Merideth Addicott    Neuroscience
Advisor: Dr. Donald Dougherty

Biphasic effects of alcohol on response inhibition

Alcohol produces stimulant effects on the ascending limb of the breath alcohol curve (BrAC) and sedative effects on the descending limb. We investigated whether self reports of stimulation and sedation would correspond with performance impairments on a model of impulsivity during the ascending and descending BrACs. Fifteen male and 15 female social drinkers completed two days during which they received either 0.8 g/kg of alcohol or placebo. A self-report measure (Biphasic Alcohol Effects Scale) and response inhibition task (GoStop Impulsivity Paradigm) were administered at baseline and on the ascending and descending limbs of the BrAC. Relative to baseline, reports of stimulation increased during the ascending limb while reports of sedation increased on both the ascending and descending limbs of the BrAC curve. Impairments in response inhibition performance were greatest during the descending limb. Multilevel regression within-subjects analysis revealed a significant correlation between sedation scores and impairments in response inhibition.

Elizabeth Akins    Molecular Medicine
Advisor: Dr. Purnima Dubey

Non-invasive bioluminescent imaging: a window into tumor rejection

Current means of evaluating the efficacy of CD8+ T cells in tumor rejection do not adequately reflect the plasticity of the immune system. We developed a system to visualize the role of CD8+ T cells in tumor rejection using non-invasive optical imaging. Bone marrow stem progenitors are transduced in vitro with lentiviruses that express Firefly luciferase behind the murine CD8 promoter and enhancer. Marked bone marrow cells are transduced into syngeneic recipients, and reconstitute the periphery with luciferase expressed specifically in CD8+ T cells. Reconstituted animals were challenged with a tumor that is rejected or a tumor that grows progressively. We visualized the localization of CD8+ T cells to the tumor site during the process of tumor rejection. We also detected CD8+ T cells at the site of the progressor tumor. Our novel system will permit kinetic, non-invasive evaluation of immunomodulatory treatments affecting CD8+ T cell rejection of solid tumors.
Bioinformatics: Protein spot identification tool

Proteins are macromolecules made up of amino acids and have important functions including catalyzing reactions, protection, and signal transduction. Identifying proteins that are important for a particular response/function involves the use of 2-dimensional gel electrophoresis for separation of different proteins and utilizes two characteristics of protein: pI and molecular weight (MW). Identifying a protein spot of interest from a 2D gel biochemically is cumbersome and time consuming. This project aimed to develop software to aid in rapid protein identification using evaluated pI and MW compared against the Swiss-Prot protein database. Development of the software involved an interdisciplinary software engineering effort combining biology, computer science, and physics students. Ultimately, this resulted in two functional software products which combined theoretical and practical approaches to protein identification. The resulting software is ideally suited to accomplish the initial motivating research goals.

Treating Autism with Music Therapy

Music has been viewed as a healing force throughout history, but only over the last century has it been used as a therapeutic tool in clinical settings. This poster explores research done on elements of music therapy, facets of autism, and the efficacy and benefits of the treatment with autistic patients.
Wilderness Therapy: Approaches, Effectiveness, and Analysis

The purpose of this research is to investigate the approaches, effectiveness and analysis of wilderness therapy programs for adolescents. The main types of therapy being used in the field today are examined and the research findings are discussed. Initially an assessment of the true definition of wilderness therapy and a background of its history are given to better fully understand its scope. After the background information, the review explains the types of clients that typically are participants in wilderness therapy and looks at traditional therapy methods versus wilderness therapy methods. The various types of approaches used in the field are then discussed. The research on the effectiveness of wilderness therapy programs is examined and the analysis of research in the field is discussed. Finally further recommendations for future research are given.

Optical Trapping and Torquing of C60 Nanorods

We have optically trapped and studied C60 polymer nanorods with diameters of 300-500 nm and lengths of 1-3 microns. The primary goal is to measure opto-electronic properties of the C60 polymer rods. This is accomplished by observing the rotational motion of the rods in a water sample when a light torque is applied. We also hope to report on opto-electronic properties of even smaller rod-shaped objects (of diameters less than 100 nm).

