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Northeastern Research Symposium

Center for Excellence in Wireless & Information Technology

Stony Brook University

April 9th, 2011
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Keynote Speakers Biographies

**Paul Greengard, PhD**  
*Rockefeller University*

**Lecture Title:** Tales of Two Maladies: Alzheimer’s Disease and Depression

Dr. Paul Greengard is Vincent Astor Professor of Molecular and Cellular Neuroscience at The Rockefeller University and Director of the Fisher Center for Alzheimer’s Research. After Dr. Greengard received his Ph.D. from The Johns Hopkins University in 1953, he spent five years training at the University of London, Cambridge University and the National Institute of Medical Research. Before joining Rockefeller in 1983, he was Director of Biochemistry at the Geigy Research Laboratories and then Professor of Pharmacology and Psychiatry at Yale University.

His interests have ranged from basic neural explorations to the development of therapeutic agents for the treatment of neurological and psychiatric diseases. In 2000, he was awarded the Nobel Prize in Physiology or Medicine for his contributions to elucidating how neurotransmitters work in signal transduction in the nervous system. Dr. Greengard is currently involved in a large collaborative effort to identify all of the expressed genes in individual cell types that have been implicated in various neuropsychiatric disorders.

**John H. Marburger, III, PhD**  
*Stony Brook University*

**Lecture Title:** A Different Take on ‘Understanding Science’

John H. Marburger, III, was Stony Brook University’s third president from 1980 to 1994, and subsequently the Director of Brookhaven National Laboratory and Science Advisor to the President and Director of the White House Office of Science and Technology Policy during both terms of the George W. Bush Administration. As a professor and dean of the College of Letters, Arts and Sciences at the University of Southern California in the 1960’s and 70’s, Marburger co-founded USC’s Center for Laser Studies and conducted research in laser physics and engineering. He earned an A.B. degree in physics from Princeton University, and a Ph.D. in applied physics from Stanford. Since the 1980’s Marburger has served multiple roles at the interface between science and society, and continues to speak frequently on science policy.

**Grigori Enikolopov, PhD**  
*Cold Spring Harbor Laboratory*

**Lecture Title:** Stem Cells of the Adult Brain

Professor Grigori Enikolopov received his Ph.D. degree in molecular biology from the Institute of Molecular Biology of the Russian (USSR) Academy of Sciences in Moscow. In 1989 Dr. Enikolopov was invited by Dr. James Watson to join Cold Spring Harbor Laboratory as a Visiting Scientist and in 1993 he joined the faculty of CSHL. He is a Visiting Scholar at Stony Brook University and Faculty Member and Instructor of the Watson School of Biological Sciences and of the graduate programs in Neurobiology, in Genetics, and in Pharmacology at Stony Brook University.

Dr. Enikolopov is a recipient of numerous grants and awards and is an author of more than 100 publications. He holds several patents and is a founder of two biotechnology companies. His research focus is on neural and hematopoietic stem cells, generation of new neurons in the adult brain, molecular basis of mood disorders, and new therapies for brain disorders.
**Schedule of Events**

8:45 AM – 9:25 AM  Registration & Breakfast
9:30 AM – 9:45 AM  Opening Remarks
9:45 AM – 10:25 AM  Keynote Lecture: John H. Marburger, III, PhD  

**A Different Take on ‘Understanding Science’**

10:25 AM – 11:30 AM  Poster Session A
11:30 AM – 12:10 PM  Keynote Lecture: Grigori Enikolopov, PhD  

**Stem Cells of the Adult Brain**

12:10 PM – 12:35 PM  Student Lecture: Yan Leyfman  

**Cancer Stem Cells: A Novel Target for Drug Development**

12:40 PM – 1:50 PM  Lunch
1:50 PM – 2:30 PM  Keynote Lecture: Paul Greengard, PhD  

**Tales of Two Maladies: Alzheimer’s Disease and Depression**

2:30 PM – 3:40 PM  Poster Session A
3:40 PM – 3:55 PM  Intermission
3:55 PM – 4:10 PM  Closing Remarks

**Institutions Represented**

- Brigham and Women’s Hospital
- Brookhaven National Laboratory
- Bryn Mawr College
- California Institute of Technology
- Cold Spring Harbor Laboratory
- Columbia University
- Connecticut College
- Cornell University
- CUNY Lehman College
- CUNY Queens College
- CUNY York College
- Duke University
- Emory University
- Fairfield University
- Fordham University
- Hampshire College
- Harvard University
- Ithaca College
- Johns Hopkins University
- Massachusetts Institute of Technology
- Medical College of Wisconsin
- Monmouth University
- National Institutes of Health
- NYU College of Dentistry
- Princeton University
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- Stanford University
- Stony Brook University
- SUNY Oswego
- SUNY Plattsburgh
- SUNY Purchase
- University of Colorado at Boulder
- University of Pennsylvania
- University of Rhode Island
- Weill Cornell Medical College
- Wells College
- Yale University
Latent and lytic cycles are characteristic of life-long herpesvirus infections. The gammaherpesviruses establish latency in memory B cells, where the virus genome is not integrated and viral gene expression is tightly regulated without producing infectious virus. This is in contrast to lytic replication where transcription of all genes occurs in a regulated cascade, viral DNA is replicated, and infectious virus is released. One of the objectives was to examine the kinetic profiles of transcripts during lytic infection and during reactivation from latency using a custom-designed tiled microarray. Reactivation of murine gammaherpesvirus 68 (MHV68) in A20 HE cells, a mature B cell line that maintains the virus in a latent state was induced by treatment with 12-O-Tetradecanoylphorbol-13-acetate (TPA). We developed and validated quantitative RT-PCR assays to confirm microarray results. We found that many viral genes had similar kinetic profiles during de novo lytic infection and reactivation from B cells. However, M1, mK3, ORF18, ORF75A and ORF75B have distinct transcription profiles during reactivation. Nuclear factor kappaB (NF-κB) transcription factors regulate cellular gene expression, playing an important role in MHV68 latency. The impact of inhibiting NF-κB on driving reactivation was examined by treating the A20 HE cells with the NF-κB inhibitory molecule Bay 11-7082 alone, or the combination of TPA and Bay 11-7082. We found that Bay11-7082 enhanced virus production and viral gene expression at later timepoints after TPA stimulation. We conclude that the tiled microarray is an effective tool for studies of viral gene regulation by host signaling pathways such as NF-κB.
Design Methodology for an Ultra-Low Power Phase-Locked Loop (PLL) Circuit in CMOS Technology with Application to Biomedical Wireless Systems
Garrett Bischof, Ben Scholnick, and Emre Salman (project advisor)
Electrical and Computer Engineering, Stony Brook University

The design and verification of an ultra low power phase-locked loop (PLL) with application to biomedical systems is presented in this paper. An example application could be a blood sugar monitoring device that can be implanted under the skin to take measurements of a patient’s blood sugar. In such a system, PLL is used both to synthesize a clock signal from a reference signal and to recover the clock signal from a corrupted incoming data signal. The recovered clock signal is then used to sample the data and produce a clean data signal. The circuit works by comparing the input data stream with the output of the voltage controlled oscillator (VCO) using a phase and frequency detector (PFD). Any difference in the phase or frequency of the two inputs causes a predictable output voltage which is used to adjust the frequency of the VCO, thereby eliminating the adverse effects of environmental variations.

The PLL architecture discussed in the paper therefore consists of five blocks: PFD, charge pump, loop filter, VCO, and divider. The charge pump and loop filter are included to significantly improve the acquisition range of the PLL. A second order loop filter is adopted to not introduce stability issues. The divider at the output of the VCO is used to multiply the clock frequency, synthesizing the required system clock by the biomedical chip.

A systematic PLL design methodology is introduced where the first step is a high level characterization of the system in Matlab. This step ensures that the system is stable and fundamental constraints can be satisfied, i.e., system is capable to achieve the lock condition. Furthermore, a high level jitter analysis is also achieved in this step. The second step involves the transistor level implementation in Cadence using CMOS technology to achieve the remaining design constraints such as power dissipation. Several circuit level techniques are proposed to achieve ultra low power such as lowering the power supply voltage when feasible. Finally, the third step is the physical layout of the system and post-layout verification that considers the parasitic effects. Specific design constraints include a maximum of 5mW for power consumption, temporal jitter less than 2% of the clock period, and VCO frequency between 500 and 800 MHz.
**Project Category: Biochemistry and Venoms**

*A rapid and sensitive fluorometric method for the quantitative analysis of snake venom metalloproteases and their inhibitors*

J. E. Biardi\textsuperscript{a,b}, K. T. Nguyen\textsuperscript{b}, S. Lander\textsuperscript{a*}, M. Whitley\textsuperscript{a}, and K. P. Nambiar\textsuperscript{b}

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Metalloproteases are responsible for the hemorrhagic effects of many snake venoms and contribute to other pathways that lead to local tissue damage. Methods that quantify snake venom metalloproteases (SVMP) are therefore valuable tools in research on the clinical, physiological, and biochemical effects of envenomation. Comparative analysis of individual, population, and species differences requires screening of large numbers of samples and treatments, and therefore require a method of quantifying SVMP activity that is simple, rapid, and sensitive. This paper demonstrates the properties of a new fluorometric assay of SVMP activity that can provide a measure of metalloprotease activity in one hour. The assay is reliable, with variation among replicates sufficiently small to reliably detect differences in between species ($F_{19,60} = 2924$, $p < 0.001$), even for those venoms with low overall activity. It is also sensitive enough to detect differences among venoms using < 2 ng of whole venom protein. We provide an example use of this assay to detect the presence of natural SVMP inhibitors in minute samples of blood plasma from rock squirrels (*S. variegatus*), a natural prey species for North American rattlesnakes. We propose this assay is a useful addition to the set of tools used to characterize venoms, as well as high-throughput screening of natural or synthetic inhibitors, or other novel therapeutic agents against SVMP effects.

**Project Category: Neuroscience and Motor Neurons**

*Achieving Stable Motor Neuron Cultures by Inhibition of the Notch Pathway*

Tara Pesce\textsuperscript{*}, Bethany Kerner, Christopher Henderson

Department of Neuroscience, Columbia University, New York, NY

Studying motor neurons in vitro is a powerful tool to understand motor neuron diseases such as amyotrophic lateral sclerosis (ALS). Since motor neurons cannot be taken directly from patients, those derived from embryonic stem (ES) cells can be used to screen for drugs to be used as therapy. Currently, it is difficult to efficiently make pure, stable cultures of motor neurons from ES cells, hindering the study of diseases such as ALS. Notch signaling maintains pools of progenitors throughout development in order to ensure that the correct numbers of different neural cell types are generated, and it is therefore possible that in culture it may play a similar role, preventing complete differentiation of ES cells into postmitotic cells such as motor neurons. In this study, we treat mouse and human embryoid bodies (EBs) with DAPT, an inhibitor of the Notch pathway, to determine if its addition to cultures of motor neurons can increase their purity. Analyses of markers for both progenitors and neurons using the Multi Wavelength Cell Scoring application module in Metamorph demonstrate that inhibition of the Notch pathway with DAPT in vitro has a direct effect on neural specification, showing promise for the use of this compound in the optimization of neural differentiation protocols.
**Introduction of Adaptive Stratified Hypotheses Tests into Genome-Wide eQTL analysis**
Sarah Urbut*, Narayanan Raghupathy, John Storey  
Department of Molecular Biology, Princeton University, Princeton, NJ

The availability of genotype and gene-expression data across many tissue types and organisms has enabled the quantitative study of associations between levels of gene expression and polymorphisms at particular loci. Expression quantitative-trait loci, or eQTL, serve as markers of local and distal gene-expression association, and coordinating such loci with both gene expression data and disease status provides tremendous biological insight about molecular disease pathways and serves to increase our understanding of genotypic risk. However, detecting distal associations requires a much lower significance threshold due to the considerably increased number of statistical tests, and the prevalence of local associations is far greater than the prevalence of distal associations. Consequently, statistical power is diminished when examining both local and distal associations in the same statistical test. We introduce a new method to stratify local and distal association tests and thus preserve the false-discovery rate while increasing the sensitivity of detected local associations. We will apply our method to gene expression data from human lymphoblastoid, liver, and yeast cell lines and hope to identify additional significant gene-SNP associations. This work has profound implications for achieving heightened understanding of the underlying components of complex biological pathways and diseases without losing any statistical specificity.

