then be compared to experimental results from both a quantitative and qualitative standpoint.

56

Quasar Absortion Line Analysis

Daniel Owen, Advisors: Dr. Sandhya Rao, Dr. David Turnshek, University of Pittsburgh

Foot progression angles are one method of evaluating gait and a surgical procedure that improves patients' leg alignment, such as a tibial osteotomy, may affect the foot progression angle. In order to have accurate data that is comparable to other studies, review of the scientific literature found an accepted definition of the angle and a normative foot progression angle. Experimentally, reflective markers on bodily landmarks were tracked as eight tibial osteotomy patients walked along an instrumented walkway until three trials of kinematic data were collected via PEAK5 software, both pre-operatively and post-operatively. A MATLAB program written for this experiment included an anthropometric correction of the landmark locations to the accepted

normative sites. For each patient, averaged midstance angles were computed and a t-test was performed to test for statistical significance. Preliminary results suggested that a tibial osteotomy had no effect on the foot progression angle.

57
Sensing Biomolecules with Conjugated Polymers
Laura Anzaldi, Palwinder Kaur, Min Liu, and Dr. David H. Waldeck, University of Pittsburgh

Recent studies have announced that the fluorescence of conjugated polymers in the presence of particular biomolecules is quenched and that this characteristic can be harnessed to make biomolecular sensors. The purpose of this project is to compare two conjugated polymers, specifically a carboxylate polymer and a sulfonate polymer, as fluorescence sensors for certain biomolecules. This project explores how the two studied conjugated polymers are suited as biosensors and the mechanism of fluorescence quenching. Experimental studies investigate fluorescence quenching in the presence of different analytes such as methyl viologen, cytochrome c, and a 3rd generation dendrimer, the relative importance of static and dynamic quenching, and how ionic strength affects the polymer's biosensing capability.

58
Designing a Tutorial on Conductors and Insulators
Caitlin Holmes, Dr. Chandralekha Singh, University of Pittsburgh

The goal of physics education research is to identify sources of student difficulties in learning physics and to design and assess curricula and pedagogies that may significantly reduce the difficulties. This project focuses on the design of a tutorial to help students understand the operational differences between insulators and conductors. We will first attempt to identify the common difficulties and misconceptions held by students and create a tutorial that forces students to examine and correct these misunderstandings. The effectiveness of the tutorial will be measured by designing and administering a pretest and a posttest before and after the students use the tutorial. We will also interview a few students in depth using a think-aloud protocol to understand the rationale for their responses.

59
Self-Assembled Monolayers On Nickel
Sanora Olday, Dr. Ellen Gawalt Duquesne University

The purpose of this project is to develop self-assembled monolayers on Nickel with different acids and using different methods. Two methods were used, the Dipping Method and the Spraying Method. The Dipping Method is accomplished by placing Nickel substrates in 3mM THF solutions of the solution of the organic acid. The Spray Method involves the 3mM spraying on the solution Nickel and placing in the oven to dry. The three acids were Bromodoecanoic Acid, Aminododecanoic Acid, and Steric Acid. Using the FRIT, the conformation of the alkyl chain is studied. A peak in the IR spectrum at 2911 cm -1 for Aminododecanoic Acid, 2911 cm -1 for Bromododecanoic Acid, and 2917 cm -1 was assigned to the CH 2 anti-symmetric of the CH 2 Group. This stretching frequency indicates that the methylene groups are in an all-trans conformation. For Spraying Method, peaks were found at 2916 cm -1 for Aminododecanoic Acid. No C-H anti-symmetric stretch was observed for Stearic Acid indicating that it had not adhered to the surface.