The Effects of Problem-Based Learning on Student Engagement and Motivation

Little evidence in the literature supports the frequent claim that Problem-Based Learning (PBL) increases student intrinsic motivation in the high school classroom. This study tested this assumption by comparing student on-task behavior in PBL classrooms versus traditional teaching methods in high school biology classrooms. Six classrooms were randomly divided into treatment variables and then each exposed to a one-day lesson on animal behavior. Surprisingly, PBL classrooms showed more variance in student on-task behavior than traditional classrooms. This variance was also uneven and obscured comparisons across all classes used. However, the most controlled comparisons possible with classes that were most similar showed no significant difference between on-task behavior in PBL classes and traditional classes.
Differential roles of MyD88 and Type I IFNR in dendritic cell maturation in response to Listeria monocytogenes

Listeria monocytogenes (L.m.) is an intracellular pathogen with potentially serious consequences in immuno-compromised individuals. Components of L.m. such as the peptidoglycan cell wall, are known to trigger Toll-like receptor (TLR) signaling through TLR2 requiring the adapter protein MyD88. In addition, L.m. have been shown to initiate a second signaling pathway upon bacterial cytoplasmic entry characterized by the induction of Type I IFN. We have previously shown that cytoplasmic entry of L.m. enhances DC maturation induced by the bacterial infection. In order to determine the relative contribution of signaling through TLR vs. cytoplasmic surveillance pathways to DC maturation, we have utilized mice lacking either the ubiquitous TLR adapter protein MyD88 (MyD88-/-) or the receptor for Type I IFN (an essential mediator of Type I IFN signaling, IFNR-/-). Our data reveal that costimulatory molecule expression (CD40 and CD86) induced by L.m. is predominantly MyD88-independent and IFNR-dependent. In contrast, inflammatory cytokines such as IL-12, IL-6, and TNF-α produced as a result of L.m. infection are MyD88-dependent and IFNR-independent. T cell priming induced by L.m.-infected DC was also investigated. These findings highlight the importance of both MyD88 and Type I IFN signaling pathways to DC maturation in response to the intracellular pathogen Listeria monocytogenes.
Using molecular dynamics to predict communication networks in an aminoacyl-tRNA synthetase

Long-range functional communication is a hallmark of many enzymes that display allostery, or action-at-a-distance. Many aminoacyl-tRNA synthetases can be considered allosteric, in that their trinucleotide anticodons bind the enzyme at a site removed from their catalytic domains. Such is the case with E. coli methionyl-tRNA synthase (MetRS), which recognizes its cognate anticodon using a tryptophan residue located 50 Å away from the site of tRNA aminoacylation. A lack of structural information and a fundamental understanding of how MetRS and tRNAMet interact have limited the success of efforts to deconvolute this communication-at-a-distance theory. Both wet bench and computational approaches have been used to dissect the proposed interaction network in MetRS. Although experimental methods such as mutation of specific amino acids provide significant data, they are labor intensive and sometimes yield incomplete information about interacting residue pairs. On the other hand, computational methods yield information about interacting pairs and less labor intensive. Preliminary molecular dynamics (MD) simulations using NAMD not only offer a validation for previous biochemical data concerning MetRS but also guide new experiments aimed at dissecting long-range communication in this essential enzyme.
Antibody responses and growth properties of the paramyxovirus Simian Virus 5 and an rSV5-P/V mutant that blocks type I interferon signaling in mouse cells