**An Orthologue of the Apicomplexan Vaccine Candidate Phosphoprotein P0 is Present at the Cell Surface in the Alveolate Protist, Tetrahymena thermophila.**  
J. Schumacher*, C. Satchwill, S. Canton, K. Babcock and L.A. Hufnagel  
Department of Cell and Molecular Biology, University of Rhode Island, Kingston, RI 02881

Phosphoprotein P0 (P0) is a conserved ribosomal protein that has been found at the cell surface in parasitic protozoa, including Plasmodium falciparum. In Plasmodium, antibodies to P0 have been found to block entry of the parasite into host cells. P0 is considered to be a possible target for development of vaccines against apicomplexan parasites. Tetrahymena thermophila is a ciliated protist belonging to the Alveolata, the clade to which the apicomplexans belong. We conducted a protein BLAST analysis of the published T. thermophila genome and identified a single orthologue of P0 (e-value = 2.7x10^{-35}). Alignment analysis using Clustal W2 shows that the Tetrahymena orthologue (TtP0) shares a highly conserved central region but is more divergent in its N-terminal and C-terminal regions. Analysis of the predicted sequence of TtP0 using a protein motif finder program revealed arginine-rich RNA-binding domains, domains that interact with ribosomal proteins P1 and P2, and ribosomal L10 and 60s motifs. To determine whether TtP0 can also occur at the cell surface in T. thermophila, immunocytochemical experiments were conducted on cells fixed and labeled in the presence and absence of detergent and methanol. Detergent/methanol-treated cells showed nuclear and cytoplasmic labeling, whereas in the absence of detergent/methanol strong labeling was localized to the anterior surface of the cells. Our findings suggest that T. thermophila may be a good model system in which to further investigate the role of P0 at the cell surface and the mechanisms for transfer of P0 to the surface.
Artificially Layered PbTiO/CaTiO Superlattices
Jonathan Daley*, John Sinsheimer, Youcef Benkara, Sara Callori, Matthew Dawber
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It has been shown that in artificially layered PbTiO/SrTiO superlattices, a form of improper ferroelectricity occurs where the rotations of the oxygen octahedra at the interfaces couple with the polar mode and increase the ferroelectric polarization of the material when the layers are very thin. PbTiO/CaTiO superlattices grown on SrTiO substrates are also highly likely to display this kind of behavior, as the CaTiO ground state is dominated by rotational distortions. This system should also play host to a competition between in-plane ferroelectricity (as CaTiO is subjected to a large tensile strain when grown on SrTiO) and out-of-plane ferroelectricity (the usual result when in PbTiO is grown on SrTiO). Using off-axis RF magnetron sputtering, we have produced high quality superlattices of PbTiO/CaTiO with various layer thicknesses on SrTiO substrates with SrRuO bottom electrodes. The samples were analyzed using x-ray diffraction, electrical measurements, and atomic force microscopy. Our experimental results reveal a fascinating transition region at certain ratios of the relative layer thicknesses.

Assessing Biological Uptake of Antimony, Copper, Lead, and Zinc at a Shooting Range Using Laser Ablation ICP-MS
Jeremy Koelmel*, Dulasiri Amarasiriwardena
School of Natural Science, Hampshire College, Amherst, MA 01002

Lead and antimony contamination of shooting ranges is a major environmental concern. We investigated soil Pb and Sb uptake and distribution in Hey-scented ferns (Dennstaedtia punctilobula) by laser ablation inductively coupled plasma mass spectrometry (LA-ICP-MS) in shooting range fern samples (n=31). Nitric acid and ammonium acetate extractable soil Cu, Pb, and Sb, concentrations were determined (n=34). Nitric acid extractable Cu, Pb, and Sb, average soil concentrations were 17.6 ± 17.5, 47345 ± 4149, and 8.6 ± 7.5 mg/kg, respectively for shooting range sites and 4.7 ± 0.4, 21.9 ± 10.8, and 0.08 ± 0.01 mg/kg for control site. Linear correlations of Cu, Pb, Sb, and Zn were highly correlated ($r^2$ > 0.5, p << 0.001) suggesting metal variation based on lead shot distribution in the shooting range. Cross and longitudinal sections of Hay-scented fern rhizomes and stems were analyzed to determine Cu, Pb, Sb, and Zn distributions at micrometer resolution using LA-ICP-MS. The distribution of Pb followed an exponential decrease from the epidermis to the end of the outer sclerotic cortex cells ($r^2$ > 0.65) and increased by up to 359% in the living starchy cortex suggesting Pb uptake across the rhizome epidermis and bioconcentration in the living tissue. The inner endodermis and starchy cortex had higher levels of Pb than vascular tissue implying potential excretion from vascular tissue. The results of our technique advance the spatial resolution of multi-element bioimaging, discerning system wide bioconcentration and transport of metals in ferns.
**Balance during Rotations in Dance: A Physical Analysis**
Melanie Lott*, Kenneth Laws
Department of Physics, Bryn Mawr College, Bryn Mawr, PA

Pirouettes, or turns on one foot, are one of the most common movements in all forms of dance. Currently, dance educators teach dancers to attempt to achieve a balanced position at the onset of rotation and maintain the body configuration, as opposed to correcting an imbalance with small adjustments during the turn. Many, even advanced, dancers have significant difficulty performing more than a two or three turn pirouette before losing balance, despite continued trial and error efforts to improve.

A theoretical model of a dancer in standard pirouette position was created to determine the mechanics of toppling during a pirouette. Body segment parameters (mass, length, radii of gyration) were based on anatomical data and adjusted for sex, total body mass, and height. The principal moments of the inertia tensor were determined for several hypothetical dancers, and rigid body equations of motion numerically solved to simulate topple angle vs. time. If a dancer’s body begins the turn displaced only one degree from vertical, it was found that she/he topples to an unrecoverable angle after 1.66s (small, female) or 1.54s (large, male). For typical rotation rates (~2 rev/sec), these dancers would fall out of a pirouette after little more than three rotations. These results demonstrate the difficulty of achieving many rotations when the body is held rigidly. To consistently perform more than a triple pirouette, dancers should be taught strategies for regaining balance while turning. An experimental study is underway to determine what adjustment strategies successfully lead to more balanced pirouettes.

**Biochemical Diversity in the Rainforest: Discovery of an Anti-fungal Endophytic Natural Product**
Alicia Darnell1*, Kaury Kucera1, Scott Strobel1
1Molecular Biophysics and Biochemistry, Yale University, New Haven, Connecticut

Though tropical rainforests hold enormous potential as a source of biological diversity, research into the biochemical potential of these biodiversity hotspots is just beginning. Endophytes, fungal organisms that live within inner plant tissues, occupy an ecological niche, subjecting them to evolutionary pressure towards the production of natural products, for the purpose of competition against neighboring populations of microorganisms. This selective pressure makes endophytes an ideal experimental system for natural product discovery. This project aims to discover bioactive natural products that inhibit the growth of the human pathogenic yeast *Candida albicans*. From a crude extract of natural products produced by a fungal organism (may be a novel genus of fungus through BLAST genomic analysis), I used thin layer chromatography and high performance liquid chromatography (HPLC) to purify a compound strongly active against *Candida albicans*. Using high-resolution mass spectrometry, I determined the mass of this potentially novel compound to be 457.2910 m/z. With a sample of purified compound, future analytical chemistry will yield an accurate $^1$H-NMR spectrum, and attempts at x-ray crystallography may exactly determine a chemical structure for this bioactive natural product. Characterization of bioactivity against strains of drug-resistant *Candida albicans* will be completed through ongoing experimental collaboration with the director of Infectious Disease at the Cincinnati Children’s Hospital, Margaret Hostetter. Through final characterization of the bioactivity of this compound and characterization of its chemical structure using $^1$H-NMR and x-ray crystallography, I hope to discover a novel natural product that is strongly active against the human pathogenic yeast fungus *Candida albicans*. 
Quantifying c-Fos in VTA DA Cells in Relation to Reward-Related Learning
Karen Kest¹, Dan Hong Chen²*, Ivonne Cruz², Robert Ranaldi²
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²Department of Psychology, Queens College, NY

Neutral stimuli associated with unconditioned stimuli (USs) acquire the ability to act as conditioned stimuli (CSs), which can elicit behaviors similar to the US with which they are associated. The mechanisms by which this occurs are not fully known. We have previously proposed that the US and CS signals converge on dopamine (DA) cells of the ventral tegmental area (VTA), where coincident activity leads to strengthening of CS synapses and the acquisition of the ability by the CS to activate VTA DA cells. In the present experiments we hypothesized that a food-associated CS (light) would acquire the capacity to activate VTA DA cells. In experiment 1, rats were allowed to eat or not eat food (US) in a test cage. In experiment 2, rats were trained to retrieve a food pellet after a light presentation (CS) and then tested for the acquisition of the food checking response with only CS presentations. Eating food (US) caused a significantly greater number of VTA DA (TH-labeled) cells to express c-Fos than not eating. Whether light presentations (CS) cause a significantly greater number of VTA DA (TH-labeled) cells to express c-Fos remains to be determined since experiment 2 is still ongoing. Thus far, the findings support our model of convergent US/CS activity in VTA DA cells.

Characterizing Scattering Property of Random Media from Phase Map of a Thin Slice: the scattering-phase theorem and the intensity propagation equation approach
*Mariam Iftikhar¹, Bianca DeAngelo², Grant Arzumanov², Patrick Shanley², Zhang Xu³, and M. Xu²
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We report first a new derivation of the scattering phase theorem and provide, for the first time, the correct relation between the variance of phase gradient and the reduced scattering coefficient. The scattering-phase theorem is then applied to investigate bulk light scattering property from the phase map of thin slices of issue phantoms measured by a differential phase interference (DIC) microscope using the intensity propagation equation approach. The scattering coefficient, the reduced scattering coefficient, and the anisotropy factor of the sample obtained with this approach is compared to known scattering property of the bulk samples.
**Effects of LED and Halogen Operatory Lights on Resin Composite**

Bapanaiah Penugonda¹, Anuja Patel¹, Marie Congiusta³

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² 2nd year Graduate Student, NYU Collage of Dentistry, New York, NY
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The aim of this study was to examine the effects of halogen and LED operatory lights on the curing of resin composite by measuring the hardness after exposure during varying time intervals. The study also investigated the depth of cure by testing the hardness on the top and bottom of specimens of 2mm, 3mm, and 4mm thickness. Specimens were fabricated by molding Ultradent-A1-Amelogen Plus resin composite into three cylinders with diameter of 5mm and thicknesses of 2mm, 3mm and 4mm. These specimens were exposed, from a distance of 2.5 feet, to 4 different operatory lights: A-Dec 571 halogen, Pelton-Crane SP18 LED (high, medium and low intensity), and Capsera 5500K and 4500K LED (high and low intensity). Specimens were exposed to one light source for durations of 3, 5 & 10 minutes to measure curing ability. Barcol Hardness Impressor GYZJ 934-1 was used to measure top and bottom hardness of all 216 specimens of resin composite immediately after exposure. There were significant differences at p < 0.05 level per light source, thickness of specimen, and exposure time using the SPSS three-way analysis of variance. All LED light sources at low intensity did not cure resin composite regardless of exposure time or specimen thickness. Halogen light exhibited highest BH profile for most thicknesses and exposure durations, followed by Pelton-Crane (PC)-SP18 LED (high intensity). Capsera 5500K LED (high intensity) had lower BH profile than halogen and PC-SP18 (high intensity), followed by PC-SP18 LED (medium intensity).

**Conformational Study of trans-1,2- and cis-1,3-Cyclohexanedicarboxylic Acids in Water and DMSO Using NMR Spectroscopy**

Alejandro J. Garza¹*, Mrinmoy Nag², William Carroll², John D. Roberts²

¹ Departamento de Química, Tecnológico de Monterrey, Monterrey NL, Mexico
² Department of Chemistry, California Institute of Technology, Pasadena, CA

Carboxylic acid groups in cyclohexane rings are generally believed to be far more stable (~2 kcal/mol) in equatorial than axial positions because of 1,3-syn-diaxial repulsions. In this work, we determined the populations of diaxial (aa) and diequatorial (ee) conformers present in trans-1,2- and cis-1,3-cyclohexanedicarboxylic acids (CDCAs) and their salts in water and DMSO, and demonstrated that a diaxial conformation (normally assumed to be completely insignificant for these compounds) might be favored depending on solvent properties and ionization state. Using vicinal proton-proton NMR coupling constants ($^3J_{HH}$), in conjunction with the Karplus and Altona equations, we found a strong preference for the diequatorial conformer (>90% ee) in water and DMSO for both diacids and their salts, except for the trans-1,2-dianion in DMSO, which was found to be substantially diaxial (55% aa). Additionally, the ratios of the ionization constants ($K_1/K_2$) for these diacids in water indicated an absence of intramolecular hydrogen bonding ($K_1/K_2 < 10^4$) for both diacids, and the case was the similar for the cis-1,3-CDCA in DMSO. However, this ratio increases drastically for the trans-1,2-isomer in DMSO ($K_1/K_2 = 2 \times 10^6$), whose monoanion appears to be hydrogen bonded in this solvent.
Detection of Significant Sub-Cluster in Biological Data
Guoli Sun
Department of Applied Mathematics & Statistics, Stony Brook University, Stony Brook, NY

Hierarchical Clustering (HC) allows one to reveal and visualize relations between complex, multi-dimensional data items, and to explore data for sub-clusters, without specifying the number of sub-clusters in advance. For this reason, HC is widely used in biology. However, identification of distinct sub-clusters in biological applications of HC is predominantly qualitative and intuitive. Therefore, a novel quantitative statistical method is developed for identifying significantly distinct sub-clusters (branches) of a hierarchical tree. Among potential applications of the method is phylogeny of tumor cell population and gene expression profiles.

Determine the role of miR-17~92 cluster of microRNAs in Myc-induced B cell lymphomas
Ping Mu1, Yoon-Chi Han1, Doron Betel2, Aleco D’Andrea1,4, Evelyn Yao1, Massimo Squatrito1, Paul Ogrodowski1, Elisa de Stanchina3, Chris Sander2 and Andrea Ventura1
1Cancer Biology and Genetics Program,
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The miR-17~92 cluster is frequently amplified or overexpressed in human cancers and has emerged as the prototypical oncogenic polycistron microRNA. miR-17~92 is a direct transcriptional target of c-Myc and experiments in a mouse model of B cell lymphomas have shown cooperation between these two oncogenes. However, both the molecular mechanism underlying this cooperation and the individual miRNAs that are responsible for it, are unknown. By using a conditional knockout allele of miR-17~92, we have previously shown that sustained expression of endogenous miR-17~92 is required to suppress apoptosis in Myc-driven B cell lymphomas. Furthermore, we have shown that among the six miRNAs that are encoded by miR-17~92, miR-19a and miR-19b are absolutely required and largely sufficient to recapitulate the oncogenic properties of the entire cluster.