60
Determining Affinity of DNA Binding Agent by a Restriction Exonuclease Protection Assay
Timothy R. McFadden and Steven M. Firestine. Duquesne University , Project SEED

The goal of my research is to determine how effective different compounds are at binding to double stranded DNA. To do this, a restriction exonuclease protection assay is employed. In this assay, specific concentrations of the compound are incubated with DNA and digested by a restriction enzyme. If the drug binds to the DNA effectively, it will prohibit the restriction enzyme from cleaving the DNA strand. After digestion occurs, electrophoresis is employed to determine how much of the DNA is cleaved by the enzyme. The gel is analyzed

to determine what percentage of the DNA remained uncut and the higher the percent of uncut DNA, the more effective that drug is at binding to DNA. We have analyzed two compounds for their binding to linear plasmid DNA, pUC19. Compound **1** displayed a K of 3.3x10 6 M -1 , close to the previously measured value. Compound **2** is currently under investigation.

61
Does black cohosh accelerate tumor metastasis via regulation of prostaglandin levels?
Erica Sparkenbaugh, PI: Dr. Vicki Davis Department of Pharmacology and Toxicology, Duquesne University

Since black cohosh is a natural supplement for reducing menopausal symptoms, many women believe it is safer than hormone replacement therapy regarding breast cancer risk. However, MMTV- *neu* mice treated with black cohosh had an increase in mammary tumor metastases compared to untreated mice. Since increased prostaglandin levels have been linked to metastatic disease, we will determine if levels of PGE 2 in mammary and tumor tissue of mice treated with black cohosh are increased compared with untreated mice. PGE 2 levels will be determined using a PGE 2 immunoassay designed for testing PGE 2 levels in serum, optimized for mammary and tumor tissue. PGE 2 levels will be normalized to total protein level. Increased levels of PGE 2 in mammary and tumor tissue are expected from the black cohosh treated mice. This study will determine if black cohosh increases mammary tumor metastasis by increasing PGE 2 levels. If so, women may be able take Cox-2 inhibitors with black cohosh to counteract this adverse effect.

62
ß-Galactosidase ELISA of ERIN mice in determining estrogen's effect on cataracts
Katie Couture, PI: Dr. Vicki Davis Duquesne University

Estrogen influences many tissues in both males and females, including the eye. Estrogen is thought to protect the eye against age-related cataracts, possibly through direct interactions with its receptors in the eye. In this study, a mouse model is used to detect the locations of functional estrogen receptors (ER) in the eye. My work on this study focuses on transgenic indicator mice (ERIN) that have an incorporated estrogen promoter linked to the reporter gene beta-galactosidase (ß-gal). The levels of ß-gal expressed in the eye will be examined using a ß-gal ELISA (enzyme linked immunosorbent assay) kit. Estrogen stimulation of ß-gal levels will determine which tissues in the eye (i.e., lens, cornea, retina) are able to directly respond to estrogen. These studies will then be expanded to examine ?-gal expression in bitransgenic mice with aberrant ER expression. These studies will help in our goal to understand the protective effect of estrogen in the aging eye.

63
Isolation and characterization of vitellogenin in two North American salamander species, Ambystoma tigrinum and Cryptobranchus alleganiensis
Lisa Mangus, Dr. Kyle Selcer, Duquesne University

Vitellogenin is the egg yolk precursor protein produced by the liver of female oviparous vertebrates under estrogen stimulation. Previous work has shown that vitellogenin can be used as a biomarker for exposure of animals to environmental estrogens, which are chemical agents capable of disrupting endocrine pathways. These compounds may have deleterious effects on humans and wildlife. Our lab has been developing assays to detect the vitellogenin protein and hepatic mRNA in various aquatic vertebrates after stimulation by estrogen and estrogenic agents. In this study, we have successfully isolated and characterized the vitellogenins of two North American salamanders, the tiger salamander (Ambystoma tigrinum), and the hellbender (Cryptobranchus alleganiensis). The protein was analyzed using SDS-PAGE and DEAE chromatography, followed by N-terminal sequencing. The resulting sequences showed significant homology with the known vitellogenin sequence of Xenopus laevis (African clawed frog). An RT-PCR assay was conducted with female and estrogen-treated male salamanders using degenerate primers designed from known vitellogenin cDNA sequences of various amphibian and fish species. The cDNA obtained from these reactions was sequenced, compared to the known Xenopus laevis (African clawed frog) vitellogenin sequence, and found to have strong homology.

