

*COLLEGE OF THE HOLY CROSS*

**Eighth Annual  
Undergraduate  
Summer  
Research  
Symposium**

September 7, 2001  
Swords Atrium  
2:00 - 4:00 pm



Sponsored by

Richard B. Fisher Research Fellowship

*Members of the College of the Holy Cross Community,*

*We welcome you to the 2001 Undergraduate Summer Research Symposium. Now in its eighth year, the Undergraduate Summer Research Symposium is a College-wide event that brings together faculty and students from all of the disciplines at Holy Cross. The Undergraduate Summer Research Symposium allows students the opportunity to celebrate their own, friends' and colleagues' accomplishments. In addition, it provides an opportunity for students to discuss the possibility of conducting research with a faculty member during the upcoming year. We hope you enjoy the impressive collection of research brought together here.*

*Professor Madeline Vargas  
Professor Timothy Roach.  
2001 USRS Organizing Committee*

Posters

1. **ASSAY FOR NOVEL POLYGLUTAMINE EXPANSIONS; THE SEARCH FOR NEW ATAXIA GENES**, *Amy Vashlishan, Lippard Center for Clinical Investigation, Dept. of Neurology, Yale University School of Medicine, New Haven, CT.*
2. **“MINI DISSOLUTION”: ASSESSING THE IMPACT OF KEY PARAMETERS ON LOW VOLUME DISSOLUTION TESTING**, *H. O’Donnell (1), D. Roberts (2), B. Nickerson (2), G. Steeno (3), College of the Holy Cross, Worcester, MA, Pfizer Global R&D, AR&D, Groton, CT, Pfizer Global R&D, GNS, Groton, CT.*
3. **EFFECTS OF IN VITRO AND IN VIVO ETHANOL ON THE BINDING OF 3H-PK 11195 TO THE PERIPHERAL BENZODIAZEPINE RECEPTOR IN RAT BRAIN**, *Michelle Tangredi, Department of Biology, College of the Holy Cross.*
4. **ADHESION MOLECULE EXPRESSION ON PERIPHERAL BLOOD NEUTROPHILS MAY PREDICT THE ONSET OF ARDS IN PATIENTS WITH MAJOR TRAUMA**, *L. Manzo, College of the Holy Cross, R. Thrall, Ph.D., UCONN Health Center, K. Keating, MD, Hartford Hospital.*
5. **ANXIETY ASSOCIATED WITH ALCOHOL WITHDRAWAL IS BLOCKED BY ADMINISTRATION OF PK 11195, A PERIPHERAL BENZODIAZEPINE RECEPTOR MIXED AGONIST**, *Rebecca A. Smith, Department of Psychology, College of the Holy Cross.*
6. **EFFECTS OF ESTRADIOL BENZOATE ON A DELAYED NON-MATCHING TO SAMPLE SPATIAL WORKING MEMORY IN OVARIECTOMIZED MICE**, *Olivia T. Vo and Tanya L. Barros, Department of Psychology, College of the Holy Cross.*
7. **THE EFFECTS OF SELECTIVE ACTIVATION OF THE ESTROGEN RECEPTOR (ER-) ON SPATIAL WORKING MEMORY IN THE OVARIECTOMIZED RAT**, *Melissa J. Lin, Stephanie Galica, and Kimberly Hewitt Department of Psychology, College of the Holy Cross.*
8. **FRUIT FLIES AS A BIOASSAY IN COMBINATORIAL CHEMISTRY OF ESTERS**, *Patrick S. Twomey, Department of Chemistry, College of the Holy Cross.*
9. **FREE RADICAL HALOGENATION @ A DISCOVERY LAB EXPLORATION**, *J. Rieger and Prof. Ronald M. Jarret, Department of Chemistry, College of the Holy Cross.*
10. **MIMICKING A MOTION ILLUSION: A COMPUTATIONAL MODEL OF HUMAN HEADING PERCEPTION**, *Daniel Conti and Constance S. Royden, Department of Mathematics and Computer Science, College of the Holy Cross.*
11. **BIOCHEMICAL CHARACTERIZATION AND PARTIAL PURIFICATION OF FE(III) REDUCTASE ACTIVITY IN CAMPYLOBACTER JEJUNI**, *Nicholas Guzewicz and Dr. Madeline Vargas, Department of Biology, College of the Holy Cross.*
12. **ONCOGENIC POTENTIAL OF KAPOSII’S SARCOMA-ASSOCIATED HERPESVIRUS K15 MAY BE STUDIED IN COMPARISON TO EPSTEIN-BARR VIRUS LMP2A AND HVS TIP BY THE FORMATION OF A RECOMBINANT VIRUS**, *D. Davignon, Dr. Joong-Kook Choi and Dr. Jae U. Jung, New England Regional Primate Research Center, Harvard Medical School.*
13. **PREPARATION OF RHENIUM COMPLEXES VIA A SCHIFF BASE LIGAND**, *I. Wrona and Prof. R.S. Herrick, Department of Chemistry, College of the Holy Cross.*