To further characterize miR-19a and miR-19b functions, we have now generated knock-in mice carrying targeted deletion of these two miRNAs. By crossing miR-17~92\textsuperscript{Δ19a,19b} knock-in mice to Myc-driven mouse models of human cancer we are now investigating the role of these two miRNAs in tumor initiation and progression.
Project Category: Orthopaedic Surgery and Hip and Joint Biomechanics

Developing a Cadaveric Model of Femoroacetabular Impingement: Preliminary Results on Pubic Symphysis Biomechanics

Robert Jacobs¹*, Bryan Kelly², Linda McGrady¹,³, Mei Wang¹,³, Patrick Birmingham¹
¹ Department of Orthopaedics, Medical College of Wisconsin, Milwaukee, WI
² Department of Sports Medicine, Hospital for Special Surgery, New York, NY
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Athletic pubalgia (sports hernia) is pain manifested at the pubis due to microtears of the attached musculature from abnormal pubic motion. Cam-type Femoroacetabular Impingement causes hip-labral tears and osteoarthritis, but has not yet been linked to athletic pubalgia. Developing a novel, full tissue, cadaveric model to investigate if FAI causes athletic pubalgia by causing motion of the pubic symphysis can show that FAI causes athletic pubalgia.

FAI was simulated by implanting a wooden bump at the femoral head-neck junction. 3D motion sensors were placed on a complete pelvis and femur to measure any relative motion across the pubic symphysis generated from internally rotating the femur at 90° flexion and neutral adduction via an Optotrak motion capture system. A 6-axis load cell was mounted at the distal femur to measure the torque needed to generate internal rotational angles. A miniature pressure sensor was placed in the pubic symphysis to monitor the force generated from the internal torque.

Preliminary results of one specimen, age 57, show artificial FAI causes exponential increase in symphysis pressure with internal rotation. Symphysis motion showed a relative downward rotation of 2.72° in the coronal plane and a 1.52° outward rotation in the transverse plane at maximum internal femur rotation of 50°.

This model can be used to quantify the biomechanical effects of FAI and hip version on the pubic symphysis. This model can also be used to study FAI size effect on symphysis motion, sacroiliac motion due to FAI and other pelvic joint biomechanics.
Dietary Shifts in the Ontogeny of Green Turtles (Chelonia mydas) in the Central Pacific

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Juvenile green turtle (Chelonia mydas) recruitment from pelagic to neritic developmental grounds is thought to coincide with a shift from omnivory to herbivory. The individual and population level variability of this ontogenetic shift has not been extensively studied. Palmyra Atoll National Wildlife Refuge, a remote uninhabited atoll in the Central Pacific, serves as a major foraging ground for green turtles. However, little is known about the ecology of this population. Stable carbon and nitrogen (δ13C and δ15N) isotopes provide information on diet and trophic position offering a tool to understand the foraging behavior of the Palmyra Atoll green turtle population.

Posterior (oldest tissue) and anterior (youngest tissue) scute samples were collected from live-captured green turtles (2008 to 2010). Juvenile (<60 cm), sub-adult (60 cm – 85 cm) and adult (85 cm ≤) classifications were determined using curved carapace length. Anterior scute samples were used to determine prey type (invertebrate, macroalgae, turf algae, etc) contributions to size class diet using mixing models. In addition, successive 50 µm layers were removed from each juvenile posterior scute sample allowing for an examination of resource use over time. Analysis of these layers will provide insight on the timing of ontogenetic shifts. Using δ13C and δ15N ratios to determine the spatial and temporal variation in sea turtle foraging habitat will help fill an important gap in our knowledge of sea turtle ecology. This study will also provide insight on the variation in ontogenetic diet shifts of juvenile green turtles as they recruit to neritic foraging grounds.

Differentiated CAD Cells as a Model System to Study Slit Signaling

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In the developing nervous system there are several principal processes, one of which is axon growth and guidance. Axon guidance involves the extension of axons to specific targets in response to attractive and repulsive extracellular cues. Although previous studies have identified many highly conserved families of guidance molecules, such as Ephrins and Slits, the specific intracellular signal transduction pathways downstream of these cues are not fully understood. The present study has identified CAD cells, a homogenous cell line derived from a mouse brain tumor cell line, as a model system to study signal transduction of the repulsive cue, Slit. First, RT-PCR study has revealed that both differentiated and undifferentiated CAD cells express Robo1 and Robo2, two receptors for Slit. In addition, ectopically expressed Robo1 was observed to be localized to the nerve growth cone, where Slits act to repel axons. Importantly, neurite outgrowth from differentiated CAD cells was inhibited by Slit2 in a dose-dependent fashion, which could be reversed by the addition of the Robo-Fc to the medium. Together, these findings suggest that CAD cells could be used as a model system for the study of Slit-Robo-mediated signal transduction.
Dissociating the Roles of the Cerebellum and Motor Cortex During Adaptive Learning

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Adaptation to a novel visuomotor transformation has revealed important principles regarding learning and memory. Computational and behavioral studies have suggested that acquisition and retention of a new visuomotor transformation are distinct processes. However, this dissociation has never been clearly shown. Here, participants made fast reaching movements while unexpectedly a 30-degree visuomotor transformation was introduced. During visuomotor adaptation, subjects received cerebellar, primary motor cortex (M1) or sham anodal transcranial direct current stimulation (tDCS), a noninvasive form of brain stimulation known to increase excitability. We found that cerebellar tDCS caused faster adaptation to the visuomotor transformation, as shown by a rapid reduction of movement errors. These findings were not present with similar modulation of visual cortex excitability. In contrast, tDCS over M1 did not affect adaptation, but resulted in a marked increase in retention of the newly learned visuomotor transformation. These results show a clear dissociation in the processes of acquisition and retention during adaptive motor learning and demonstrate that the cerebellum and primary motor cortex have distinct functional roles. Furthermore, they show that it is possible to enhance cerebellar function using tDCS.

Effect of Fear on Perception of Height and Distance

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The current study observed the role of trait fear in people’s perceptions of vertical and horizontal distances. In this study, we measured height estimates when viewed from above (i.e., looking down) and distance estimates when viewed horizontally (i.e., looking straight ahead). Multiple measures were utilized to evaluate both types of distances and multiple questionnaires were used to measure participants’ fear of heights (acrophobia), enclosed spaces (claustrophobia), and open spaces (agoraphobia). We found that participants overestimated vertical distance, whereas they underestimated horizontal distance. There was a significant correlation between horizontal estimates and claustrophobic fear, even after accounting for acrophobic and agoraphobic fears. Specifically, participants who reported greater claustrophobic fear showed greater underestimation of horizontal distance. This finding is especially interesting given that participants were tested outdoors, suggesting that claustrophobic fear may affect the perception of distance even when spaces are not enclosed.
Effects of Chronic Oral Methylphenidate Treatment and Abstinence on Body Weight, Food Intake, Open Field Activity, Circadian Activity, and Novel Object Recognition

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Methylphenidate (MP; Ritalin) is a psychostimulant used to treat Attention Deficit Hyperactivity Disorder (ADHD) that has received attention for possible developmental and behavioral side effects that may persist beyond treatment. Male Sprague-Dawley rats were split into three groups (n=24/group) at 4 weeks of age: control (water), low dose MP (LD), high dose MP (HD). MP was given orally using a dual bottle 8-hour limited access drinking paradigm: 4 mg/kg MP (LD) or 30 mg/kg MP (HD) during hour 1, and 10 mg/kg (LD) or 60 mg/kg MP (HD) hours 2-8. Following 13 weeks of treatment, half of the rats in each group were subjected to behavioral testing [novel object recognition (NOR) and circadian activity]. Remaining rats went through a 5 week abstinence period, followed by behavioral testing. Food intake and body weight were recorded, as was open field activity weekly. MP dose-dependently decreased body weight during treatment. During abstinence, body weights of HD rats rebounded to that of LD rats; neither MP group returned to control weights. MP decreased food intake during treatment, specifically during earlier weeks. Circadian activity results showed that HD MP increased activity in the dark (active) cycle. Following abstinence, dark cycle activity levels decreased but remained elevated over controls, corroborating open field findings of MP-induced hyperactivity. HD MP increased center activity during treatment, suggesting an anxiolytic effect. HD MP also decreased rearing activity, suggesting reduced exploratory behavior/reactivity to or preference for novelty; this is in agreement with the dose-dependent decrease in NOR observed during MP treatment.

Effects of Embryonic Exposure to Nicotine and Anoxia on Autonomic Innervation of the Heart

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Embryonic nicotine exposure and possibly oxygen deprivation can result in decreased sensitivity of nicotinic acetylcholine receptors (nAChRs). Over 16.7% of women smoke during pregnancy, despite evidence that smoking is correlated with Sudden Infant Death Syndrome. Acetylcholine (ACh) normally slows the heart’s contraction rate (HR). If nicotine and/or anoxia exposure during heart development in chick embryos decreases sensitivity to nAChRs, the heart’s response to ACh should be reduced. Chick embryos were treated with 50 µL of 0.05M nicotine (N), 1.5 hours of anoxia (A), both (N-A), or neither (C) at Hamburger-Hamilton developmental stage 25. One day later, resting HR was recorded and compared to HR immediately after dropwise application of 0.007M ACh. Compared to C embryos (n=36), the average resting HR of N exposed embryos was 6.5% higher (n=29), N-A 4.2% higher (n=30) and A only 1.8% higher (n=32). The N and N-A groups showed an 11% decreased sensitivity to ACh when compared to C embryos. These values were all significant at p<0.05. Heart dissections revealed no significant differences in the cross-sectional area or perimeter of the heart. However, the diameter of the outflow tract was 16% narrower in N embryos than in C embryos. These results suggest that embryonic exposure to nicotine adversely affects cardiovascular development, but that a short interval of anoxia during heart development in chicks is not seriously detrimental.
Effects of Lead and Mercury on the Blood Proteome of Children
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Heavy metal exposure in children has been associated with a variety of physiological and neurological problems. The goal of this study was to utilize proteomics to enhance the understanding of biochemical interactions responsible for the health problems related to lead and mercury exposure at concentrations significantly below CDC guidelines. Blood plasma and serum samples from 34 children were depleted of their most abundant proteins using antibody-based affinity columns and analyzed using two different methods, LC-MS/MS and 2-D electrophoresis coupled with MALDI-TOF/MS and tandem mass spectrometry. Apolipoprotein E demonstrated a significant association with lead concentrations (average being one microgram/deciliter) as deduced from LC-MS/MS and 2-D electrophoresis and confirmed by Western blot analysis. Fifteen other proteins were identified by LC-MS/MS as proteins of interest exhibiting expressional differences in the presence of environmental lead and mercury. Serum proteins directly binding to lead are currently being investigated. The study is the first in the field of proteomics to study toxicology of heavy metals in blood in a general population of children. It is the first to statistically relate a cardiovascular protein Apolipoprotein E with sub-clinical blood Pb levels, as per CDC guidelines. These findings also support previous evidence from our group that have associated lead exposure in children with an increase in risk factors related to cardiovascular disease.

Effects of Red-Cone Photoreceptor Loss on Photoreceptor-Horizontal Cell Connectivity in Zebrafish Retina
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The retina is responsible for the initiation of visual information processing. Photoreceptors first detect light, and the visual information is transmitted to bipolar cells, ganglion cells, and eventually to the visual cortex of the brain. To assist in detecting light contrast and possibly color, horizontal cells modify the data stream along specific photoreceptor-bipolar cell synapses. In zebrafish, the four horizontal cell types each synapse to a pre-determined photoreceptor type. The Dowling lab is interested in the maturation of the retina at the molecular level. Of particular interest is the partial optokinetic response b (pob) gene, a recently discovered gene that renders homozygous recessive mutant zebrafish blind to red light. In these mutants, red-light sensing cone photoreceptors form at 3 days post-fertilization (dpf) but die by 5 dpf. However, the secondary effects that pob mutation has on the horizontal cells have yet to be explored. By inducing only red-sensitive cone death, the pob mutation can present insight into whether horizontal cells are dependent on their photoreceptor for survival, whether they can alter their photoreceptor connectivity should their pre-determined photoreceptor die, or whether they take an alternative action. It is hoped that increasing our understanding of retinal development and possible plasticity will yield information into the structure and ultimately the mechanics of the visual information pathway.
**Electron Spin Resonance Dating (ESR) Deep Sea Sediment: A Core Analysis of Benthic Foraminifera**

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Foraminiferal analyses can provide data about changes in ocean chemistry, circulation, and world climate, if they can be dated accurately. Reliable dating requires dates from at least two different methods, but foraminifera (forams) older than 50 ka can currently only be dated by $^{230}$Th/$^{234}$U, if they contain enough U. Electron spin resonance (ESR) dating can date calcite from planktonic forams, molluscs, and corals up to at least 200 ka, but ESR has not been tested on benthic forams. ESR dating uses a radiation-sensitive signal formed in the mineral in response to sedimentary and internal radiation. A new protocol for ESR dating forams was developed using two samples of *Nuttalides umbonifera* and *Cibicidoides wuellerstorfi* specifically picked for ESR dating from Core EW9209-1JPC drilled on the Ceará Rise, central Atlantic. Although the samples are still being ramped to improve the accuracy of accumulated dose calculation, BF1 (478-492 cm depth) yielded a LU age of 250 ± 96 ka, while BF2 (560-570 cm) dated at 171 ± 19 ka. These ages agree well with the known ages for the sediment at these core depths. Although other tests will ascertain the reliability of this new application generally, these are the first successful ESR dates using benthic foraminifera.