64
Organelles Effecting Gap Junction Morphology
Leon S. Sanders III, Beth Nickel, Dr. Sandra A. Murray Department of Cell Biology and Physiology, University of Pittsburgh , School of Medicine Pittsburgh , PA

Our interest is in the mechanisms by which gap junctions are assembled and degraded. We used three different imaging techniques (time-lapse video microscopy, immunocytochemistry and transmission electron microscopy) to assess gap junction plaque dynamics. Gap junction plaque assembly, internalization and interaction with cytoplasmic structures were analyzed in adrenal cortical cells transfected with a cDNA encoding a green fluorescent protein tagged connexin 43 construct (Cx43-GFP). On several occasions gap junction plaques fragmented into smaller gap junction plaques that remained at the cell surface or resolved to make a larger plaque. We observed gap junction plaques being internalized into the cytoplasm of one cell to form what we believe is an annular gap junction. Spherical cytoplasmic organelles were seen associating with gap junctions, sometimes causing a change in the gap junction. Some of the annular gap junction associated structures were identified as lysosomes, lipid vesicles and early endosomes. Actin filaments were observed associating with both gap junction plaques and annulars. Associations between lysosomes and annular gap junctions support speculations that annular gap junctions are degraded by lysosomes, and may play a role in gap junction protein turnover.

65 Direct Free Radical Comination Synthesis of Tetraaryldiboron Organics
Joseph E. Winans, Glenn C. Schott Jr., and Dr. T.J. Weismann Duquesne University, Department of Chemistry & Biochemistry; Crompton Corporation

Attempts to prepare symmetrical tetraaryldiboron organic compounds have failed owing to the instability of intermediates in the synthesis process. We have encountered success in producing the desired products via recombination of highly reactive radical intermediates produced from diarylboron halides and sodium-potassium alloys. The details of the synthetic process are described along with the results of configurational studies and theoretical predictions of orientations of the product molecules. The tetraarylborons are chemically significant in shedding light on the nature of the bond between the two boron atoms – i.e. single or double bond. Isolation of crystalline product and successful x-ray determination and interpretation are presented.

66
Regulation of Glycerophosphoinositol Production in *Saccharomyces*
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Phosphatidylinositol (PI) is a critical membrane component of the yeast *Saccharomyces cerevisiae* . Not only doe PI act as a precursor to several other phospholipids, but it also can be deacylated to form extracellular glycerophosphoinositol (GroPIns). The production of extracellular GroPIns is a major catabolic pathway in *S. cerevisiae* , accounting for approximately fifty percent of the phosphorus and inositol lost from PI during its growth in rich medium[1]. Extracellular CroPIns production is proposed to be the result of the activity of phospholipases localized in the plasma membrane and/or periplasmic space 2,3 . We have examined the effect of inositol and phosphate availability on the production of GroPIns and other inositol-containing compounds. Preliminary results indicate that a wild type strain produces the most the most GroPIns when grown in high phosphate, inositol-containing medium. Some strains bearing deletion mutations in genes known to regulate phospholipid or phosphate metabolism exhibit an aberrant pattern of GroPIns production.

67
Purification and characterization of SilE
James M. Irwin, Dr. Charles Dameron Duquesne University

Silver compounds are often used in burn wards and hospitals as antimicrobials to help treat patients; however some pathogens have developed a resistance towards silver. Silver resistant pathogens have caused the deaths of many burn victims and even been responsible for the closing of some hospital wards. In order to study this problem a closer look has been taken at the Ag(I) –resistant gene cluster known as Sil. This cluster contains a total of nine genes. In this study, the protein encoded by the first gene, SilE, was investigated because of

its proposed role in the binding of multiple metal ions and in their transportation to a silver ATPase. My goal is to isolate the SilE protein and attempt to characterize its physical and metal binding properties. My goal co-insides with the overall project goal, which is to understand the mechanism of the Sil system and eventually find a way to circumvent its silver resistance.