## ASSAY FOR NOVEL POLYGLUTAMINE EXPANSIONS; THE SEARCH FOR NEW ATAXIA GENES

*Amy B. Vashlishan*

*Lippard Center for Clinical Investigation, Dept. of Neurology  
Yale University School of Medicine, New Haven, CT*

14. **PREPARATIONS FOR LASER COOLING OF RB ATOMS USING STABILIZED DIODE LASERS AND A MAGNETO-OPTIC TRAP**, *Peter Harris and Dr. Timothy Roach, Department of Physics, College of the Holy Cross.*
15. **UNDERSTANDING THE WATER/ACETONITRILE INTERFACE USING MOLECULAR DYNAMICS SIMULATIONS**, *Dan Kirchoff and Ramona Taylor, Department of Chemistry, College of the Holy Cross.*
16. **ON THE MEASUREMENTS OF SMALL AMPLITUDE SIDE-BRANCH SPACING AT THE DENDRITE TIP**, *S.L. DeChiaro, K.A. Gormley and M.B. Koss, Department of Physics, College of the Holy Cross.*
17. **SUBSTRATE-INDUCED RESPIRATION FOR DETERMINING EUKARYOTE:PROKARYOTE RATIOS IN SOILS**, *B.G. DeGasperis, C. Rice and E. Brennan, Kansas State University, Manhattan, KS.*
18. **IONIZATION STATES OF ATOMS IN AN ASTROPHYSICAL PLASMA**, *Carolyn M. Berger, Professor Randy Ross, Department of Physics, College of the Holy Cross.*
19. **MOLECULAR DYNAMICS INVESTIGATIONS OF ETHANOL VIA AQUEOUS ETHANOL SOLUTIONS**, *Ethan Stewart, Roseanne Shields, and Prof. Ramona Taylor, Department of Chemistry, College of the Holy Cross.*
20. **CALCULATING THE THERMAL FIELD SURROUNDING DENDRITES**, *John T. Giblin, Jr. and Matthew B. Koss, Department of Physics, College of the Holy Cross.*
21. **QUANTUM SCATTERING IN TWO DIMENSIONS**, *John T. Giblin, Jr. Bradley Schuller and Dr. Janine Shertzer Department of Physics, College of the Holy Cross.*
22. **ALKENE SYNTHESIS IN THE ORGANIC CHEMISTRY LABORATORY**, *James Conley and Prof. Ronald Jarret Ph.D., Department of Chemistry, College of the Holy Cross.*

Polyglutamine expansions are expanded runs of the amino acid glutamine in a transcribed protein, which result from repeats of the nucleotide triplet CAG in messenger RNA. By an unknown mechanism thought to involve gain of function or toxicity of the mutated protein, these expansions of glutamine tracks cause neurodegeneration. Polyglutamine repeats are responsible for several types of inherited neurodegenerative diseases including Huntington's disease (HD), Myotonic Dystrophy, and several forms of ataxias. Spinocerebellar Ataxia (SCA) is a group of such diseases that have been linked to 15 different loci in the human genome. Seven genes for different types of SCAs have been identified, all of which are genes encoding polyglutamine expansions. The patients in this study have tested negative for all known SCA/polyglutamine expansion genes. By isolating proteins from patients' blood samples and Western blotting with an antibody that recognizes polyglutamine expansions, I sought to determine if these families have a novel polyglutamine expansion. Failure of this monoclonal antibody, mAb1C2, to bind to any proteins in the patient blood samples indicates that the tested patients have no polyglutamine repeats detectable by this assay. Analysis of the same patients at the DNA level is being undertaken as a basis of comparison and confirmation of these results.

**“Mini Dissolution”: Assessing the Impact of Key Parameters on Low Volume Dissolution Testing**

*H. O'Donnell (1), D. Roberts (2), B. Nickerson (2), G. Steeno (3)*  
*College of the Holy Cross, Worcester, MA*  
*Pfizer Global R&D, AR&D, Groton, CT*  
*Pfizer Global R&D, GNS, Groton, CT*

Dissolution is a common analytical procedure used in the pharmaceutical industry to assess solid dosage form properties. The extent and rate that a tablet dissolves in a given medium is measured. The medium is chosen based on properties of the drug and formulation. (solubility, stability, immediate vs. extended release, etc.)

During the development of Compound X, small volume dissolution was used for some of the clinical formulations. The low volume vessels are non-compendial (e.g. not recognized by United States Pharmacopeia). In order to file a new drug application dissolution method with small volume vessels, significant supportive data justifying their use is required. The group wanted to investigate the fluid dynamics of the low volume “mini-disso” apparatus by empirically studying the effects of key parameters on the dissolution rate of three different types of tablets. This would move toward finding a calibration method, and in the future making low volume dissolution a USP-compendial method.