**Elucidating the mechanism of Mesenchymal Stem Cell retention in capillaries after systemic injection**

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Mesenchymal stem cells (MSCs) or bone marrow derived stromal cells have the ability to differentiate into osteocytes, chondrocytes and adipocytes, among others. Their minimal immunogenic response, convenient isolation and ability to expand in culture make them excellent candidates for use in regenerative medicine. MSCs are being tested in over 100 clinical trials for treatment of a variety of diseases including bone, cartilage and cardiovascular diseases. However, these trials have led to mixed results due to lack of efficacy. This is in part due to the immediate retention of MSC in the microvasculature of the lungs, liver, kidney, and spleen, leaving < 1-2% free to target damaged tissues. MSC retention can be attributed to size, deformability, or adhesion. Since MSCs are defined by their adhesive properties, we investigated the role of adhesion in MSC retention, which was previously a challenge given that there are multiple adhesive interactions that mediate MSC-endothelial cell interactions. To address this, we developed a novel approach to abolish the adhesive properties of MSCs by conjugating a protein repellent polymer (Poly Ethylene Glycol) to the surface. On testing our engineered cells in vivo, we observed that non-adherent MSCs had similar blood residence time and tissue distribution to unmodified MSCs suggesting that cell adhesion is not a major contributor towards microvasculature retention. We are currently investigating the role of MSC size and deformability as potential factors for microvasculature retention. These experiments will help us elucidate the mechanism for MSC entrapment and successfully develop novel therapeutic approaches for delivery strategies.
Experimental Study of the Onset of Nucleate Boiling in a Prototypical Research Reactor Coolant Channel
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A major obstacle for converting remaining highly enriched uranium (HEU)-fueled research reactors to low enriched uranium (LEU) fuel is that conversion will result in a loss of reactor performance. One method for improving core performance with LEU fuel is to increase the power level of the reactor. However, in research reactors using plate-type fuel elements, power density is limited by constraints on heat removal, with the limiting criterion being the onset of nucleate boiling (ONB). This research project investigates the onset of nucleate boiling in an MITR-II coolant channel. Experiments are performed using a flow loop with a test section prototypical of flow channels found in high performance research reactors. With the use of high speed video, the heat flux and temperature at ONB are determined for typical research reactor conditions, i.e. a mass flux of around 2000 kg/m²·sec and a subcooling of about 60 °C at atmospheric pressure. Results are compared to predictions such as that found with the Bergles-Rohsenow correlation. In general, such correlations are found to be overly conservative, which may allow for power uprates in plate-type research reactors. This would provide for more incentive to transition to LEU fuel, thereby reducing proliferations risk worldwide.

Exploring Gastric Cancer Oncogenes using Cultured Models of the Stomach
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Heliobacter Pylori (H. Pylori) is a Gram-negative bacterium that can inhabit various locations in the stomach and is responsible for ulcers and some cases of stomach inflammation. H. Pylori is also capable of producing cytotoxin associated protein A (CagA). Individuals infected with CagA positive H. Pylori show increased risk of developing gastric cancer. To determine the role of CagA in gastric carcinogenesis, recombinant retroviruses that express CagA were constructed. Cultures of wild-type gastric cells were then infected with the CagA retroviruses to elucidate whether CagA alone is sufficient to cause altered cell morphology. Independent review by a pathologist, as well as immunofluorescence and immunohistochemistry will verify cell transformation. To further ascertain CagA’s role in the development of gastric cancer and the relationships between CagA and other tumor suppressor oncogenes, we plan to transform gastric cells that have a mutation in p53 and/or constitutively active KRas in order to see whether CagA has a role in gastric carcinogenesis in conjunction with other mutations.
Flexible Hybrid Cystoscopy/Optical Coherence Tomography for Early Bladder Cancer Diagnosis and Guided Tumor Resection

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Early diagnosis is crucial to the cure of bladder cancer. Cystoscopic optical coherence tomography (COCT) is a new technique that enables noninvasive and high-resolution cross-sectional imaging of bladder in vivo. Results of our preclinical and clinical studies revealed that MEMS rigid COCT was able to significantly enhance white-light cystoscopy for early bladder cancer diagnosis and tumor resection. To further explore COCT for outpatient diagnoses of early bladder cancers and other urological diseases, we developed a new flexible OCT catheter which is fully compatible with commercial flexible cystoscopes. Fig 1 illustrates our newly designed flexible COCT. With a miniature high-speed linear translation stage, the side-view COCT probe provides a large field of view (e.g. 8×2mm²) per OCT scan. Since the probe size is only φ2mm, it can be inserted in the instrument channel of a commercial flexible cystoscope and guided by white light for bladder imaging and tumor diagnosis.

![Fig. 1 – Flexible COCT probe (φ2mm)](image1)

![Fig. 2 – COCT image to show a TCC (left) and normal bladder wall (right); U: urothelium; LP: lamina propria; M: muscularis)](image2)

Fig 2 exemplifies an in vivo clinical result acquired by flexible COCT. The high resolution (~10µm) and large field FOV (8×2mm²) of the flexible probe allow physicians to image the transition between normal bladder and the lesion to better diagnose TCC and identify the margin to assist tumor resection. The large field of view, high resolution and the flexibility render it a potential candidate for enhancing bladder cancer management in the future.
Highly Effective Essential Oils Prevent Spread of Methicillin Resistant Staphylococcus aureus (MRSA) and Methicillin Sensitive Staphylococcus aureus (MSSA) in Hospital Admitted Patients

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Methicillin Resistant Staphylococcus aureus (MRSA) is a staph bacterium resistant to strong antibiotics classified as beta-lactams, such as oxacillin, penicillin and amoxicillin. Methicillin Sensitive Staphylococcus aureus is a type of staph infection that is moderately sensitive to antibiotics. Hospital acquired MRSA (HA-MRSA) is typically contracted by patients who have invasive medical procedures or weakened immune systems; HA-MRSA infections can cause severely life threatening complications, such as bloodstream and surgical site infections or pneumonia. Previous research conducted with 54 essential oils revealed excellent antibacterial activity with seventeen of these oils. The seventeen oils were further tested on four known strains of MRSA, as well as MSSA and Methicillin Resistant Staphylococcus epidermidis. Ten of these oils proved to have excellent antibacterial activity on three out of the four strains. These ten oils were also tested on 12 patient samples which included MRSA and MSSA. Plates with Mueller-Hinton II medium were overlaid with each of the 12 patient samples. Sterile blank discs (6 mm) saturated with 5 µL of each of the ten oils and a disc containing the antibiotic standard vancomycin (30 µg) was positioned on the plates. Diameters of zones of inhibition were measured after 24 hours of incubation at 37°C. Based on this study, all ten oils showed higher effectiveness inhibiting MRSA and MSSA growth than vancomycin, which is the currently used standard for treatment. Essential oils could be particularly beneficial towards treating hospital patients with MRSA or MSSA infections in underdeveloped countries where antibiotics are not readily available.

Immunohistochemical Analysis of Proliferating Skin Micrografts in a Full-Thickness Porcine Wound Model

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Regeneration of skin after major burns and other trauma wounds is a major obstacle of clinical treatment. The common six-fold skin expansion ratio used clinically is often not sufficient to cover the defect. In a pig model we have previously shown that minced skin micrografts can regenerate the epidermis when transplanted in a 100-fold expansion ratio in a wet environment, independent of orientation (dermal side up or down). On post-operative day 14, transplanted wounds showed 100% re-epithelialization, while the un-transplanted control group showed only 56% re-epithelialization (p<0.0001). In the current study the migration and proliferation process of micrografts was illustrated using immunohistochemical staining methods. A Ki-67 and pancytokeratin assay showed proliferation of the basal keratinocytes within the micrografts. Using a tri-chrome staining, the transplanted collagen-rich dermal component of the micrograft was viewed being expelled from the wound through the epidermis by post-operative day 14. The number of blood vessels in the wounded tissue was compared using antibodies directed against the endothelial marker Von Willebrand factor (vWF). On post-operative day 10 there were 3.0±0.2 vessels per mm² in the subepidermal plexus of the transplanted wound compared to 1.7±0.5 in the non-transplanted control wounds (p<0.005). No statistical difference was observed in wounds 21 or 123 days after transplantation. A basement membrane was identified using a collagen IV staining as early as day 6 after transplantation. Combined these immunohistochemical stainings demonstrate that micrografts migrate and proliferate in a wet environment, independent of orientation, on the bottom of the wound.
Testing the waters: a closer look at the physical chemistry of Fairfield University’s storm water effluent

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The objective of this project is to monitor physical and chemical parameters of surface waters on the campus of Fairfield University. Beginning in 2009 a set of nine monitoring sites was established within the campus watershed. A database of site specific and overall water quality is continually updated with weekly monitoring of phosphorous, nitrogen, dissolved oxygen, salinity, conductivity, temperature, and pH. This database is being used to evaluate current landscaping and maintenance practices (snow management, lawn fertilization, landscape maintenance) for their effects on water quality. We are also using the database to monitor acute impacts of current construction projects on campus. Student researchers have received additional training to expand monitoring to include coliform bacteria, protist diversity, and C/BOD that will begin in Fall 2011. This project is serving as a model of community engaged scholarship (CES) as one approach to achieve Fairfield University’s strategic goal of integrating living and learning at the undergraduate level.

Insights into Oncogene Addiction in Melanoma

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Melanoma, most aggressive type of skin cancer, is highly resistant to chemotherapy. Oncogene addiction is observed in many types of cancer, including melanoma, in which cells develop an addiction to a particular gene, and the disruption of this oncogene can cause sudden death in tumor cells. In approximately 60% of melanoma patients the tumor cells are addicted to BRAF oncogene due to V600E mutation, which allows mutated cells to bypass normal cell-cycle checkpoints and proliferate uncontrollably. Recognition that the survival mechanism of melanoma cells can be effectively inhibited through MEK inhibition can lead to insights into the possible mechanisms for melanoma drug resistance.

An imbalance between the expression levels of pro- and anti-survival proteins creates an oncogenic shock resulting in cell death. In melanoma cell line WM239A response to MEK inhibitor resulted in a shift from survival to apoptosis at 12hrs after the treatment, shown by down-regulation of p-AKT, NFkB RelA and mcl-1 and up-regulation of bim. Apoptosis was evident from the cleavage of PARP and caspase-3. This implies that the melanoma cells, oncogene-addicted to MEK/ERK, shift to AKT pathway when ERK levels are repressed. Next, high cellular apoptosis might be obtained if the cells are first treated with a basal amount of MEK inhibitor and then with a higher concentration of inhibitor. This approach is based on the hypothesis that a smaller amount of MEK inhibitor would induce a constant ERK expression, and then treatment with a higher concentration might be more effective in disrupting the oncogenic pathway.
**Project Category:** Biochemistry and Ribosome Studies

**Investigating Inhibition of Prokaryotic Translation by Natural Products from Rainforest Endophytes**

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Identifying and characterizing natural products that inhibit biochemical processes such as ribosomal translation has long been valued as a means of elucidating cellular mechanisms and providing novel sources of molecular therapeutics. The search for novel antibiotics has identified many clinically essential small molecule prokaryote-specific ribosome inhibitors and provided insight into the structure and function of the ribosome. Regulation of eukaryotic protein synthesis has become a novel target for cancer therapies and antiviral agents. In this study, natural products from Ecuadorian rainforest endophytes were screened in a luciferase DNA transcript-based translation and detection assay using E. coli ribosomal extracts in an attempt to identify novel inhibitors of prokaryotic protein translation. Potential inhibitors were then subject to a transcription inhibition counterscreen to rule out inhibition due to transcription disruption and/or general nucleic acid intercalation or binding.

**Project Category:** Biology and Genetics

**Investigation of the Presence of the Risk Taking Gene in Winter Athletes Competing in Lake Placid, New York**

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The study being conducted is the investigation of the Risk Taking/Thrill Seeking gene, DRD4, within the genomes of winter athletes competing in Lake Placid, New York. The project consists of collecting DNA samples from these winter athletes by having each athlete, who is willing to partake in the experiment, sign a consent form allowing the use of their DNA. Samples collected have included members of international bobsled and skeleton teams and non-competitive individuals serving as controls. The procedure has been accepted by the Committee on the Protection of Human Subjects (COPHS). Participants will swish a 0.9% saline solution in their mouths, and then expel the solution into 50ml conical tubes with corresponding numbered labels. DNA samples will be amplified using the polymerase chain reaction (PCR) technique. The participants’ DRD4 genes will be analyzed for the number of tandem repeats, indicative of the Risk Taking/Thrill Seeking behaviors. Analysis will include use of an Agilent Bioanalyzer and a Molecular Gel Documentation System. Data will allow an extension of a 2010 project involving a snowboarder population from Whiteface Mountain, Lake Placid, New York.
Isolation and Purification of Metalloproteinase Inhibitors from Small Mammal Prey of Venomous Snakes

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The purpose of this study was to isolate and purify the protein responsible in the California ground squirrel (Spermophilus beecheyi) for inhibiting snake venom metalloprotease (SVMP) activity. While current clinical treatment to snake bites relies on the use of antibodies harvested from inoculated domestic animals, our goal is to characterize innately expressed S. beecheyi SVMP inhibiting proteins as a novel alternative lead for snake venom therapy. A Bio-Rad BioLogic DuoFlow chromatography system was used in multi-step purification strategy in order to isolate and concentrate protective serum proteins from whole blood. The first phase is affinity chromatography on a HiTrap Blue column. Fractions containing inhibitory activity are further separated using anion exchange chromatography on a UNO Q1 anion exchange column. This step has isolated serum proteins from S. beecheyi that inhibit metalloproteinases in the venom of the sympatric northern pacific rattlesnake (Crotalus oreganus oreganus). We are applying this protocol to check for SVMP inhibitors in plasma samples from other small mammals subject to snake predation. We hope to better evaluate the biochemical makeup of these proteins so that innate venom resistance in mammals can be better understood.