68 Developing Chemical Crosslinking and Mass Spectrometry for Large Protein Structure Determination

Jean E Schneider, Guangyu Zhu, Brianne S Raccor, Billy W Day University of Pittsburgh Department of Pharmaceutical Sciences

Dynein heavy chain (HC) is a 530 kDa subunit of the microtubule-associated, motor protein dynein. Dynein HC is a potential cancer target because of its vital role in the cell cycle, yet little is known about its structure. While the amino acid sequence of dynein HC has been determined, an understanding of the spatial configuration of the peptide backbone is lacking. However, the size of dynein makes traditional methods for tertiary structure determination impractical. Recent studies have demonstrated an alternate method based on amino acid specific cross-linking and mass spectrometry. A chemical cross-linking reagent features dual lysine reactivity and covalently binds to primary amines separated by 5-10A. After cross-linking the protein is digested and peptide fragments are purified and sequenced by liquid chromatography mass spectrometry (LC-MS). The distance constraints between lysine residues provide initial parameters for computational structure determination.

69

Contralateral Compensation in Stair Climbing After Unilateral Ankle Arthroplasty

Scott Kramer, Mark C. Miller, Derek Dazen Virginia Tech and Duquesne University

Performance of stair climbing after total ankle arthroplasty is an important measure of patients' abilities. Fourteen patients wearing low cut shoes ascended and descended a set of four steps one year after unilateral ankle arthroplasty with a semi-constrained system. The functional range of motion (ROM) at the knee and ankle were computed by gathering kinematic data via PEAK5 motion analysis system. The angle between the foot and direction of motion (progression angle) was calculated by inputting the kinematic data in a MATLAB program specifically written for this experiment. Progression angle measures the compensation achieved by external rotation of the foot. After three trials of data were collected for each patient, looking at both operated and un-operated sides, results suggested that increased knee flexion compensated for loss of ankle movement during ascent, while an increase in progression angle was used to compensate in descent. Patients' contralateral abilities may be necessary for a successful total ankle arthroplasty.

70

Synthetic Studies Toward the Generation of Deoxystreptazolin Derivatives

Mary B. Martucci, Dr. Kay Brummond, Dr. Donald Probst, University of Pittsburgh

Streptazolin is a natural product with anti-biotic and anti-fungal activity, and various derivatives have been synthesized which show increased activity. Our research focuses on developing a rapid synthesis of deoxystreptazolin derivatives. This strategy centers around the selective addition of an allyl borane to an aldehyde followed by a Rhodium-catalyzed cyclization to generate the core structure of deoxystreptazolin. This core can then be derivatized to numerous deoxystreptazolin analogues.

71

Analysis of the NSF REU Chemistry Applicant Pool: What is the Demand for Undergraduate Research?

Devin Coon, Joseph J. Grabowski Department of Chemistry, University of Pittsburgh

On behalf of the NSF's REU Leadership Group in Chemistry, we have gathered aggregate information on applicants to Chemistry REU sites for three different years (2001, 2003-04). The focus of our project is to analyze these statistics to gain insight into the demands and needs for summer REU positions (i.e., a "demand survey"). Among the issues we are analyzing the data for are similarities and differences between applicants from Research Intensive

Institutions (RIIs) and Primarily Undergraduate Institutions (PUIs), how broadly students apply, and whether offers are made to the same small fraction of applicants. In addition to collecting "short form" data from the majority of sites, more extensive demographic data was collected from a small number of sites for a detailed look at a portion of the applicant pool. We anticipate that our analysis can be used by the NSF as they allocate their limited resources among their many programs.

72

Testing the New Long-Range Model for Membrane Protein Folding

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Understanding the folding process of membrane proteins is a fundamental biomedical challenge that has lagged behind that of soluble proteins due to the hydrophobic nature of the membrane proteins. The shape a protein takes after undergoing the folding process determines the function of the protein. A new model for membrane protein folding has been proposed that states that long-range interactions between amino acids from both loop and transmembrane helices take place during the very early stages of folding, before and during the formation of helices. To test this model, we use a computational method to predict protein folding nuclei from native state structures that is based on a constraint network model of freely rotating rods. This method uses an all-atomic analysis of the rigidity and flexibility of protein structures, which includes specific hydrophobic, polar and charged interactions. The objective is to test the validity of the new model.