Parameters to be investigated were paddle height, paddle speed, and sampling zone. The information gained was unprecedented, and proved useful to the department for justification of testing low dose formulations using this non-compendial dissolution method.

It was determined that paddle speed had the most effect on the percent of drug dissolved, paddle height had a smaller, but still significant effect on percent drug dissolved, and sampling zone had a very small effect (not significant in practice) on percent drug dissolved.

**Effects of In Vitro and In Vivo Ethanol on the Binding of <sup>3</sup>H-PK 11195 to the Peripheral Benzodiazepine Receptor in Rat Brain**

*Michelle Tangredi*  
*Department of Biology, College of the Holy Cross*

A similarity exists in the behavioral effects produced by alcohol and the neurosteroid positive modulator of the GABA<sub>A</sub> receptor, allopregnanolone (3 $\alpha$ -OH-5  $\alpha$ -pregnan-20-one). Alcohol has been found to increase allopregnanolone levels. This effect may occur via activation of the peripheral benzodiazepine receptor (PBR) that is located on the mitochondria of glial cells in the brain. The present study investigated the effects of the in vitro and in vivo addition of ethanol on the binding characteristics of PBR in the brain. Rat brain tissue samples were incubated in increasing concentrations of ethanol (1-600 mM) for 1 hour before assessing PBR binding using 1nM of <sup>3</sup>H-PK 11195. In a separate experiment, an acute dose of alcohol (0.5 g/kg, 2.0 g/kg) was administered in vivo one hour before rats were terminated to assess binding using <sup>3</sup>H-PK11195 (0.1875 @ 6 nM). High concentrations of alcohol in vitro decreased binding of <sup>3</sup>H-PK 11195 to cerebral cortical homogenates. In hippocampus, the effects were biphasic in that they increased with the concentrations of alcohol up to approximately 127 % of control values (in 50 mM of EtOH) and then decreased under high concentrations of alcohol (significant at 600 mM EtOH). No changes were observed in cerebellar homogenates. The increase in PBR binding by alcohol suggests that alcohol may activate neurosteroidogenesis by an allosteric interaction that increases the binding affinity of the PBR for an endogenous ligand. The decrease in PBR binding seen with high alcohol concentrations suggests that alcohol may bind directly to the PBR (and thus increase neurosteroid production) or that it produces a general disruption of the cellular membrane that interferes with ligand binding. In contrast to the in vitro results, no significant differences in binding were found after the in vivo administration of alcohol, although slight decrease in the number of PBRs was found in hippocampus. Alcohol's effects on the PBR may depend on its continued presence or perhaps the two doses used in vivo may represent two points on an inverted U-shaped curve that fall on either side of a possible peak.

This research was funded by a grant from the National Science Foundation and a Fisher Summer Research Fellowship.

**Adhesion Molecule Expression on Peripheral Blood Neutrophils  
May Predict the Onset of ARDS in Patients with Major Trauma**

*L. Manzo, College of the Holy Cross*  
*R. Thrall, Ph.D., UCONN Health Center*  
*K. Keating, MD, Hartford Hospital*

Acute Respiratory Distress syndrome is a potentially lethal event that occurs in many patients during traumatic hospitalization. Unfortunately, while the symptoms are well documented, the exact etiology of the syndrome remains unclear and thus prediction of onset is only a guess at best. Studies as far back as 1991 have shown data that suggests a role for activated neutrophils (PMN) in the pathogenesis of ARDS. Neutrophils are already known to be important players in the general inflammatory process and are often the cause of damage caused by inflammation. Hence it is possible that they are also the cause of damage seen in ARDS. Studies have suggested that adherence of PMN to pulmonary artery endothelial cells followed by release of reactive oxygen species may be the trigger that induces a leaky capillary state in the pulmonary circulation during the beginning of the syndrome. This adherence is regulated by expression of adhesion molecules (CD18, Mac-1, LFA-1, and selectins) on the surface of the PMN. The current study seeks to use this information as a possible tool to predict the onset of ARDS. If upregulation of neutrophils is in fact a marker of ARDS, the expression of adhesion molecules can be used to predict its manifestation in trauma patients. This study aims to show PMN infiltration into the lung as a possible marker in the development of acute respiratory distress syndrome. We hypothesize that neutrophil infiltration caused by expression of adhesion molecules is an early event in developing ARDS. Thus it should be possible to use the expression of adhesion molecules as a tool to predict the onset of the syndrome.