Localization of HSP25 and p-HSP25 and Actin in C2C12 Myoblast Cell Development

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C2C12 cells are derived from mouse myoblasts and are capable of differentiating into skeletal muscle in three defined stages: myoblast, early myotube and late myotube. Actin, a cytoskeletal protein, functions in contraction and movement. Heat shock protein 25 (HSP25) is a cytoskeleton-stabilizing molecular chaperone that binds/caps F-actin under cellular stress, preventing depolymerization. HSP25 phosphorylation alters actin dynamics by reducing inhibition of depolymerization. Fluorescence microscopy is used to examine the role of HSP25 phosphorylation on actin filaments during C2C12 myogenesis. We hypothesize that phosphorylated-HSP25 (p-HSP25) would release from actin filaments, thereby affecting HSP25 cellular localization.

C2C12 cells were cultured on coverslips. Cells were imaged at days 1, 3, 5, 7 and 9. Immunofluorescence was used to visualize F-actin (phalloidin) and anti-HSP25/anti-phospho-HSP27ser82. The secondary antibody was goat-anti-rabbit-IgG AlexaFluor 488 and nuclear stain was DAPI. Cells were imaged with a Leica epi-fluorescence microscope for fluorochrome image direct overlay.

Developmental differences in colocalization exist between actin and p-HSP25/unphosphorylated-HSP25 developmentally. Most interesting differences occur between p-HSP25 and HSP25 on days 5-9 of development. P-HSP25 localization at focal points appeared, while HSP25 colocalized with actin at days 5 and 7 and then migrated to nuclear localization on day 9.

Phosphorylation causes a significant change in HSP25 localization. Focal point p-HSP25 localization suggests a focal adhesion plaque function, independent. HSP25 appears to maintain the actin binding function until day 9, and then carries out molecular chaperone functions in the nucleolus. Additional analysis will be done to conclude precise function of p-HSP25 focal point localization.
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Plant community structure and composition can be altered for a number of reasons such as succession, invasion, or changes in climate or hydrology. This study sought to identify community changes that have occurred over the past thirty years in Ausable Marsh, a large, complex wetland on Lake Champlain. Field maps of plant communities from a study in 1978 were digitized in GIS, where random nested plots were generated in each stratum identified. Preliminary results from the first of two field seasons (2010 and 2011) show that Sørensen's similarity index between 7 sampled strata and their 1978 counterparts varied. Overstory similarity was relatively high, with most strata over 60%. Due to lack of reference data, midstory and herbaceous layers could not be compared in all strata. However, in those that could be compared, similarity was low (mostly under 40%) indicating that community changes have occurred in these layers. Among the major changes were the spread of non-native species such as European frogbit (Hydrocharis morsus-ranae L.), which was not present in the baseline data, and purple loosestrife (Lythrum salicaria L.), which greatly increased its range in the marsh. Native species such as wood nettle (Laportea canadensis [L.] Weddell) also increased in abundance. This project will set up a long-term research study that will enhance our ability to record and understand large-scale shifts in diversity and ecosystem function in wetland habitats of the “Sixth Great Lake.” It can also provide critical information in developing a management plan for non-native species in the marsh.

Fabrication of Ultrasharp Carbon Fiber Tips for Scanning Probe Microscopy
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The scanning tunneling microscope (STM) and atomic force microscope (AFM) have greatly contributed to the investigation of material properties at the nanoscale. Both of these instruments use a sharp conducting tip in order to probe the surface at the atomic scale. Since the tip’s physical and chemical properties determine the resolution capacity and stability of the measurement system, several techniques have been developed to fabricate these probes. We will describe the use of a single sharpened carbon fiber as a probing tip. We start with a commercially available carbon fiber with an 8 µm diameter. We will describe an electrochemical etching setup by which these tips can be sharpened cleanly to below 50 nm. Our setup uses two films of etchant suspended in stainless steel electrodes that are vertically separated. This technique has the advantage that the etching process is stopped as soon as the tip separates into two parts, yielding a smooth, sharp apex. We will describe the use of these tips in both AFM and STM instruments.
MicroRNA Expression Through Muscle Stem Cell Fate Decisions
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Postnatal growth, maintenance and repair of skeletal muscle is performed by rare adult stem cells, termed satellite cells, that are maintained as a quiescent stem cell population. Upon muscle injury satellite cells rapidly activate, a dynamic process involving differential expression of over 4,000 genes. Though transcriptional control likely accounts for some of this, post-transcriptional regulation has recently been found to play an important role. One such mechanism is microRNA (miRNA) mediated gene silencing. MiRNAs are a novel class of small (18-22 nucleotides) non-coding RNAs that act as post-transcriptional regulators. MiRNAs associate with the RISC-complex, guiding the targeting of complementary mRNAs and leading to their translational inhibition and degradation. Prior computational analysis predicted a number of miRNA candidates, and additional research narrowed this group to 12 potential regulators. MiRNA expression was assayed in whole muscle as well as isolated satellite cell samples at specific time points selected to model key events and fate decisions in satellite cell activity: namely activation, commitment and proliferation. Whole muscle samples were obtained from the tibialis anterior of wild-type mice post-injury following local injection of BaCl_2 while activated satellite cells were isolated and cultured. Quantitative PCR (qPCR) analysis of all samples was performed in triplicate using perfectly complementary miRNA primers. Analysis of qPCR data revealed differential expression patterns that correlated with published data for select miRNAs, and in addition new expression patterns in miRNAs previously uncharacterized in satellite cells. Furthermore, novel comparative expression patterns in both whole muscle and satellite cell samples were observed.

Migration Aids Pathogen Persistence
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Viruses frequently mutate to gain the ability to infect new hosts; however virus emergence (defined as sustained, epidemic infection), is rare in nature. This experiment aims at understanding the patterns of viral growth in new host population. Recent reports suggest that new hosts represent sink habitats for emerging viruses. Here, effects of virus migration into sink populations is determined by establishing simple models of sink and source populations that mimic pathogen and host interactions in nature. It is hypothesized that migration is positively correlated with evolutionary adaptation in sinks. Hypothesis was tested by manipulating the rate of migration from sources into sink populations growing on a novel host. Absolute fitness was determined for all treatments following 200 generations of adaptive evolution. Absolute fitness is calculated as W_{abs} = \ln \left( \frac{N_f}{N_i} \right) where initial inocula N_i = 10^5 and N_f is the total number of progeny produced in a overnight culture. Results showing a positive relationship between migration rate and absolute fitness will be construed as support for the hypothesis.
Multiphase Comparison of Period-Luminosity and Period-Color Relations
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**Graduate Institute of Astronomy, National Central University, Jhongli, Taiwan

The Cepheid Period-Luminosity (PL) relation is of paramount importance in Astrophysics in establishing the extra-galactic distance scale that can be used to estimate Hubble’s constant to less than 5% accuracy. Previous work over the last 70 years has indicated that the PL relation is linear. Here we present convincing evidence that the Cepheid PL relation in the Large and Small Magellanic Clouds is a highly dynamic quantity which varies considerably with pulsation phase. For many pulsation phases, it is highly nonlinear. We also find strong evidence of a metallicity dependence.

Nanoparticle-enhanced Photoacoustic Stimulus for Osteodifferentiation
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Aim: A novel nanoparticle-enhanced photoacoustic (PA) effect, for osteodifferentiation of bone marrow derived marrow stromal cells (MSCs) grown on single-walled carbon nanotube (SWCNT) and poly(lactic-co-glycolic acid) (PLGA) composite films is introduced in this study.

Methods: MSCs grown onto glass coverslips, PLGA and PLGA-SWCNT were photoacoustically stimulated for 10 minutes per day for 4, 5 and 9 consecutive days with a 527nm Nd: YLF laser (200ns pulse duration, 10Hz). Three similar groups were used as baseline controls without PA stimulation. For the experimental groups and the baseline controls MSCs were grown in media without osteogenic culture supplement. For the positive control MSCs were grown in media containing osteogenic culture supplement (0.01 M β-glycerophosphate, 50 mg/l ascorbic acid, 10⁻⁸ M dexamethasone) to induce osteodifferentiation chemically.

Results and Discussion: Alkaline phosphate, calcium and osteopontin assays were used for quantifying the osteodifferentiation of MSCs. The PA stimulated groups showed up to 350% increased calcium content compared to the positive control after day 15. The stimulated PLGA-SWCNT group had 130% higher calcium content than the stimulated PLGA group. Compared to the positive control the stimulated groups showed up to 7 folds higher osteopontin content by day 15. Qualitative alizarin red staining of the extracellular matrix further reinforces these results. The study concludes that nanoparticle-enhanced photoacoustic effect could be used to develop biophysical strategies for osteodifferentiation in engineering scaffolds instead of conventional biochemical strategies.
HIV-1 Requires Host Proteins for Successful Infection and Replication: Validation of Candidate Genes Identified in a Genome-Scale RNAi Screen

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Acquired immunodeficiency syndrome (AIDS) has claimed more than 25 million lives since its characterization in 1981. The main causative agent, human immunodeficiency virus (HIV)-1, requires host cell factors for successful infection and replication. Since 2008, three separate groups have performed genome-wide RNA-interference screens with the goal of identifying human genes required for HIV-1 replication and infection. While all three groups discovered ~300 genes with diverse cellular functions, the overlap between the studies was disappointingly low. We conducted our own genome-wide RNAi screen using short hairpin RNA and an HIV reporter virus expressing red fluorescent protein, and discovered 559 mapped genes whose knockdown resulted in a ≥3-fold decrease in HIV reporter infection. Potential genes required for HIV replication were validated using an HIV reporter virus expressing a drug selectable marker. Results indicate that mRNA reduction of DYNLL1, ELP4, and CCDC13 increases resistance to HIV infection, suggesting these genes may be required for HIV replication.

Natural Movement Behavior in the Eastern Chipmunk (Tamias striatus)

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Studies have used the movement and behavior of wild and laboratory animals in various tests, such as open field arenas, hole-board tests or mazes, to determine their personality, or behavioral syndromes. The purpose of this study is to determine the correlation, if any, of the results from these man-made environments and the movement behavior of an animal in its natural habitat. In this trial study, eastern chipmunks, Tamias striatus, are trapped and run through an open field arena and maze to determine a personality score for their movement in these tests. The individuals are then radio-collared, released, and telemetrically located to observe their movement in their natural environment. Initial results have indicated that the six individuals tested at this point score similarly to other studies in their personality evaluations. An activity/boldness temperament trait is suggested from results of the open arena test. Tracking of their wild movement will be resumed in the early spring, when they come out of hibernation. We expect to see a correlation between their movement behavior in the tests and that in the wild. Such a correlation would allow for the movement behavior of animals in the wild to be determined through a simple test. These tests could be used as a tool in conservation efforts to determine the movement of animals, especially those that disperse or migrate and have habitats that are being fragmented.
**Project Category:** Biology and Neurobiology

**Nicotinic Acetylcholine Receptors Mediated Presynaptic Calcium Signaling Along Ventral Hippocampal Axons**

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The main function of the presynaptic neuronal nicotinic acetylcholine receptor (nAChR) is to increase neurotransmitter release and enhance presynaptic transmission. Our research focuses on presynaptic nAChR mediated calcium influx and signaling mechanism in which nicotine and acetylcholine activates nAChRs and enhances glutamatergic synaptic transmission. We developed *in vitro* microslices of subiculum/CA1 region of the ventral hippocampi (vHipp) from wild-type (WT) mice. Neuronal projection fibers were grown from the cultured microslices. The immunostaining data demonstrates that these projections from vHipp can be labeled with pan-axonal marker, identifying those that are axons. Furthermore, these glutamatergic axons could also be labeled with primary and secondary antibodies against several nAChR subunits, including α7, α5, and α4. Our ongoing study focuses on the usage of calcium imaging to find and monitor nicotinic induced calcium signaling on the presynaptic glutamatergic terminals, in which calcium enters or increases within the presynaptic terminal through several direct and indirect mechanisms. This research of neuronal nAChR and its role in calcium signaling relates to the study of schizophrenia, patients of which show a significant dependence on nicotine.