73

Modeling Transcription Factor Binding Sites with Dependencies

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Protein-DNA binding is essential to transcriptional control, a key mechanism of the gene expression regulation. In general, computational models have the potential to efficiently model transcription factor binding sites (TFBSs), though the complexity of the interactions in some cases pose a major challenge. Basic models consider each position of a TFBS to contribute independently to protein binding. This project looks into modeling dependencies between positions in the TFBS. The use of mutual information content will elicit dependencies between different positions in a collection of binding sites for a given transcription factor. The significance of these values is determined by comparing known MIC values to a distribution of semi-randomly generated values. Scoring methods will be used considering dinucleotide and trinucleotide dependencies as well as independent positions to create a more accurate TFBS model. Finally, the accuracy of these models are tested compared to strictly independent models.

74

Stochasticity in NF-?B Regulation

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The nuclear factor ?B (NF-?B) family of transcription factors is important in the expression of many genes, including several involved in the immune response. A model was recently proposed that approximates this pathway using ordinary differential equations. The basic processes included in that model are those of NF-?B and its activator, I?B (IKK), as well as its inhibitors, A20 and I?Ba. Because this model uses ordinary differential equations, there is no inclusion of noise and fluctuations which often have great effects on biological systems. We

converted the ordinary differential equations into stochastic differential equations, allowing us to study the possible implications of noise on the deterministic model by analyzing the qualitative differences in the dynamics of the system.

75
Weighted Probability in Absolute Entropy Calculation of a Lattice Model
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The absolute free energy, F, is a criterion of stability, thus calculating F is mandatory for defining the native structure of a protein. F=E-TS, where E is the average energy, T is the absolute temperature and S is the absolute entropy. In simulations it is easy to calculate E but very difficult to obtain S, hence F. A new method for calculating S suggested recently by Meirovitch's group is tested as applied to a self-avoiding-walk on a square lattice, which constitutes a simplified model for a denatured protein. Understanding protein folding is essential for future applications of molecular medicine and disease research.

76
Solvent entropy estimation at the nanosecond timescale in molecular dynamics simulations
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Solvent entropy is recognized as the driving force of protein folding, and we propose that native folds are the ones that maximize solvent entropy. Quantitative descriptions of this process have been proposed, but current experimental methods do not have the detail or speed to probe the exact changes in solvent entropy during folding. This project uses the molecular dynamics program CHARMM to simulate polypeptides solvated by explicit water. An index of solvent entropy is monitored over the course of the simulation. This project is a test bed for developing more atom-realistic quantitative solvent-entropy simulations. Validation of this method can be used to develop new folding simulations driven by solvent entropy. Such accurate simulations can ultimately lead to protein structure prediction from amino acid sequence alone.

77
Homology Modelling of Melatonin Receptors
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G-protein coupled receptors (GPCRs) are targets for 50% of all existing medications, and are thought to be in equilibrium between an active and inactive state. GPCRs are characterized by the presence of seven transmembrane helices composed of hydrophobic sequences; however, the actual sequence identities vary greatly. The melatonin receptors, specifically the MT1 and MT2 receptors, are of particular interest because their structures have not yet been determined. MOE and Modeller were used to both align the sequences with a template sequence, bovine rhodopsin, and then create a model using its structure. Two specific motifs of the melatonin receptor are of interest: the "aromatic cluster" motif and the "N(P)XXY" motif in transmembrane 7, both of which are found in GPCRs. Similarities and contrasts between GPCRs/Melatonin and Modeller/MOE will be presented.

78
An Efficient Monte Carlo Algorithm for Simulating Michaelis-Menten Enzyme Kinetics

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Many reactions in biochemical networks involve enzymatic catalysis, and can be described by standard Michaelis-Menten kinetics. Numerical simulation of the underlying mechanism can be inefficient with either continuous or Monte Carlo algorithms, because of unmatched timescales (stiffness) of the rates involved. Often, the rate of enzyme-substrate dissociation is much higher than the rate of product creation. In this study, removal of the explicitly simulated reversible intermediate was investigated, in order to reduce stiffness and allow for longer timesteps. Reaction rates were adjusted to compensate for lack of the reversible step. Monte Carlo simulations of traditional Michaelis-Menten kinetics were compared to simulations using the new algorithm over a range of timesteps. The results demonstrate the correctness and increased simulation efficiency of the new algorithm, which ultimately may be incorporated into simulation programs such as MCell.