**Anxiety Associated with Alcohol Withdrawal is Blocked by  
Administration of PK 11195, a Peripheral Benzodiazepine  
Receptor Mixed Agonist**

*Rebecca A. Smith*  
*Department of Psychology, College of the Holy Cross*

Withdrawal from chronic alcohol exposure produces an increase in anxiety and a decrease in convulsant threshold. Past research suggests that alcohol withdrawal causes a decrease in neurosteroidogenesis, possibly through a decrease in peripheral benzodiazepine receptor (PBR) levels. Peripheral benzodiazepine receptors mediate the production of neurosteroids, compounds that are potent GABA<sub>A</sub> receptor positive modulators with anxiolytic and anticonvulsant properties. The purpose of this experiment was twofold: (1) to determine if PK 11195, a PBR ligand, has an effect on the anxiogenic response to alcohol withdrawal; and (2) to further examine the mixed-agonist profile of PK 11195 to determine if alcohol withdrawal affects the pharmacological properties of the drug, making it more or less of an agonist. This study exposed male Long Evans rats to alcohol in the form of a liquid diet over a period of 14 days. Withdrawal was induced by removing the liquid alcohol diet and approximately 12 hours later, subjects were tested in the novel open field, the elevated plus-maze and the social interaction test one hour after receiving an injection of PK 11195 (0, 5, 10, or 20 mg/kg). Results show that alcohol withdrawal produced anxiety in the elevated plus-maze and social interaction test while decreasing activity in the novel open field. PK 11195 caused a reduction of anxiety in alcohol withdrawn rats in the elevated plus-maze at doses of 10 and 20 mg/kg. In the social interaction test, PK 11195 blocked alcohol-withdrawn anxiety at 5 and 10 mg/kg. In addition, the anxiolytic effect of PK 11195 measured in control animals was not evident in alcohol withdrawal. Thus, these results suggest that alcohol withdrawal elicits a decreased sensitivity to the agonist effects of PK 11195.

This research was supported by a grant from the National Science Foundation and a Fisher Summer Research Fellowship.

## Effects of Estradiol Benzoate on a Delayed Non-Matching to Sample Spatial Working Memory in Ovariectomized Mice

*Olivia T. Vo and Tanya L. Barros*

*Department of Psychology, College of the Holy Cross*

Although estrogen is commonly associated with reproductive functions, it has been shown to also influence learning and memory. Previous investigations have studied the effects of chronic estradiol administration on non-spatial learning tasks using genetically engineered knockout mice that lack either the functional estrogen receptor- $\alpha$  or - $\beta$  subtype. This work has begun to unravel the relative contributions of the estrogen receptor subtypes in mediating the cognitive enhancing effects of estrogen. This research was the first step towards work examining the acute effects of estradiol on spatial working memory in the ER- $\beta$  knockout mice. Thus, we sought to establish the parameters for facilitative effects of estradiol benzoate (EB) in the estrogen receptor- $\beta$ -wild type strain of mice (ER- $\beta$ WT). Acquisition of a spatial win-shift task was first completed, followed by tests using a delayed non-matching to sample test (DNMTS) in a water escape Y-maze apparatus. Five and four days before the DNMTS, animals received an injection of EB (5  $\mu$ g/0.1 cc, SC) or the vehicle (10% DMSO, 90% sesame oil) 5 and 4 days before the test. This cycle of acquisition, injection, and DNMTS tests was repeated three times. In the first cycle, acute EB injection increased the number of errorless trials at 60 and 120 sec delays, relative to vehicle injected animals. On the second test, EB only facilitated retention of the spatial working memory at the 60 sec delay. By the third test, EB reduced the number of errorless trials, but only at the 15 and 30 sec delays. Over repeated testing, it became apparent that EB-treated animals maintained a steady level of performance. However, vehicle animals learned the task and were able to perform better, eventually, at the same level as the EB animals. These results, have established that will test the effects of EB on spatial working memory in ER- $\beta$  knockout mice. If EB continues to improve memory in ER- $\beta$  knockout mice, then we will conclude that it is the alpha receptor subtype that mediates the cognitive enhancing effects of estrogen

## The Effects of Selective Activation of the Estrogen Receptor (ER- $\beta$ ) on Spatial Working Memory in the Ovariectomized Rat

*Melissa J. Lin, Stephanie Galica, and Kimberly Hewitt*

*Department of Psychology, College of the Holy Cross*

Much research has been done to demonstrate that estrogen selectively enhances performance on tasks that are dependent on working memory. In concordance with other researchers, our laboratory found that estradiol benzoate (EB) administration to ovariectomized rats elicited facilitative effects on a spatial working memory. The effects of estrogen on memory function can be mediated by one of two estrogen receptor subtypes, alpha (ER- $\alpha$ ) or beta (ER- $\beta$ ). In these experiments we tested the effects of selective ER- $\beta$  agonists on spatial working memory. The hypothesized similarity of the agonist-induced effects to those observed following EB treatment would strongly suggest that the ER- $\beta$  plays a role in the cognitive enhancing effects of estrogen. Twenty-four ovariectomized rats were habituated in the radial arm maze (RAM) for fifteen minutes for five days, then given a win-shift task during acquisition for three days. The following day, injections of vehicle (0.2 cc, SC), EB (10  $\mu$ g/0.2 cc), or one of three ER- $\beta$  selective compounds (10 mg/kg) were administered. Injections were repeated 24 hours later. Four days after the second injection, animals were tested in a delayed non-matching to sample task. Relative to vehicle treated animals, EB injections increased the number of correct responses at 15, 30, and 60 sec delay intervals. By comparison, only one of the ER- $\beta$  agonist (WAY 201353) improved working memory at 15 and 30 sec delays. The other ER- $\beta$  compounds (WAY 166818 and WAY 200070) only improved memory at the 60 sec delay. Because the selective ER- $\beta$  agonists produced only a partial enhancement, these results suggest an additional role for ER- $\alpha$  in mediating the cognitive enhancing effects of estradiol. This research was supported by a grant from the Wyeth-Ayerst Women's Health Research Foundation and a Fisher Summer Research Fellowship.