**Project Category:** Biogeochemistry

**Occurrence of Fecal Indicative Bacteria (FIB) in Jamaica Bay: Consequences of Nutrients Loading**

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Increase of both organic material and nutrients in estuaries due to urban anthropogenic activities, poses serious threats. The impact is manifested in enrichment of bacterial activity, and increase in BOD leading to potential oxygen depletion, both in the water column and sediment. This is relevant in coastal area of New York City such as the Jamaica Bay, ~73 sq. km wetland estuary environment, receives large inputs of the nutrients from several point and non-point sources. Improvements in storm water retention infrastructure by the NYC Department of Environmental Protection are expected to reduce the loading of pathogenic bacteria such as fecal coliforms and enterococci. This study attempts to capture the broad spectrum of nutrients and microbial contamination, by periodically collecting samples from various mixing zones (high to low) and locations close to point sources in Jamaica Bay area. Lachet nutrient analyzer and IDEXX method have been used for nutrient analysis and water microbiology respectively. Preliminary scanning of microbe levels in the nearshore surfacewater showed high frequency and range of concentrations. Fecal coliform, Escherichia coli and Enterococci were consistently higher than previously reported. Fecal coliform concentrations were well above the state bathing standard, with a geometric mean of 1200 counts/100 mL. Enterococci concentrations were found to be an order of magnitude higher than previous concentrations at 3 counts/100 mL. Based on these preliminary results, further investigation on water quality, as well as sediment analysis of FIB is required, to understand the extent of nutrients loading and bacterial contamination both temporally and spatially.
**Project Category:** Biomedical Engineering and Cellular Biomechanics

**Osteoblast Precursor Cells Need the Pyrophosphate Transporter ANKH in order to Sense and Respond to Mechanical Stimuli**

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Like virtually all cells in the body, osteoblast cells have a primary cilium protruding outward serving as an antenna, allowing it to receive signals and thereby respond dynamically to its environment. The primary cilium is an extracellular organelle extending outward from the basal body and is built from a microtubule-based cytoskeleton. Osteoblasts are constantly exposed to fluid shear forces from pulsing L-C fluid that is caused by daily physical activity, such as walking or running. The pyrophosphate transporter ANKH is found in the base of the primary cilium. Here we show a preliminary study for the effect of disabling the ANKH protein in primary cilia on flow response to osteogenic markers. Further studies will seek to understand the exact role of the protein as a mediator of mechanosensing in bone cells.

**Project Category:** Biology and Developmental Genetics

**Overlapping but distinct roles of Odd-paired and D-Stat in gene activation during Drosophila segmentation**

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The Drosophila sloppy-paired-1 (slp1) gene provides an attractive model for investigating the mechanisms of regulation by Runt, a member of a transcription factor family with critical roles in animal development and human disease. The slp1 expression pattern consists of 14 two-cell wide stripes in the posterior half of each parasegment in the early Drosophila embryo. Runt works with the Zn-finger transcription factor Odd-paired (Opa), to activate the two-cell wide odd-numbered stripes, but the factor responsible for activation of the even-numbered stripes is not yet established and has been referred to as Factor X.

Embryos that are mutant for opa fail to express the odd-numbered slp1 stripes and also show reduced expression of the even-numbered stripes, indicating that Opa contributes to Factor X activity. We have demonstrated that D-stat, a transcription activator in the Drosophila JAK-STAT pathway, also contributes to Factor X activity.

Previous work in the laboratory identified two distinct upstream cis-regulatory elements that contribute to the expression of the even-numbered slp1 stripes and are thus direct targets of Factor X. We examined the expression pattern of slp1 and different slp1-lacZ reporter genes in embryos that are mutant for opa alone, unpaired (unpaired encodes a ligand that activates the JAK-STAT pathway) alone, and embryos doubly mutant for these two factors. Our result suggests that Opa plays a major role in activating both even-numbered and odd-numbered slp1 stripes while D-stat is able to interact with the distal enhancer of slp1 to activate the even number stripes when opa is not present. We hope that defining the specific roles of Opa and D-stat in slp1 activation will provide a foundation for future studies that are relevant to understanding the roles of homologs of these transcription factors in human development and disease.
**Project Category:** Organic Chemistry and Coupling Reactions

**Picolinamide Derivatives as Ligand for Ullmann Couplings**

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The use of N-phenyl picolinamide with copper powder in aryl homocouplings has been surveyed in order to increase the scope of Ullmann type C-C bond formations. The Ullmann type C-C bond formations are achieved at room temperature with the addition of N-phenyl picolinamide in high yields. Several factors including solvent, time, substrate and copper source are optimized for the use of N-phenyl picolinamide as a ligand. Critical structural features of N-phenyl picolinamide are illustrated by compare yields between differing derivatives.

**Project Category:** Conservation Biology

**Population Genetics of the Asian Golden Cat**

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The Asian Golden Cat (*Catopuma temminckii*) is a small felid native to Southeast Asia. The International Union for Conservation of Nature currently lists this species as “near threatened” due to destruction of its forest habitat as well as poaching. This elusive cat avoids areas of human activity, making it difficult to accurately census. We hypothesized the existence of distinct populations within its range. To test this hypothesis, we analyzed 53 scat samples from Laos, Myanmar, and Bhutan by extracting DNA from each sample, sequencing a small region of four mitochondrial genes (ATP6, 16S, 12S, and CytB), and genotyping 12 microsatellite loci. We also used PCR to determine sex of the scat samples. The genetic program Cervus 3.0 (Kalinowski et al. 2007) revealed 43 distinct individuals. These data allowed us to run multiple population genetic analyses to determine population structure and diversity. Population aggregation analysis, using mitochondrial genes, revealed haplotypes unique to each region. This analysis also showed evidence of gene flow between populations as well as low levels of inbreeding. Microsatellite data allowed us to identify relatedness between individuals, as well as contribute to our understanding of the overall genetic diversity of the populations. Our study is the first population level analysis of Asian Golden Cats using non-invasive genetic techniques. Results from this study will help identify distinct Asian Golden Cat populations and inform conservation strategies designed to protect those unique populations.
**Precursor Chemistry of Narrow Band Gap Nanocrystals and their Morphology dependent Optical Transition**

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Narrow band gap semiconductors are interesting materials for their optical and electronic applications such as field-effect transistor and photovoltaic devices. We study colloidal synthesis of lead chalcogenide nanocrystals, especially focusing on how to design precursors of them to control their morphology, as well as how to understand precursor decomposition and morphology evolution. Nuclear magnetic resonance spectroscopy, absorption spectroscopy, transmission electron microscopy, X-ray diffraction, and thermogravimetric analysis mass spectrometry show how to correlate precursor decomposition and morphology evolution of lead selenide nanocrystals, implying a possible mechanism involving diethylamine as an important by-product. Size and shape dependent optical transition in lead selenide nanocrystals show how we can understand their electronic structures, following their steady-state and time-resolved spectroscopy, and quantum yield measurement. This fundamental study of narrow band gap semiconductor nanocrystals in synthesis, precursor chemistry, materials science, and spectroscopy would open a new opportunity to engineer the properties of materials for a variety of applications.

**Promoting Neural Regeneration in Parkinson’s Disease with C3 Lentiviral Vectors**

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Parkinson’s disease, a degenerative disorder of the central nervous system (CNS), is marked by decreased motor function and coordination because of loss of dopaminergic neurons. Neural regeneration is inhibited in the injured adult CNS due to down regulation of growth factors and complex extracellular inhibitory signals. RhoA GTPase is an important inhibitory signal convergence point, and therefore an attractive therapeutic target. Previous studies have successfully obtained axonal regeneration by inhibiting RhoA with C3 transferase, with limited success due to the enzyme’s poor cellular permeability and short-term expression. This study explored a novel axonal regeneration approach, based on the delivery of C3 transferase into the CNS utilizing lentiviral vectors (FUGW, FU(C3GFP)W, FU(GFP)W, FU(IgkTATC3)W, FU(C32AGFP)W) in order to produce constitutive, sustained cellular expression of C3. Because of overly high rates of C3 expression in vitro, lentiviral vectors were modified to be specifically doxycycline-inducible. Dosage experiments were conducted to identify that 1-2μg/ml of doxycycline was the ideal concentration to use in vitro. Several doxycycline-inducible C3 lentiviral plasmids were constructed, confirmed through sequencing, and successfully transfected into PC12 and 293 T cells. ICC was performed to visualize C3 and/or GFP expression in PC12 and 293 T cells. Morphological changes were observed in cells transfected with C3. Achieving constitutive, sustained production of C3 transferase through plasmid development and subsequent lentiviral generation is an important milestone in exploring the full regenerative and therapeutic potentials of RhoA inhibition.
Regenerative Shock Absorber based on Motion Magnification
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As a vehicle travels down a road, its suspension system is responsible for damping the vibrations induced by the road’s irregularities to achieve rider’s comfort. Typical suspension systems dissipate the vibration energy into wasteful heat energy through fluid frictions or dry friction. As estimated, the amount of energy wasted by all four shock absorbers for a typical passenger car is on the order of 200-1600 watts. By developing a regenerative shock absorber to recover the vibration energy, we could increase the vehicle fuel efficiency by approximately 4%. In this study a regenerative shock absorber has been designed and tested. Unlike the linear electromagnetic prototype we developed previously, here we proposed an improved design by transmitting the linear motion experienced within the shock to rotational motion through the use of a rack, pinion and miter gear assembly. Higher power output and energy density have been achieved.

Relational Memory for Manipulated Scenes in Rhesus macaques
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Relational memory is the ability to associate multiple distinct elements into a coherent representation. Previous studies have shown that human subjects demonstrate relational memory for items in a complex scene by preferentially viewing objects in repeated, altered scenes in comparison to those in unmanipulated scenes. However, amnesic patients who had sustained damage to the hippocampus did not demonstrate this type of memory, indicating that this is hippocampal-dependent. In this study, we examined the ability of Rhesus macaques to demonstrate relational memory by viewing a manipulated region of a repeated scene, compared with a repeated unmanipulated scene. Four head-fixed monkeys performed a free-viewing task where they were presented complex scenes and were allowed to freely view these images for 10 seconds on a 19in CRT monitor. Each trial included two images, a novel image then followed by a repeated scene with or without manipulation. Manipulated images were defined by movement or replacement of an object to a new location or with a novel object, respectively. Eye movements were recorded with an infrared eye-tracking system. We found that monkeys spent more time viewing the manipulated objects than when they were unmanipulated, both when moved and replaced by a new object (p<.001). This effect was significant within 1s following stimulus onset (p<.01), indicating quick recognition of the manipulation. These data demonstrate that monkeys are able to form memories for relational aspects of visual scenes. We are currently investigating the neural signals within the hippocampus that may support relational memory encoding and retrieval.
**Project Category: Neuroscience and Spinal Cord Injury**

**Restoring locomotion after spinal injury: Histological analysis of Neurotrophin-treated spinal transected adult rats**

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Our research shows that rats with thoracic spinal transections, treated with brain-derived neurotrophic factor (BDNF) via an adeno-associated virus (AAV) vector (AAV-BDNF), regain treadmill and overground hindlimb stepping. Stepping ability was never restored in control rats, while rats treated with Neurotrophin-3 (NT-3) walked on the treadmill only with excitatory cutaneous input (tail pinch). Our electrophysiological experiments suggest that recovery of hindlimb stepping may be related to changes in spinal neuron excitability. In particular, AAV-BDNF-treated rats displayed significantly higher motoneuron excitability than controls, whereas AAV-NT-3 rats had reduced excitability, possibly explaining why they required tail pinch to step. Interneurons are less electrophysiologically accessible; therefore we used immunohistochemistry to understand how spinal interneurons are affected by these treatments.

Previous studies show that potassium-chloride cotransporter (KCC2) downregulation enhances excitability by reducing synaptic inhibition. Our histological data in spinal injured rats demonstrates the least KCC2 staining in motoneurons of AAV-BDNF rats, intermediate levels in AAV-NT-3 rats, and the most in control rats. Thus both BDNF and NT-3 may reduce synaptic inhibition and improve stepping. Further studies are needed to link these results to behavioral observations. We plan to combine the use of the KCC2 antibody with another antibody that recognizes the activated form of the BDNF receptor, trkB. Using these techniques we expect to determine which motoneurons and interneurons are activated by BDNF and whether these cells display reduced KCC2. Success in this endeavor will provide better insight into how neurotrophins modify spinal circuits to improve stepping after spinal cord injury.

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**Project Category: Genetics and Reproduction**

**Role of Accessory Gland Proteins in Early Release of Sperm from the Female Reproductive Tract**

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Sperm storage is a universal phenomenon in organisms with internal fertilization. In the fruit fly *Drosophila melanogaster* (D.mel), receipt of proteins originating from the accessory gland of the male reproductive tract (referred to as Acps), are required for females to store sperm. In addition to their role in sperm storage, Acps also orchestrate numerous other female post-mating responses such as inducing ovulation and egg-laying. A D. mel female stores sperm in her seminal receptacle and paired spermathecae. She can store up to 1000 sperm after a single mating. Females who re-mate preferentially utilize the second male’s sperm for fertilization. A recent study has shown that the second male gains this precedence in by causing an immediate release of some of the previously-stored sperm into the lumen of the uterus, followed by physical displacement of some of the remaining sperm from the female’s storage organs. The triggers and mechanism of the initial expulsion are unknown. We wished to determine the potential role of Acps and sperm in this process. To address this, we utilized males expressing a protamine-GFP transgene, which allows easy visualization of sperm nuclei. The expulsion of GFP-sperm was compared in females re-mated to normal (control) males relative to the level of sperm—expulsion in females mated to males we generated that transferred neither sperm nor Acps, or Acps but not sperm, or sperm but only a subset of Acps.
Simultaneous Energy Harvesting and Vibration Control of Civil Structures
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Vehicles and some civil structures, such as tall buildings and bridges are subjected to large vibrations due to the road irregularity and dynamic wind load, respectively. Engineers use viscous damper to dissipate the vibration energy into heat waste, in order to reduce the vibration for the purpose of keeping occupant comfort and safety. Instead of dissipating the energy, we developed an energy regenerative system to recover the energy loss in vehicle and civil structure vibration while effectively reducing the vibration at the same time. It is composed of a retrofit electromagnetic transducer with high energy density, electric circuits and vibration control unit. With the semi-active and self-powered active vibration control algorithms, the vibration mitigation is further enhanced while the energy is harvested. We also estimated the power that we can harvest from the vehicle and civil structures by simulation. We estimated that the energy harvesting in a typical vehicle under normal driving condition is 100 to 400 watts, which can increase the fuel efficiency of a hybrid car by 4-8% and the traditional cars by 2-4%. Typical 10-100KW energy harvesting is expected in the building vibration which varies with the height of the tall building and wind load.