The battle between the host cell type I interferon (IFN-I) response and viral strategies for counteracting this innate response has been a focus of our lab, particularly with respect to how this interaction affects the adaptive immune response. We have tested the hypothesis that paramyxovirus vectors that differ in their ability to block IFN-I pathways will elicit differential antibody responses. We have analyzed the adaptive response to infection with wild type Simian Virus 5 (rSV5-WT), which does not block IFN-I signaling in mouse cells, and an rSV5-P/V mutant (rSV5-P/V-N100D) that blocks murine IFN-I signaling. Infection of BALB/c mice with rSV5-WT elicited a potent antibody response that was a mixture of IgG1 and IgG2a isotypes, suggesting a mixed TH1/TH2 response. By comparison, rSV5-P/V-N100D elicited overall slightly higher levels of both IgG1 and IgG2a, with the isotype ratio indicating a further shift toward a TH2 response. Under low MOI conditions in vitro, these viruses demonstrated differential growth kinetics, which correlated with their ability to counteract IFN-I. Analysis of the growth kinetics in mouse lungs revealed similar titers for each virus throughout the time course, which did not mirror the differential growth kinetics observed in tissue culture. We present a model for the relationship between in vivo innate immune responses and adaptive antibody responses elicited by SV5 vectors that differ in their ability to counteract the IFN-I response.

Analysis of Bacillus globigii spores by capillary electrophoresis

Bacillus globigii (Bg) spores are used as a stimulant for Bacillus anthracis (Ba) due to their similar shape, size, and cellular makeup. It is imperative in today’s world that detection of harmful airborne or solution-based microbes can be made quickly and efficiently. The likeness of Bg spores to Ba spores allows researchers to investigate real air or solution matrices for the presence and detection of pathogenic spores. Traditional methods of detection can take three days and require pure colonies. In an effort to keep up with public security a system is needed that can provide faster and more reliable identification of spores. The utility of capillary electrophoresis (CE) to separate and detect low levels of spore concentrations will be evaluated. CE with laser induced fluorescence detection enables interactions between dyes and spore surface proteins to be observed with greater fluorescence occurring upon binding of the dye to protein.
Ibotenic acid lesions in the prelimbic and infralimbic areas of the medial prefrontal cortex differentially affect cocaine self-administration reinforced on a progressive ratio schedule

Repeated injections of cocaine produce an augmented locomotor response. This form of behavioral sensitization has been proposed as a model for examining changes which occur during the addiction process. Previous studies have shown that excitotoxic lesions of the infralimbic or prelimbic subregions of the medial prefrontal cortex diversely affect the development of locomotor sensitization. Here we tested whether these two structures are involved in sensitization to the reinforcing effects of cocaine. Rats received chronically indwelling jugular catheters and bilateral ibotenic acid or control lesions into either the prelimbic or infralimbic cortex. Rats were then trained to self-administer cocaine (1.5 mg/kg/infusion) on a progressive ratio schedule. Cocaine-reinforced breakpoints significantly increased over 14 days of testing in the control group, while neither the prelimbic nor infralimbic lesion groups demonstrated this sensitized responding. However, the prelimbic lesion group reached significantly higher breakpoints on the first testing day than the other groups. These data suggest that locomotor sensitization data do not predict changes in cocaine reinforcement and also illustrate that prelimbic and infralimbic prefrontal areas are differentially involved in cocaine addiction.

Ferritin inhibits the cleavage of High Molecular Weight Kininogen by Elastase and Mast Cell Tryptase

Ferritin is a ubiquitous protein known primarily for its role in iron storage. Our lab previously described a novel interaction between ferritin and high molecular weight kininogen (HK), a cofactor in the intrinsic coagulation cascade. HK is cleaved by the serine protease kallikrein to release the pro-inflammatory peptide bradykinin (BK). Kallikrein, however, is unable to cleave oxidized HK potentially produced during inflammation. Conversely, elastase and mast cell tryptase can cleave oxidized HK, thereby providing an alternative HK cleavage mechanism with significance at sites of inflammation. We report that ferritin can retard the cleavage of both native and oxidized HK by elastase and tryptase. Ferritin reduced the initial rates of elastase and tryptase-mediated HK cleavage by 45-75%. The ability of ferritin to impede HK cleavage is most likely mediated through a direct ferritin/HK interaction. Collectively, these results imply that ferritin may modulate the cleavage of HK at sites of inflammation.
Colleen Warner Colaner
Communication
Advisor: Dr. Ananda Mitra