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## **Fruit Flies as a Bioassay in Combinatorial Chemistry of Esters**

*Patrick S. Twomey*

*Department of Chemistry, College of the Holy Cross*

Combinatorial chemistry is becoming a widely used technique in industry today. The purpose of this research was to find an efficient means by which students could be exposed to the ideas of combinatorial chemistry in the lab. For the research, I made a library of twenty-five esters, and their respective batches. These were tested for purity using GC-MS and IR spectroscopy. I then used fruit flies as a bioassay for the esters hoping that isoamyl acetate (banana oil) would attract them. However the fruit flies proved not to be a good bioassay.

The research was good however in that a larger array of esters was found for the students thus exposing them to a more diverse sampling of smells and a better understanding of esters. Likewise a more efficient means of making the esters was found. Rather than making the esters by the Fischer esterification, esters were made by acyl substitution which proved to be easier and produced a larger array of esters.

This research was funded by Fisher Summer Research Fellowship

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## **Free Radical Halogenation @ A Discovery Lab Exploration**

*J. Rieger and Prof. Ronald M. Jarret*

*Department of Chemistry, College of the Holy Cross*

Through this research it was hoped to expand upon the free radical halogenation lab currently used by first semester Organic Chemistry students. Presently free radical chlorination is demonstrated with only two chemicals. Five additional chemicals were tested to determine the feasibility of adding some to the lab, and to discover whether any of these chemicals demonstrated a preference for substitution at the benzylic position. Free radical bromination was also explored in the hopes of demonstrating the difference in selectivity between chlorine and bromine.

All products were analyzed by GC-MS for identification. It was found that for most chemicals tested free radical chlorination was the more successful procedure, giving clearer results than free radical bromination. Of the new chemicals tested tetralin gave the most promising results, illustrating the favorability of substitution at the benzylic position and the higher selectivity of bromine.

We thank Pfizer for financial support.

## Mimicking a Motion Illusion: A Computational Model of Human Heading Perception

*Daniel Conti and Constance S. Royden*  
*Department of Mathematics and Computer Science*  
*College of the Holy Cross*

Much research has been done regarding a human observer's ability to judge direction of motion, or heading, based on visual stimuli. In other words, how do humans know which way they're moving based on what they see? Even when we're physically not moving, visual stimuli can be created to give the appearance of motion. A common example of this is the screen saver of a star field. The stars on the computer screen move in a radial pattern moving outward from the center of the screen. The viewer perceives this as motion through space. From this same scene, the viewer could be asked to indicate where they are headed based on the star field's movement. The question is how well can they judge their heading.

Psychophysical experiments have shown that a human can judge heading fairly accurately based on visual stimuli (Royden et al, 1994). However, in a specific case studied by Charles Duffy and Robert Wurtz (1992), humans were asked to judge heading based on a radial optic flow field, like the screen saver of the star field, combined with overlapping lateral motion, like dots moving horizontally across the screen. The visual stimulus creates an illusion of heading direction biased in the direction of the lateral motion.

We examined the responses of a computer model for computing heading given the same visual stimuli as given in the above mentioned experiments. The computer model uses motion-opponent operators similar to cells in the brain which respond to motion stimuli. Using a motion field as input, the model computes an estimated direction of heading. This is much like a human asked to point in the direction they are headed. When compared to the human data, we show that the computer exhibits biases similar to those seen in humans. These results suggest that such a model may accurately describe the neural mechanism used in human heading computations.

We'd like to thank the National Science Foundation for their financial contributions for the funding of this research.

## Biochemical Characterization and Partial Purification of Fe(III) Reductase Activity in *Campylobacter jejuni*

*Nicholas Guziewicz and Dr. Madeline Vargas*  
*Department of Biology, College of the Holy Cross*

*Campylobacter Jejuni* is a microaerophilic, gram-negative pathogen causing symptoms such as fever, bloody diarrhea, headache, abdominal pain, and nausea. Our laboratory has successfully predicted and demonstrated the ability of the genus *Campylobacter* to reduce Fe(III) due to its close phylogenetic relationship with the known Fe(III) reducer *Wollinella succinogens*.