Single-molecule Conductance of Disubstituted Stilbenes
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This poster details the single-molecule electrical measurements of disubstituted stilbenes using STM-based break junctions. Results show that 4,4'-dithiomethylstilbene has an unusually high bias dependence. The interpretation of this result is that the Fermi level or work function of the gold contact electrode is aligned properly with the Highest Occupied Molecular Orbital (HOMO) of the molecule, which allows for resonant tunneling through the system and a greater bias dependence. Further experimentation showed that the 3,4'-disubstituted stilbenes formed molecular junctions and measurable conductance - despite resonance predictions. In this case, the molecules chemically bind to the gold electrodes through both linker groups, but conduct through only the 4-substituted linker group. This experimental evidence broadens our understanding of fundamentals governing single-molecule conductance and may lead to predictive power in single-molecule design.
Site Specific de novo DNA Methylation Markers Regulate the Transcriptional Silencing of Retroviruses by Embryonic Stem Cells

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Embryonic stem cells (ESCs) are potently able to silence retroviral genes following an infection by targeting a highly conserved retroviral primer-binding site (PBS) sequence and subsequently recruiting epigenetic modifiers to block gene expression. A complete understanding of the underlying mechanism of this process may lead to new methods for blocking the effects of retroviral infection in differentiated cells. To assess the role of sequence-specific DNA methylation in the PBS-mediated silencing of integrated proviral DNA by ESCs, both mouse ESCs and mouse fibroblasts were infected with modified Moloney-murine leukemia viruses containing either a wild type or mutant PBS sequence, and sorted based on the virus used in the infection and on cellular expression of a GFP reporter gene delivered by the infecting virus. DNA was extracted from all eight groups and treated with sodium bisulfite. Viral LTRs and structural sequences were amplified and cloned in bacteria. Sequencing analyses of the cloned fragments were then performed, indicating that differing patterns of DNA methylation in the cytidine residues of cytidine-phosphate-guanidine (CpG) islands in these sequences were responsible for the phenotypic variation observed among cell types and groups following an infection. The findings contribute to explaining downstream effects of the PBS-mediated silencing pathway, and further the understanding of gene regulation in ESCs.

Solid State NMR and X-Ray Diffraction Studies of SnF2 and PbF2 as Cathode Materials in Lithium Ion Batteries

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Energy storage systems play an important role in the reduction of the global dependence on fossil fuels. They are essential components for the implementation of renewable energy sources and electric vehicles. Lithium ion batteries are the most desirable form of energy storage because of the high energy and power densities. Conversion materials, specifically nanocomposite metal fluorides, show great promise due to their high theoretical capacities, which mainly arise from the multi-electron transfer per redox center. The main challenge with conversion materials is the poor capacity retention compared to commercially available intercalation materials, such as lithium cobalt oxide (LiCoO2) and lithium iron phosphate (LiFePO4). Due to the size of fluoride nanocomposites, there is a lack in fundamental understanding of the conversion mechanism and phase distribution of these compounds.

Tin fluoride (SnF2) and lead fluoride (PbF2) nanocomposites were prepared and characterized via x-ray diffraction. Electrochemical analysis was also performed. Magic angle spinning nuclear magnetic resonance (MAS NMR) was used to probe the local structure of these compounds at various stages during an electrochemical cycle. Specifically, two dimensional magnetization exchange technique was employed for the first time to better understand the phase distribution. Techniques such as scanning transmission electron microscopy (STEM), electron energy loss spectroscopy (EELS), and energy dispersive x-ray spectroscopy (EDS) were used to support conclusions drawn from the NMR experiments. The current study suggests the SnF2 system has better reversibility than the PbF2 system likely due to the close proximity of SnF2 domains and electrochemically formed LiF domains.
Spatial Organization of Myelinated Axons at the Ultrastructural Level
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Myelinated axons are long processes from neurons involved in the conduction of electrical signals and communication in the brain circuit. In a volume of the neocortex revealed using electron microscopy, trajectories of nonfasciculated myelinated axons are observed to intersect and form numerous touches between each other. These touches may be the sites of adhesion and the basis of a scaffold consisting of myelinated axon that supports the structural integrity of the neuropil. A structural framework would contribute to the arrangement of neuronal cell bodies and extensions and would imply a novel organizational principle for the structure of brain circuits.

An implication of a scaffold of myelinated axons is that the number of touches observed in the volume is significantly higher than the number expected from a random arrangement of myelinated axons. To test the scaffold hypothesis, myelinated axons were modeled geometrically as rigid tubes shaped similar to the observed axonal morphology, and a Monte Carlo simulation was designed to compute the probability that randomly positioned myelinated axons form at least the observed number of touches. Based on this computational method, the probability of at least the observed number of touches is $P = 0.25$, implying the myelinated axons in the volume are not organized to form a scaffold, and that myelinated axons with fixed trajectories are randomly positioned within a small volume. The results suggest that the trajectories of myelinated axons are not determined by any factor other than the connectivity between the original cell body and synaptic target.

Structure-Activity Relationship of Kinesin Spindle Protein Inhibitors Promoting Neurite Growth in Embryonic Stem Cell-Derived Mouse Motor Neurons
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Axonal regrowth by CNS neurons is an important therapeutic target for spinal cord injury and other neurodegenerative diseases. When adult CNS tissue is damaged, regeneration is hindered by several factors: poor intrinsic growth in quiescent neurons, low levels of neurogenesis from endogenous neural progenitor cells, and injury response mechanisms. Moreover, otherwise promising therapeutic grafts of embryonic stem cell-derived motor neurons (ES-MNs) into injury sites in the spinal cord have been ineffective in restoring synapses with target muscles due to myelin-associated inhibition by proteins in white matter, including myelin-associated glycoprotein (MAG). We used a cell-based model of myelin inhibition by MAG-expressing CHO cells as an assay system to screen for small molecules promoting neurite growth in ES-MNs. A preliminary high-throughput screen had identified an inhibitor of kinesin spindle protein (KSP) as a candidate for drug development. To gain insight into the SAR of KSP inhibitors, we performed dose-response tests of structurally analogous compounds and distinct KSP inhibitors on MAG CHO models. Results indicate that modification of an amide group can improve compound potency. Further tests are needed to determine the potential of KSP inhibitors as drug candidates.
Synthesis of Small Molecule HIV-1 Entry Inhibitors: Region III Analogs of NBD-556

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The Human Immunodeficiency Virus (HIV-1) now persists on a pandemic level, currently affecting 33 million people worldwide. In the initial stages of infection, a glycoprotein on the HIV-1 viral surface, gp120, undergoes a recognition event with CD4, a receptor protein on the cell membrane of T cells. Because the CD4 binding site of gp120 is highly conserved among many viral isolates, potential small molecule inhibitors of this recognition event are less prone to mutational resistance. It is hypothesized that if this recognition event can be blocked, then it may be possible to reduce infection rates of healthy T cells, thus leading to a decrease in blood viral load. A small molecule, NBD-556, was discovered in 2005, and inhibits HIV-1 from entering human T cells by targeting the gp120 glycoprotein of HIV-1. Through rational design guided by computational models based on an X-ray crystal structure of the proteins that mediate viral entry, analogs of NBD-556 that have been found to bind to gp120 with greater affinity than the parent compound, have been synthesized. The affinities of these novel analogs for gp120 were determined by Isothermal Titration Calorimetry (ITC), and their ability to inhibit viral entry was assessed by a cell-based assay. One compound, AWS-I-91, was found to exhibit the highest binding affinity for gp120 of all the compounds synthesized to date (Kd = 0.19 uM). Consequently, following an iterative manner of synthesis and refinement, AWS-I-91 provides a potential benchmark for future structural optimization.

Using supercritical fluid technology to develop a biomimetic 3D porous scaffold for bone tissue engineering

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The key to designing a suitable material for bone replacement is to mimic the mineral component and the microstructure of natural bone. The novel artificial bone scaffold should have good mechanical properties, high porosity, bioactivity, and controllable degradation kinetics. In this work, a three-dimensional scaffold based on a polymer phase consisting of only naturally-derived components (gelatin and cornstarch) and a mineral phase (hydroxyapatite (HA)) was produced using supercritical CO2 as the foaming agent. Pore size and distribution, mechanical properties, bioactivity and degradation rates were studied. SEM analysis so far showed a homogeneous pore size distribution within the 3D structure and a decreasing pore size with increasing HA:polymer content.
Adhesion, Spreading, and Alignment of Osteoblasts on Various Surface Topographies

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According to the National Institutes of Health, osteosarcoma is the most common type of bone cancer in adolescents; however the cause is still yet unknown. In this study, three types of cells were examined: rat osteosarcoma cells (ROS), a mis-functional subclone of murine osteoblasts (sub. 24, MC3T3-E1), and a functional subclone of murine osteoblasts (sub. 4, MC3T3-E1). From observing the adhesion, spreading, actin alignment, and migration of these cells on various engineered micro-topographies, it may be possible to elucidate how they differ in their functional pathways and what triggers them to differentiate properly along the osteoblast lineage.

The topographies in the study were fabricated in polydimethylsiloxane (PDMS) using standard photolithography techniques, forming distinct micro-patterns. The patterned and non-patterned surfaces were functionalized with fibronectin, an extracellular matrix (ECM) protein vital to cell adhesion. Cells were plated on the substrates and maintained under standard tissue culture environment. Once the cells were fully attached, immunofluorescence microscopy was employed to visualize initial cell adhesion and spreading, as well as alignment of actin fibers in relation to PDMS patterns. Phase contrast time-lapse microscopy was used to monitor live cell migration while image analysis was done using ImageJ software.

Cell spreading was considerably different between the two MC3T3 subclones and the ROS cells, and differences were also seen in cell alignment along the micro-patterns and migration speeds of the cells. These discrepancies in adhesion, spreading, alignment, and migration will help elucidate the mechanisms that control mitotic functions and lead to proper bone mineral formation.
The Effects of Ambient Processing Conditions on the Exciton Lifetime of Poly 3-Hexylthiophene Using Femtosecond Upconversion Fluorescence Spectroscopy
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Blends of organic semiconductors such as poly 3-hexylthiophene (P3HT) and phenyl-C61-butyric acid methyl ester (PCBM) have shown great promise for use in photovoltaics (PV). However, a major barrier to high device efficiency is that bound electron-hole pairs (excitons) are produced in P3HT upon light absorption instead of free charges. This condition requires a complex energy conversion process to break excitons and produce electrical current, a process sensitive to the morphology of both the P3HT layer and the P3HT/PCBM interface. This project attempts to isolate the dependence of the exciton lifetime on P3HT oxidation and morphology from the complicated interfacial dynamics by fabricating and processing single-component devices under ambient conditions. We use femtosecond up-conversion fluorescence spectroscopy to correlate the total exciton lifetime in P3HT films to the overall PV efficiency in identically processed blend devices. Our studies found that a noticeable increase in the fluorescence decay rate due to oxidation was only seen after weeks of oxygen exposure, indicating slow time-scale kinetics. Aluminum deposition caused a dramatically longer fluorescence lifetime, from 35 to 55 ps in fresh films and 23 to 92 ps in oxidized films. Once annealed, the samples exhibited a faster fluorescence lifetime decay rate, yet slower than as-spun samples. Our results indicate that both oxygen content and sample morphology can dramatically affect the exciton lifetime and as a result, their diffusion length in PV devices. With a deeper understanding of these effects, more effective processing procedures can now be developed to make the next generation of organic photovoltaics.