Side by side or one step behind: The effects of Evangelical Christian gender beliefs on family typology

The proposed study seeks to investigate the relationship between religious gender role ideologies, family communication patterns, and family type. Consistent with a traditional mediation model, the analysis in this study will come in two parts. First, gender role ideology will be used as a predictor variable in gauging the type of communication present within families; communication patterns will be measured according to three levels as defined by the General Theory of Family Communication: expressiveness, structural traditionalism, and conflict avoidance. Gender role ideologies, which will be limited in this study to Evangelical Christian beliefs on husband-wife interaction, will be measured on a continuum of Complementarianism (hierarchical roles) to Egalitarianism (mutual roles). Secondly, the relationship will be assessed between communication patterns and family type. Family type will be characterized according to the Circumplex Model of Family Systems. Relationships between the named variables will be measured through cross-sectional survey research and qualitative interviews with married couples.

Melissa Daly
Biomedical Engineering
Advisor: Dr. Joel Stitzel

A Controlled, Repeatable Approach for Measuring Pulmonary Contusion

Complications due to blunt-chest trauma are a major factor in determining the survival of car crash victims. One of the major injuries sustained from blunt-chest trauma is lung contusion. The amount of lung contusion present in a trauma victim may be a good way to assess the likelihood of that victim developing further complications, such as acute respiratory distress syndrome (ARDS) or pneumonia. To better understand this, the clinical environment needs a controlled, accurate approach for measuring contusion in an efficient manner. Traditional x-rays cannot be used for this because there is no good way to determine the three-dimensional volume of the contusion from one or two two-dimensional slides. However, Computer tomography (CT) can be used to create three-dimensional volumes. The mission of this research is to develop a method of measuring pulmonary injury using CT so that a predictive algorithm can be created to predict whether a patient will develop ARDS.
Vesicular stomatitis virus matrix protein plasma membrane microdomain organization during virus assembly

Enveloped viruses acquire their envelopes from host cell plasma membranes. The plasma membrane is not uniform, but contains a lateral organization of membrane microdomains with a distinct protein or lipid concentration compared to the overall composition of the membrane. Membrane microdomains are budding sites for many enveloped viruses. Vesicular stomatitis virus (VSV), the prototypical negative-stranded RNA virus, buds from membrane microdomains enriched in the viral envelope glycoprotein (G protein). The VSV matrix (M) protein brings the viral nucleoprotein core to the plasma membrane during assembly. However, a direct interaction between M protein and G protein has been difficult to establish. M protein may interact with G protein through lipid microdomains. Therefore, viral protein incorporation into organized membrane microdomains may be critical for the efficient assembly of enveloped viruses. Immunogold-labeling electron microscopy showed M protein partitions into membrane microdomains that are separate from G protein membrane microdomains, which may cluster to form virus budding sites.
Amniotic Fluid Derived Stem Cells are a Potential Source for Cardiac Therapeutics

Cell therapy has been proposed as a means to promote the regeneration of damaged heart muscle. We have established lines of broad spectrum multipotent stem cells derived from primitive fetal cells present in human and mouse amniotic fluid (AFS). These cells can be induced to differentiate in vitro into a wide variety of cell types, including all three embryonic germ layers. In this study, we hypothesize that AFS cells can be used for cardiac regeneration.

We utilized treatment with 5-aza-2-deoxycytidine to induced cardiogenic differentiation. The cells were analyzed for expression of myogenic and cardiogenic markers. AFSC-derived cardiomyocytes were seeded on collagen scaffolds and preconditioned in a bioreactor system with cyclic strain stimulation, mimicking the wall motion of the native heart muscle. Lastly, we used an ischemic injury model in mice to test the ability of the cells to survive and integrate after direct injection into the myocardium.