We measured NADPH-, NADH-, and hydrogen-dependent Fe(III) reductase activities in crude cell-free extracts, and whole cells. NADH and hydrogen-dependent activity was negligible in both cases suggesting that neither serve as a direct donor. NADPH-dependent activity was measured at 298.49 mUnits/mg protein for the extract and 155.76 mUnits/mg protein for whole cells. Activity was also measured in the soluble and membrane fractions separated by ultracentrifugation of the cell free extracts. Approximately 99% of NADPH-dependent Fe(III) reductase activity was localized to the soluble fraction. As a first step in purifying the protein(s) responsible for Fe(III) reductase activity, crude extracts were separated on native gels and stained for enzyme activity. Electroeluted activity bands were separated on denaturing SDS-PAGE and silver stained. Bands of interest consistently appear at 45,000, and 29,000, and 22,000 daltons.

Our results represent a first step at understanding the role of Fe(III) reduction in the colonization and pathogenesis of *Campylobacter* infections which could lead to possible treatments and/or prevention.

This research was funded by a Fisher Summer Research Fellowship and the Biology department.

**Oncogenic Potential of Kaposi's Sarcoma-Associated Herpesvirus K15 may be studied in comparison to Epstein-Barr Virus LMP2A and HVS Tip by the Formation of a Recombinant Virus**

*D. Davignon, Dr. Joong-Kook Choi and Dr. Jae U. Jung  
Division of Tumor Virology, The New England Regional Primate  
Research Center, Harvard Medical School*

The numerous  $\gamma$ -herpesviruses have been shown to cause many serious illnesses in both humans and animals. They infect B or T cells and have large, double-stranded DNA genomes that are difficult to manipulate in the laboratory and must be manipulated in fragments that are later allowed to recombine. Of special interest in this study was Kaposi's Sarcoma Associated Herpesvirus (KSHV), specifically the genes involved in the oncogenicity of the virus. The K15 gene of is structurally and functionally similar to the LMP2A gene of the Epstein-Barr Virus (EBV) and the Tip gene of Herpes Virus Saimiri (HVS.) At present, no cell culture system will support the growth of KSHV, so we intend to study it in the context of a recombinant HVS genome in comparison with the related genes Tip and LMP2A as well as mutant forms of all the genes.

The desired genes and respective deletion mutants were amplified by PCR and cloned into a recombination-competent bacterial plasmid containing HVS sequences from which the HVS Tip gene had been deleted. The positive clones were transformed into *E. coli*, grown overnight and DNA was extracted. The genes and neighboring HVS sequences were inserted into cosmid DNA. Positive clones will be verified, the cosmid will be inserted into owl monkey kidney cells for recombination with the additional overlapping cosmids comprising the HVS genome. The recombinant virus will then be allowed to grow to an appropriate titer whereupon we shall infect New World Primates. Necropsies of the afflicted animals will allow us to understand more specifically the pathogenicities induced by KSHV K15. We expect to see the development of lymphomas similar to those seen previously in humans and animals infected with these gamma-herpesviruses

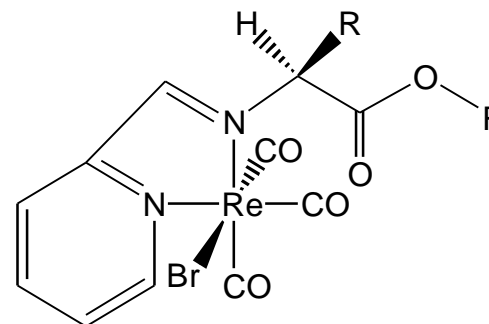
**Preparation of Rhenium Complexes via a Schiff Base Ligand**

*I. Wrona and Prof. R.S. Herrick*

*Department of Chemistry, College of the Holy Cross*

The goal of this study was to examine whether an amino acid could be attached to a metal center. Previous group members have been able to bind amino acids to metals such as molybdenum(0) and tungsten(0) via a Schiff base ligand. The present research focuses on rhenium(I) complex. There is an apparent color difference among these complexes; molybdenum and tungsten compounds are burgundy in color while rhenium compounds are fluorescent orange. A general structure of a rhenium(I) complex can be seen below. Compounds prepared include  $\text{Re}(\text{CO})_3\text{Br}(\text{pyca-xxx})$  where xxx= ala-OEt, asp(OMe)-OMe, -ala-OEt, GABA-OMe, val-OMe. Results of successful syntheses will be presented. We would like to thank the Dreyfus Foundation for funding this research.