The impact of genetic variation in glycerol-3-phosphate dehydrogenase activity on longevity and metabolite pools in the context of diet composition in Drosophila melanogaster
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Previous studies have found that diet composition, alone and in combination with overall caloric intake, modulates lifespan in a range of organisms. Increasingly protein-rich, balanced diets reduce the longevity of flies, while carbohydrate-rich, imbalanced diets do so to a greater extent. An energy state regulator, glycerol-3-phosphate dehydrogenase (Gpdh) controls the amount of triglyceride in metabolism and acts as a cofactor shuttle in flies. We hypothesize that genetic variation in Gpdh will modify the effect of diet on lifespan, presumably by impacting downstream neurosecretory and transcriptional mechanisms. Using Drosophila melanogaster, three Gpdh genotypes possessing 100%, 50%, and 10% activity were created through P-element excision. We confirm that increasing nutrient content in a cornmeal/agar-based diet reduces longevity of flies. However, lower Gpdh activity extends fly lifespan on low (4g yeast, 4g sucrose) and high nutrient (16g yeast, 16g sucrose) diets. The inverse effect was observed for flies on an “obesogenic” diet (40g sucrose, 2.5g yeast), where lower Gpdh activity reduces lifespan, possibly due to accumulation of metabolites. Genetic predisposition to obesity and type 2 diabetes is frequently studied in humans. The predisposition may have arisen from neutral or advantageous genetic variants in the cycling feast and famine of nature, which now exhibit detrimental effects in the nutrient excess of the modern diet. This study is thus of potential biomedical interest, as our data models this possibility. Additionally, we present data regarding the effects of varying Gpdh activity on triglyceride and glycogen storage in the context of diet, as well as starvation resistance.
The Influence of Sialylated Intravenous Immunoglobulin on the Interaction Between C1 and C4 in the Classical Complement Pathway

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We are examining the mechanism of action of Intravenous Immunoglobulin (IVIG). IVIG is prepared from the pooled antibody containing fraction (gamma globulin or IgG) of thousands of blood donors. It has been found empirically to down-regulate inflammation in many inflammatory and autoimmune diseases. Naturally occurring complement proteins act to destroy invading microorganisms and induce inflammation and IVIG is known to block complement action. It has been shown that IVIG can be separated into sialic acid rich and sialic acid poor molecules and that the sialic acid rich molecules have all of the anti-inflammatory activity. We determined which of these fractions blocks complement action. We first examined the effect on the classical pathway of complement action in an Enzyme-Linked Immunosorbent Assay (ELISA). To immune complexes formed with BSA and anti-BSA on a microtiter plate was added sequentially C1 and C4 in the presence of varying dosage of sialylated or non-sialylated IVIG. We used a rabbit red cell lysis to examine the effect of IVIG on the alternative pathway of complement action. Lysis of rabbit erythrocytes was unchanged in the presence and absence of IVIG. However, sialylated IVIG blocked the C1-C4 interaction and less C4 was found bound to the ELISA plate. The non-sialylated IVIG was not active. Therefore, sialylated IVIG not only blocks inflammation in autoimmunity, but it also blocks the interaction between C1 and C4 and inhibits the Classical Pathway. This may be part of its mechanism of IVIG action. We will now determine whether other complement binding steps are blocked.

The Relationship Between Chest Compression Depth and Complete Chest Recoil During CPR Varies by Rescuer Type and CPR Technique

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Introduction: We tested the hypothesis that there is a relationship between chest compression depth and frequency of complete chest recoil (CCR), dependent on rescuer type and CPR technique.

Methods: This randomized prospective trial was performed on an electronic manikin (Laerdal Skill Reporter™). Thirty laypersons trained in CPR and thirty EMS providers performed three minutes of CPR using the American Heart Association recommended standard hand position followed by three minutes of an alternative hands-off technique (lifting the subject’s hands completely off the chest during decompression). Compressions >38 mm were considered adequate depth and chest recoil < 1 mm from baseline was considered CCR.

Results: Laypersons using the standard hand position had the highest incidence of CCR with adequate depth (24%) and a significantly lower incidence of CCR with inadequate depth (21%), (P<0.0028). EMS providers had the opposite finding. EMS providers using the standard hand position had a lower incidence of CCR with adequate depth (12%) and a significantly higher incidence of CCR with inadequate depth (18%), (P<0.0001). The hands-off technique provided an extremely high incidence of CCR (>92%) with both adequate and inadequate compression depth for laypersons and EMS providers. For the hands-off technique, these differences were not statistically significant.

Conclusions: There is a statistically significant relationship between chest compression depth and frequency of CCR using the standard hand position which varies by rescuer type. The hands-off technique resulted in a high incidence of CCR. This information may assist in developing improved CPR education and training for rescuers.
Triazole as an Alternative to Water in Fuel Cell Membranes

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Current proton exchange membrane fuel cell technology poses a few problems due to the usage of water as proton transport. This study aims to ameliorate these problems by using triazole as a substitute for water as the main proton transport method. 1,2,4-Triazole was mixed with commercially available poly-flourinated sulfonic acid membranes (Nafion NRE 212 and 3M-825) at different molar ratios. The proton conductivities of each sample were tested, at 50 °C, 85 °C and 120 °C at varying humidities. Thermo-gravimetric analysis (TGA) was run after each sample was tested in order to determine the actual ratio of Triazole:Polymer and the difference in the membrane before and after proton conductivity testing. The proton conductivities tests showed an insignificant difference between the different molar ratios. The largest difference in proton conductivities was between Nafion and 3M-825 where 3M-825 had better conductivities than Nafion. The TGA showed that after humidification, all excess triazole is removed making the membrane a 1:1 salt explaining the static conductivities.

Using Nano-Hydroxyapatite as a Drug Carrier

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In this present research, different amount of BSA is incorporated with hydroxyapatite nanoparticles. The release kinetics of hydroxyapatite is carefully studied under in vitro conditions and the release profiles are acquired for three different samples. In this study, hydroxyapatite nanoparticles are synthesized using wet chemical method. The BSA concentration in each sample is 5%, 10% and 20% respectively. All samples are characterized by FTIR, TGA and XRD. After characterization, BSA-hydroxyapatite nanoparticles are dispersed in DI water. The release kinetics for three samples is determined by measuring the protein concentration in supernatants every 24 hours over a period of two weeks. Release profiles are then plotted for each sample to determine the ideal BSA to hydroxyapatite ratio.
**Project Category:** Biochemistry and Computational

*Water Diffusion In And Out Of The β-Barrel Of Fast Maturing Fluorescent Proteins.*
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Green fluorescent protein (GFP) and GFP-like proteins are commonly used in scientific research. Their utility as genetic tracer molecules, as highlighters in high resolution microscopy, and as a critical component in many modern biotechnological methods has led to an increased effort to understand their photochemistry, and to find and design new GFP-like proteins. Turbo GFP and Vivid Verde are rapidly maturing GFP-like proteins. The fluorescent chromophore is formed by an internal cyclization of the tripeptide 6S5YG67 fragment (avGFP numbering) and subsequent oxidation of the intrinsically formed structure. The chromophore oxidation is slow, and it is the kinetics of this step that is presumably improved in fast maturing GFP-like proteins. It has been proposed that water molecules can aid in proton abstraction from the Tyr66 alpha carbon atom. We have used 50ns molecular dynamics simulations of the mature and immature forms of avGFP and TurboGFP to examine the diffusion of water molecules in and out of the protein beta barrel. The simulations confirm the existence of a pore that leads to the chromophore in the rapidly maturing TurboGFP; decreased water diffusion upon chromophore formation; increased water diffusion due to the pore formation and static water molecules constrained by hydrogen bonding networks in the chromophore vicinity.

**Project Category:** Material Science

*Nanoscale Fabrication and Characterization of Epitaxial Quantum Dot Materials for Future Nanoelectronic Devices*
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Our focus here, is to address material challenges in realization of epitaxial QDs (Quantum dots) and QDMs (QD Molecules) (in GeSi/Si system) based future nanologic devices, as well as to develop new nanoscale characterization methods relevant to nanoelectronic devices. For example, the FIB (Focused Ion Beam), used for controlling nucleation of the nanostructures, inherently damages the Si substrate and, depending on the species employed, can cause unintentional doping. We are carrying out Raman and Photoluminescence (PL) studies on ion (Ga⁺, Ge²⁺ and Si³⁺) implanted Si to study structural and electronic recovery. Raman studies indicate almost complete structural recovery for ion doses up to 10¹⁴ - 10¹⁵ cm⁻² after a 10 min 600 °C anneal; while the PL spectra for Ga⁺ has only substantially recovered after a 10 min 800 °C anneal. In another focus of our work, since, Ga⁺ dopes Si, we are trying to find out what type of nanostructures self-assemble on Si (100) templated with non-invasive, isoelectronic ions (Si³⁺, Ge²⁺). Results† indicate that new nanostructures are formed on Si²⁺ templated Si surfaces. We are exploring variant structures that form as detailed functions of FIB templating conditions (ion energy, dose, species). Finally, to demonstrate localization of charge carriers in a QDM, we are studying chemical composition distribution around a QDM using AES (Auger electron spectroscopy) and EELS (Electron energy loss spectroscopy) /TEM imaging.

Another focus of our work is the development of a high spatial resolution temperature measurement technique that has many potential applications including for nanoelectronics. Here we use diffuse scattering in the TEM to measure local temperature. We have demonstrated temperature sensitivity of c. ten K and we are working towards greater sensitivity with a spatial resolution of a few nm.

† This work is in collaboration with the groups of Jerry Floro (UVa), Jennifer Gray (U. Pittsburgh) and Frances Ross (IBM).
MDMA and Cocaine Modulation of Nicotinic Acetylcholine Receptors in the Hippocampus and Striatum of the Adult Mammalian Brain: A novel mechanism?

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MDMA (Ecstasy) and cocaine are both illicit drugs that show psychostimulant activity. Although their ability to reverse and block monoamine transporters respectively throughout the brain has been established, evidence is beginning to surface showing other possible mechanisms of action involving nicotinic acetylcholine receptors (nAChRs). The goal of this project was to identify a novel role for MDMA and cocaine modulation of nicotinic acetylcholine channels in the adult mammalian hippocampus and striatum, two areas in the brain known to be both rich in nicotinic receptors and involved in addiction, motivation, and reward processes. To test for functional interaction between MDMA or cocaine and nAChRs, we examined presynaptic nAChR activation using a rubidium (Rb) efflux assay in synaptosomes. MDMA inhibited nicotine-induced Rb efflux with a 50% inactivation at 10uM, while cocaine and its primary metabolite benzoylecgonine showed 50% inactivation of these nicotinic channels at only 3uM. The antagonism of the nicotinic acetylcholine receptors in the brain could have implications for nicotinic receptor regulation. Due to the low micromolar concentrations at which this effect reaches 50% efficacy (IC50=3-10uM), psychostimulants like MDMA, d-amphetamine, cocaine, and methamphetamine may induce nicotine seeking behavior. Further investigation into the mechanism responsible for MDMA and cocaine inhibition of nicotinic acetylcholine receptors is underway.

Memory Illusions: Fonts and Serial Positions

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Memory illusions, or memories for events that never happened, have often been studied using word lists and recognition/recall tasks. The most successful method of creating memory illusions in the laboratory is the Deese/Roediger/McDermott (DRM) paradigm, in which participants are presented with a semantically related word list, often presented from highly associated words to weakly associated words, and then asked to complete a recognition or recall task. Participants overwhelmingly accept the presence of a highly associated word that was not presented (i.e., the critical lure). In fact, acceptance rates for the critical lure are often as high as acceptance rates for words presented in the middle of the list (Roediger & McDermott, 1995). Prohaska, Del Valle, and Toglia (in prep.) presented participants with word lists ordered from highly associated items to weakly associated items and asked them to indicate the serial position of the critical lures. They found that participants had a preference for the first half of the list. However, when the word lists were ordered from weakly associated items to highly associated items, participants’ preference switched to later in the list, indicating that the structure of the list affected encoding. The present research tested whether font manipulations during encoding and retrieval affect the serial position assignments and font assignments of the critical lures.
Bone marrow mesenchymal stem and progenitor cells participate in innate immune response by inducing monocytes emigration

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Inflammatory (Ly6C⁹ CCR2⁴) monocytes provide defense against infections but also contribute to autoimmune diseases and atherosclerosis. Monocytes originate from the bone marrow and their entry into the bloodstream requires stimulation of CCR2 chemokine receptors by MCP1. How monocyte emigration from bone marrow is triggered by infections in anatomically remote sites remains unclear. We demonstrate that low concentrations of TLR ligands in the bloodstream drive CCR2-dependent emigration of monocytes from bone marrow. Bone marrow mesenchymal stem cells (MSCs) and their progeny, including CXCL12-abundant reticular (CAR) cells, rapidly express MCP1 in response to circulating TLR ligands or systemic bacterial infection and induce inflammatory monocyte trafficking into the bloodstream. Targeted deletion of MCP1 from MSCs impaired monocyte emigration from bone marrow upon LPS stimulation and increased susceptibility to Listeria monocytogenes infection. Our findings suggest that bone marrow mesenchymal stem and progenitor cells respond to circulating microbial molecules and regulate bloodstream monocyte frequencies by secreting MCP1 in proximity to bone marrow vascular sinuses.
**Project Category:** Chemical Engineering and Microrheology

**Microrheology of Colloidal Dispersions with Excluded-Volume Interactions**

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Microrheology is a theoretical model and experimental technique in which the dynamic behavior of a complex fluid – colloidal particles suspended in a solvent – is interrogated by forcing a single, micron-sized probe through the medium. The suspended particles form a microstructure whose behavior strongly affects rheological properties such as viscosity and diffusion. The shape of the deformed microstructure then depends on the Péclet number - the strength of probe forcing compared to thermal forces:

\[
Pe = \frac{F_{\text{ext}}}{(kT/b)},
\]

where \(kT\) is the thermal energy and \(b\) is the bath particle size.

Probe fluctuations due to collisions give rise to the force-induced diffusion, called the microdiffusivity. Most theoretical work has focused on dilute suspensions in the absence of hydrodynamic interactions. However, many real systems, such as the interior of the cell, involve crowded environments of particles that interact via hydrodynamic and excluded-volume interactions. Previous theoretical work predicts the presence of two diffusive regimes corresponding to distinct physical processes, but recent numerical simulation was unable to capture the early-time diffusive behavior in the dilute regime. In this study, the microdiffusivity of dilute and concentrated colloidal dispersions was studied in the presence of excluded-volume interactions via Brownian dynamics simulation. Analysis revealed the presence of both short- and long-time diffusive regimes; the latter is studied as a function of \(Pe\) and the volume fraction of bath particles, \( \varphi \). The microdiffusivity is found to scale quadratically in \( Pe \) for \(Pe \ll 1\), linearly in \(Pe\) for \(Pe \gg 1\), and linearly in \( \varphi \), for all \(Pe\).