We observed that by 10 to 20 days after induction, AFSC cells stained positively for cardiomyocyte markers including troponin I, troponin T, α-actinin. RT-PCR analysis revealed expression of cardiomyocyte markers including GATA-4 and MEF2C. AFSC-derived cardiomyocytes preconditioned in the bioreactor showed muscle tissue organization and contraction. Histological assessment of AFSC-derived cardiomyocytes injected into injured mouse hearts indicated that these cells survived and integrated into the myocardium. These results demonstrate that multipotent stem cells derived from amniotic fluid can be used for cardiac regeneration. Amniotic fluid derived stem cells represent a promising novel source of cells for regenerative therapies in cardiac diseases.

Recursive Structures: Linear and Nonlinear

This poster displays the work of a master’s thesis on linear and nonlinear difference equations. Results on the maximal growth rates of certain classes on linear difference equations with applications to matrix and power series bounds will be displayed. Several asymptotic results for nonlinear difference equations will be presented as well. This work spans several research papers. Copies of papers, including other work, will be available.
Mesh development for a finite element model of the carotid artery

A technique for developing a structured, hexahedral and quadrilateral mesh for use in finite element analyses of the carotid artery is presented. The model is reconstructed from 270 Computed Tomography (CT) images (slice thickness 0.625mm) of a 57 year old male subject and extends from the arch of the aorta to the base of the jaw. The structured mesh was generated using an unstructured, automatically generated tetrahedral mesh of the intimal surface of the carotid artery and its branches. A parametric meshing software package was used to create the structured mesh, facilitating mesh density studies. The change in volume and surface area introduced when converting the mesh from tetrahedral to hexahedral elements (+1.5% change in volume, -1.4% change in surface area) is small in comparison to estimated error introduced in the segmentation process. The technique introduced will benefit finite element and fluid dynamic studies of the carotid artery investigating mechanically induced pathology at both physiologic loading rates (i.e., atherosclerotic plaque formation) and high strain rates (i.e., blunt trauma).

Keywords: finite element, mesh, parametric, carotid, hyperelastic, biomechanics

Controlling Levels of Presented Ova Peptide/MHC Complexes via Engineered Recombinant Vaccinia Viruses and Potential for Avidity Regulation

It has been well documented that high avidity CTL are the most effective cells for the clearance of virus. High avidity CTL can respond to low levels of presented peptide antigen whereas low avidity CTL require much higher amounts of peptide. A better understanding of the mechanisms involved in the generation of high avidity CTL in vivo is of importance for vaccine development. To this end, we have generated recombinant vaccinia viruses designed to express different amounts of ovalbumin peptide. Our data demonstrate that, as expected, different levels of KbOva257-264 complexes are present on the surface of cells following infection with the individual vaccinia constructs. Further, high avidity CTL recognize cells infected with the virus presenting a limiting amount of peptide more efficiently than low avidity CTL. Finally, CTL generated by stimulation with virally infected cells exhibit differential expression of the co-receptor CD8, a phenotype shown previously to correlate with differences in functional avidity. These results open the door to in vivo analyses in which the impact on functional avidity of viruses expressing distinct levels of peptide antigen will be determined.
David Hairston Neurobiology & Anatomy Advisor: Dr. Mark Wallace

Auditory and Multisensory Enhancement of Localization Ability in Music Conductors

Music conductors have unique auditory experiences, comprised not only of discriminating subtly different tones and timbres, but also of locating the spatial origins of these sounds within an ensemble setting. Such experiences may not only lead to enhanced discrimination abilities in auditory perception, but also to greater benefits from the synergistic use of auditory and visual cues. Demographically matched music conductors (>7 yrs podium experience) and control (no musical training) subjects performed a target localization task, with targets presented from locations ranging 10-40° in azimuth and their precision was assessed.