GENERAL STRUCTURE OF A RHENIUM COMPLEX



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### **Preparations for Laser Cooling of Rb atoms using Stabilized Diode Lasers and a Magneto-Optic Trap**

*Peter Harris and Dr. Timothy Roach*

*Department of Physics, College of the Holy Cross*

Very slowly moving Rb atoms will exhibit interesting wave properties. To study these properties we are working on a program to launch very cold Rb atoms at a ferro-magnetic surface. This summer was dedicated to the construction and testing of the many components necessary to complete this goal. To achieve very cold temperatures ( $< 0.1$  mK), these atoms need to be laser-cooled, requiring the ability to finely tune and adjust our lasers, therefore I worked on two important controls, the acousto-optic modulator and the temperature control device. The atoms are to be cooled inside a vacuum chamber which was constructed and tested this summer. Designs and calculations for the electromagnetic coils used to hold the atoms in place were carried out, as were the designs for the coils necessary to cancel out the earth's natural magnetic field. Finally, programs were written to give us the ability to run the experiment by computer control, providing greater accuracy and accountability for multiple trials.

We thank the Fisher and Fortin Summer Research Fellowships and The Research Corporation for financial support.

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### **Understanding the Water/Acetonitrile Interface Using Molecular Dynamics Simulations**

*Dan Kirchoff and Ramona Taylor*

*Department of Chemistry, College of the Holy Cross*

In low concentrations, acetonitrile stands straight up on the surface of the water with its CN triple bond directed into the water. However, at a mole fraction of approximately 0.07, the surface structure changes; the acetonitrile molecules undergo a "phase transition" to tilt the molecules so the methyl groups move closer to the water surface<sup>1</sup>. The cause of this phenomenon is not yet understood. Our research attempts to use molecular dynamic simulations to understand the cause of the "phase transition".

We have spent significant time gathering information, in the form of several physical properties, about simulated boxes of acetonitrile in various aqueous concentrations. One goal was to match the properties of our simulated solutions such as surface tension, dipole moment, density and diffusion constant to reported experimental results. A second long range goal has been to similarly experiment with a new potential function to more accurately model the motions of the molecules in solution.

Funding for this research was provided by the Research Corporation (#CC5158).

### On the Measurements of Small Amplitude Side-Branch Spacing at the Dendrite Tip

*S.L. DeChiaro, K.A. Gormley and M.B. Koss*

*Department of Physics, College of the Holy Cross*

Dendrites are commonly formed in metals during the solidification process. They form in pure metals as well as alloys and significantly affect material properties. The general structure of the dendrite is a smooth tip region followed by an ever expanding envelope of side-branches. The focus of this ongoing research is to analyze the tip region of dendrites in order to find out if there is evidence of side-branching in the “smooth” tip region. Over the past decade experimental, theoretical and modeling efforts have demonstrated a strong coupling between the smooth tip of a dendrite and its trailing side-branching behavior. More recently it has been reported that the dendrites do not grow at a steady-state velocity, and that there are growth velocity oscillations at the tip. Extracting a smooth curve from the photographed dendrite as a reference, we measured correlations in the deviation between the actual dendritic interface and the smooth reference as a function of arclength. These results constitute a wavenumber spectrum of perturbations at the dendrite tip. One way to quantify the side-branch structure is to measure directly the distance between adjacent side-branches, which we call the side-branch spacing,  $l$ . Preliminary results show that the inverse of these wavenumbers, which is a spacing, when scaled by the tip radius, yields  $l_{\text{tip wavenumber}}/R = 3.1 \pm 0.3$ . This is about the same as the measured side-branch spacing of  $l_{\text{side-branching}}/R = 2.9 \pm 0.3$ . This close correspondence indicates that the perturbations of the “smooth” region of the dendrite are side-branch related. This constitutes the first experimental evidence that there is side-branch activity at the tip.

### Substrate-induced respiration for determining eukaryote:prokaryote ratios in soils

*B.G. DeGasperis, C. Rice and E. Brennan*

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The substrate-induced respiration (SIR) technique of Anderson and Domsch (1973) and West (1986) for determining eukaryote:prokaryote ratios was refined for use on tallgrass prairie soils. Glucose ( $1000 \text{ mg g}^{-1}$  soil) was used to stimulate microbial metabolism. Antibiotics (streptomycin sulfate, chlortetracycline, chloramphenicol and cycloheximide) were tested at various concentrations to ascertain their effectiveness at inhibiting microbial respiration. The effects of antibiotic, optimal incubation period and method of solution preparation were also investigated. Of the antibiotics tested, chlortetracycline, was the greatest inhibitor of prokaryotic respiration. A concentration of  $8600 \text{ mg g}^{-1}$  soil was selected based on effectiveness and solubility. Of the concentrations tested,  $13333 \text{ mg g}^{-1}$  soil was selected for cycloheximide (eukaryotic protein inhibitor). Four hours was found to be the maximum incubation period which yielded a constant rate of microbial respiration. Magnetically stirring for 2 hours at 24C proved to be the most effective and practical method of solution preparation. We also applied the SIR technique to a limited sample of field-treated soils in order to explore its effectiveness at registering shifts in microbial. The effects of burning and nitrogen (N) addition on the microbial community composition were investigated. There were no significant differences in bacterial:fungal ratios (BFRATIO) in the plots studied. We found a trend with a decrease in BFRATIO with burning and an increase in BFRATIO with N addition. Field-treated samples were also tested for initial inorganic N, microbial biomass (MBM), carbon (C) and N, and total soil C and N. Burning increased MBM C and decreased MBM N. Nitrogen addition decreased MBM C and N.