79

The Effect of Non-uniform Acetylcholine Receptor Distribution in Neuromuscular Junctional Folds

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Neurotransmission is the main communicative process in the body, making it an interesting and important area of research. In the vertebrate neuromuscular junction (NMJ), miniature endplate currents (mEPCs) are produced when acetylcholine binds to postsynaptic receptor channels (AChRs) leading to channel opening. Minis exhibit a first-order exponential decay when acetylcholinesterase is inhibited; we hypothesized that this results from a combination of tortuous diffusion space and non-uniform postjunctional fold AChR distribution. This hypothesis was then tested using a large scale 3-D reconstruction and MCell simulations. A preexisting model of the NMJ with constant AChR densities was modified; the top of the folds were populated with AChRs at 7-10,000 µm 2 and the bottom was left unpopulated. Minis were simulated, and the shape of the decay phase and the variability in mEPC decay time were analyzed. Consistent with our hypothesis, an increase in first order decay phase characteristics were seen.

80

The Role of Backbone Flexibility in Protein-Protein Docking

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Protein-protein docking is one of the great modern challenges for computational biology. The Critical Assessment of Protein Interactions (CAPRI), hosted by the European Bionformatics Institute, has encouraged the community to develop methods for predicting these interactions. Current methods rely on the assumption that a protein is a rigid body. These algorithms do not perform well, especially if the protein undergoes induced fit upon binding. We propose that the use of the Gaussian Network Model can systematically identify regions of flexibility that play a role in induced fit. We shall attempt to show that the Anisotropic Network Model can generate conformations that can be used as rigid bodies in the standard protein docking protocols.

81

Computational Quantitative Structure-Activity Relationship Analyses and Docking to Tubulin of Discodermolide, Dictyostatin-1 and Synthetic Analogues

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The stabilization of microtubules leads to cell apoptosis. Therefore, microtubule stabilizers make good anticancer agents. Computational molecular models of the microtubule stabilizers dictyostatin-1, discodermolide and synthetic analogues of each were built with the Cerius 2 molecular modeling suite and analyzed for low energy conformers with the Merck Molecular Force Field. A receptor model was then generated using the superimposed structures weighted by their respective biological activities. Grid point interaction energies were calculated from the receptor model. Additional shape, electronic, and thermodynamic descriptors were calculated from the models, and the genetic function approximation was used to generate quantitative structure-activity relationship equations. The GOLD algorithm was used to dock the models to a model of the ??-tubulin heterodimer built from coordinates determined by high-resolution cryoelectron microscopy. Energetics of the different orientations within the binding site were calculated. Docking statistics were used with biological activity values in order to form a quantitative relationship.

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Characterization of Human APE/Ref-1 Protein Family

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The human APE/Ref-1 protein family is important for DNA repair rand regulation of gene transcription. 124 sequences were identified as belonging to family using the superfamily annotation of the iProClass protein database. The sequences ranged from 300 – 600 amino acids in length. An initial multiple sequence alignment was created with the T-COFFEE program and refined using the results of a MEME analysis on the unaligned sequences. This refined alignment serves as the starting point for an extensive analysis of the enzyme superfamily as well as the organization of and differences among its subfamilies. A phylogenetic analysis and a SeqSpace analysis followed to define these subfamilies and their members' sequences. The subfamilies were analyzed for their distinctive features. These features were then mapped onto a 3D structure to see how the structures differ amongst subfamilies.