All subjects were significantly more precise in localizing visual than auditory targets, and precision decreased with increasing target distance from midline. However, the conductors auditory localization was significantly more precise, particularly for peripheral targets. Additionally, conductors’ performance was significantly better with the light/sound pair than with the visual targets alone, a response enhancement not seen in the control subjects, and typically not observed in the general population. These results suggest fundamental differences not only in the auditory capabilities of music conductors, but also in the ability of these individuals to synthesize and utilize cues from multiple sensory modalities (i.e., audition and vision) to improve localization performance.

Shawnda Marie Herring Education Advisor: Dr. Robert Evans

Effects of Problem-Based Learning on Students’ Understanding of Animal Behavior

The recent trend in science education is a push towards inquiry. However, traditional labs do little to promote inquiry due to the fact answers are known beforehand and students merely go through the steps. This research looked to compare traditional labs to problem-based learning. This research sampled 150 high school biology students. Half participated in a traditional lab while the other half participated in problem-based learning. Research findings shed light on the difficulty in implementing inquiry with students who are trained in traditional styles of learning. Overall, when comparing the two groups of students, no significance was found in the achievement of each group. Yet, an interaction was found between gender and lab type. Results showed an increase in female scores but a drastic drop in male scores from traditional lab to PBL settings. This finding warrants further research.
Pair State Analysis of the Hubbard Hamiltonian in One-Dimension

Using two-electron states as the basis, we have analyzed the one-dimensional Hubbard Hamiltonian (HH) with periodic boundary conditions for many-electron systems. The N-electron energy eigenvalues are simply the sum of the pair energies (eigenvalues of the two-particle reduced HH) weighted by two-particle density matrix elements. We are investigating the possibility that this approach will lead to a useful approximation scheme. For many weakly correlated systems, the pair-energy sum can be truncated and still the ground state energy can be obtained with reasonable accuracy. For example, in the case of six sites at half-filling (with $U/t = 1$) we need only include 12 of the 45 triplet pair states and 6 of the 21 singlet pair states, and still the ground state energy can be found with only 6% error. A comparison between the exact and approximate results for this system and several others are presented.

Novel Synthesis of Nicotine Binding Receptor for Nicotinic Analog Binding Studies

A basic understanding of the differential nicotine binding in various receptor environments can serve as a design tool for nicotinic analogues, which show potential as therapeutic agents in the treatment of neurodegenerative disorders such as Alzheimer’s Disease. Our research takes a novel approach to elucidating the communication between nicotine’s two rings as the molecule participates in a recognition event with a synthetic receptor. For the purposes of characterizing this communication, electronically modifiable receptors will be synthesized in order to minimize the complications inherent in isolating and manipulating the natural biological receptor. Our current focus is the design and synthesis of two receptors, each bearing a hydrogen bond acceptor and a donor to interact with nicotine. The receptors will be constructed using palladium-mediated Suzuki coupling reactions. The receptors will be used to determine the fundamental physical parameters that typify nicotine’s binding by probing the cross-talk between the two binding sites on the nicotine molecule.
Kris Huang  Biomedical Engineering  Advisor: Dr. Daniel Kim-Shapiro

Nitric oxide red blood cell membrane permeability depends on oxygen tension

Hemoglobin (Hb) scavenging of nitric oxide (NO) can compromise its function as a vasodilator, and encapsulation in the red blood cell (RBC) preserves this function. The reduced NO scavenging by RBC-encapsulated Hb has been attributed to a diffusion-limited zone surrounding the RBC and an intrinsic NO barrier in the RBC membrane possibly involving the RBC cytoskeleton. Previously performed NO competition experiments between cell-bound and cell-free Hb found hematocrit and oxygen dependence for RBC NO uptake in the presence of cell-free Hb. The difference in bimolecular rates between oxygenated and deoxygenated Hb cannot completely account for this oxygen dependence. Thus, we performed computer simulations of the experiment to explore this discrepancy. Comparison of computational data to published observations indicates an oxygen-dependent change in membrane NO permeability of least a factor of five. The oxygen dependency of the membrane permeability may have important implications in transport of NO and other nitrogen oxides.