## IONIZATION STATES OF ATOMS IN AN ASTROPHYSICAL PLASMA

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From gaseous nebulae to stellar atmospheres to accretion disks around blackholes, astrophysical plasmas are frequently not in Local Thermodynamic Equilibrium (LTE). To determine the dominant ion of a particular element at a fixed temperature involves several different processes that affect each atom in a unique way. The processes that I have covered include collisional ionization, three-body recombination, radiative recombination, and dielectronic recombination. Non-LTE means that each ionization rate for a given process and its corresponding recombination rate are not in local thermodynamic equilibrium. We can still assume statistical equilibrium, that the total overall rate of ionization equals the rate of recombination. Thus, mathematical formulae derived from statistical equilibrium can be solved through computer programming in Fortran to determine each of the rates. Once we determine the rates, we can determine the fractional abundance of each of the ions.

My research for the summer concluded with rates applicable to the Sun's corona at a temperature around  $10^6$  K. Overall my research aims at depicting more clearly the make-up of phenomenal astrophysical plasmas, particularly accretion disks around blackholes

## Molecular Dynamics Investigations of Ethanol via Aqueous Ethanol Solutions

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The interactions of molecules between the gas and liquid interface, particularly the uptake of molecules by droplets of  $\text{H}_2\text{O}$ , are important for understanding processes involved in atmospheric chemistry. Molecular dynamics simulations can be especially helpful in the investigation of these reactions. The current model describes a large energy barrier, which the approaching molecule must overcome to solvate in water. This research focuses on systems of ethanol and water that are forced to interact. Under these conditions, a variety of physical properties can be examined.

It was found that at all concentrations, molecules of ethanol sat at the surface of the liquid/vapor interface. At a mole fraction of just 0.1, the surface of the water droplet was almost fully saturated with ethanol. It was also seen that as concentration increased, the orientation of water shifts to maximize hydrogen bonding. The energy barrier found experimentally is not seen to be explained by the interaction of ethanol at the surface of water in this simulation.

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## Calculating the Thermal Field surrounding Dendrites

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A dendrite is a crystalline solid that grows as a liquid becomes solid. These dendrites become important in many industrial purposes; for instance a machine part made of a single dendrite is far stronger than a part made from many dendrites.

During the freezing process, latent heat is liberated and moves away from the dendrite. When a liquid becomes super-cooled it is below the given freezing point, but it is still liquid and it has not given up the latent heat. A nucleation seed within the super-cooled liquid triggers the freezing process and, with in the right liquid, solidifies as a dendrite. It is well known how super-cooling correlates with the speed at which the dendrite actually expands, as well as various other growth characteristics. This project deals directly with modeling the effect the evolving latent heat has on the environment of the freezing dendrite. As the latent heat is released from the solidifying liquid, it slightly warms the surrounding material producing a changing thermal field, and thereby a thermal gradient around the dendrite. This thermal field can be calculated using the properties of the given compound and a known analytic solution that describes the freezing. Knowledge of the size of the thermal field helps to conclude the amount of time experiments can last before the dendrites become altered by the size of the growing chamber.

## Quantum Scattering in Two Dimensions

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Quantum mechanics studies the probability of finding a particle in a particular space. The functions from which these calculations can be made are solutions to the Schrodinger differential equation. Quantum scattering calculates the probabilistic properties of unbound particles. This project aims to be able to calculate the probabilistic functions as well as other information regarding unbound as they encounter a general two-dimensional potential. The Schrodinger equation, however, becomes impossible to solve analytically for more than very simplified cases; a numeric solution is necessary for almost always. The process by which we generate the numeric solution includes building a computerized numeric calculating program, an analytic test case that can be used to compare the numeric result, and refinement techniques that make the results more accurate.

## **Alkene Synthesis in the Organic Chemistry Laboratory**

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The purpose of this research project was to further examine and expand the organic discovery laboratory of alkene synthesis. The present lab exercise has students conducting a dehydration reaction of an alcohol, reducing it to an alkene. Because of rearrangement, many alkene products were formed in mixture. To correctly identify the peaks on the GC trace, each alkene needs to be synthesized through independent methods. One method that was successful involved addition of hydrogen to alkynes. An experiment using a zinc-copper couple was used giving the cis isomer.

Secondly, an experiment was devised that yielded the terminal alkene as the major product. A molecule containing a tosylate leaving group was combined with potassium-tert-butoxide as a bulky base dissolved in DMSO. This gave the terminal alkene as the major product; something that rearrangement had prevented in earlier experiments.

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