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Exploring Sub-optimal Sequence Alignments and Scoring Functions for Comparative Protein Structural Modeling

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As structural genomics initiatives gain momentum within the structure

determination community, comparative modeling of protein structures will grow both more common and more useful in informing further experimental design. A major challenge in this model construction remains the sequence alignment between the target sequence to be modeled and the template sequence upon which the model will be based. We performed comparative modeling based on sub-optimal sequence alignments between CASP5 target sequences and structural templates of 15-30% sequence identity. Ensembles of 100-500 models per target were produced and scored using a statistical potential function, after which poorly aligned loop regions of the best-scoring model were refined using *ab initio* protein folding simulations. We find that models produced through our procedure are often more accurate than those constructed from a T-coffee alignment, although our scoring process appears unable to identify the absolute best model from the ensemble.

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Application of Hydrogen Bond Analysis Techniques to Protein-Sugar Interactions

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Hydrogen bonding is an electrostatic interaction that is responsible for a wide variety of molecular properties. Hydrogen bonding is especially important in protein chemistry, as these interactions play a pivotal role in the determination of protein structure and binding specificity. The objective of this research project is to study the binding of b (1 à 4)-linked *N* -acetyl glucosamine (GlcNAc) homopolysaccharides to a chitinase-like lectin, human cartilage glycoprotein (HCGP39), a protein involved in connective tissue remodeling processes which is often overexpressed in certain types of breast and colon cancer. Through molecular docking and subsequent geometric hydrogen bond analysis and binding studies, in sight into the binding mechanism of HCGP39 and other Family 18 chitinases will be gained, and these results will be presented and discussed.

85

Heterogeneity in Acetylcholine Receptor Kinetics in MCell Simulations: Achieving Known Variability in mEPC Decay

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Vesicular release of acetylcholine (ACh) at the neuromuscular junction (NMJ) produces miniature endplate currents (mEPCs) as ACh binds to ACh receptors (AChRs). In previous MCell (Monte Carlo simulation program) simulations the observed variability of mEPC decay times was much less than experimental results, despite use of detailed cleft topology and acetylcholinesterase distribution. Thus, we hypothesize that different gating kinetics from one AChR to another may explain the experimental variability. The rates for AChR opening and closing were varied based on the known range of mEPC decay times, and then the fractional amounts of the different AChRs were varied in the postsynaptic membrane according to a Gaussian distribution. Under these conditions, simulations still could not reproduce the experimental variability in mEPC decay time, suggesting that spatial segregation of AChRs with different gating properties may also be required.

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Studies of the Hydrosilation Reactions of Diallyltrifluoroacetamide with Alkyl and Fluoroalkyl Silanes

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Studies were performed on the hydrosilation reactions of *N,N* -diallyl-2,2,2-trifluoroacetamide with chloroplatinic acid using various highly fluorinated silanes to improve the yield of the desired *bis* -[*tris* -(perfluoroalkylethyl)silyl

propyl] trifluoroacetamides. Model studies were undertaken with non-fluorous silanes to optimize reaction conditions. The results of these studies were then applied to produce compounds of the general structure (R 3 Si(CH 2) 3) 2 NCOCF 3 in which R = CH 2 CH 2 C 6 F 13 or CH 2 CH 2 C 8 F 17 . The compounds were analyzed by GC, NMR and EI-MS. These compounds have applications as effective electron spray mass spectroscopy calibration standards. Attributes include a large mass range (100-3000 Da), evenly and regularly spaced fragments, and volatility .

87

New Free-Amine Polymers and Uses in Tissue Engineering

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Although the use of biodegradable polymers such as Poly(caprolactone), Poly (lactic acid-co-glycolic acid) and Poly(lactic acid-co-lysine) in tissue engineering is not a new concept, their effectiveness is limited. As an alternative approach, the synthesis of a biodegradable, free amine-containing polymer to which essential cell-growth factors can be attached, has come to the forefront. Two similar polymers, identical with the exception of their respective protecting groups, tert-butoxycarbonyl and carbobenzyloxy, are studied within. Following the addition of the amine-protecting group, both compounds undergo the same reaction process through to polymerization. These similar polymers can then be deprotected to yield the identical free amine-containing polymer. This polymer may be studied for future use with the incorporation of amino acid sequences known to target specific cellular receptors associated with cell growth and tissue formation.

Abstracts will become available the week of July 27th

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