Melanie M. Huston  Biology  Advisor: Dr. Miriam A. Ashley-Ross

Feeding kinematics of the grotto salamander, Eurycea spelaea

Typically, troglobitic salamanders remain paedomorphic due to greater availability of prey items in the water as opposed to on the dry substrate. In contrast, the cave dwelling grotto salamander, Eurycea spelaea (Stejneger, 1893) transforms from aquatic to terrestrial despite the nutrient limitations in caves. To help establish why the grotto salamander transforms, the kinematics of both larval and adult specimens were determined using high-speed video. It was found that the larvae fed stereotypically using suction feeding as expected for larval salamanders. The larvae approached the prey and lowered the nose onto the prey. The gills depressed before the mouth opened and feeding began. Individuals varied in swallowing technique, some larvae swallowed with one hyoid depression cycle, while others used two cycles or varied between one and two depression cycles. The average time from onset of strike to contact of the prey was 37.43ms, and the average maximum hyoid depression was 0.55cm. Preliminary observations showed that the adult specimens were able to feed both aquatically and terrestrial.
Effects of Hemolysis on Nitric Oxide Bioavailability

Nitric oxide (NO) has been identified as the endothelium-derived relaxation factor (EDRF), which is responsible for smooth muscle relaxation. However, hemoglobin (Hb) is an effective scavenger of NO, which can lead to endothelial dysfunction during hemolytic conditions. There are various mechanisms that limit consumption of NO by Hb in vivo including (1) a physical barrier to NO diffusion across the red blood cell (RBC) membrane, (2) an unstirred layer creating a concentration gradient in NO outside the RBC, and (3) a cell-free zone between the endothelium where NO is made and the location of the RBCs. However, during hemolysis, these mechanisms could be compromised, reducing levels of NO reaching the smooth muscle cells. Although the importance of hemolysis in disease has been gaining attention, some believe that small amounts of hemolysis would not effect NO bioavailability in the presence of 10 mM RBC encapsulated Hb normally found in vivo.

We have performed computational modeling of NO bioavailability within blood vessels, specifically looking at the effects of hemolysis and extravasation of cell-free Hb into the endothelium. Our modeling was performed using FEMLAB software. Our model considered individual RBCs within the lumen of the blood vessel, taking into account the particulate nature of blood. We examined the effect of cell-free Hb and extravasation of cell-free Hb, which can occur during hemolytic conditions such as sickle cell disease. We have found that concentrations as low as 1 μM of cell-free Hb reduces the availability of NO. Furthermore, the effect of RBC membrane permeability diminishes as cell-free Hb reaches concentrations as low as 5 μM. Based on these calculations, we hypothesize that the scavenging of NO in the lumen by cell-free Hb during hemolysis results in drastically reduced NO bioavailability. Additionally, at low hematocrit values, cell-free Hb scavenging of NO was more efficient than at high hematocrit values. Examination of the effects of extravasation, indicate that concentrations of cell-free Hb in the endothelium as low as 1 μM further reduce the bioavailability of NO. These results support experimental ones demonstrating a major role of cell-free Hb in the pathology of hemolytic conditions.
Admixture-Adjusted Association Between the Estrogen Receptor Alpha Gene and Type 2 Diabetes in an African American Population

Evidence for association with type 2 diabetes mellitus (T2DM) has been observed in a 41 kb region spanning intron 1-intron 2 of the estrogen receptor alpha gene (ESR1) in our African American case-control population sample. Two single nucleotide polymorphisms (SNPs) in intron 2 (rs11155818 P=0.00004; and rs1033182 P=0.020) as well as three haplotype blocks of high linkage disequilibrium (LD) spanning this region (global P<0.001) were significantly associated with T2DM. The objective of this study was to adjust association analyses for the contribution of admixture. Twenty-three ancestry informative markers (AIMs) and 17 SNPs in the associated region of the ESR1 gene were genotyped in 282 non-diabetic Caucasian and 120 non-diabetic African individuals, as well as 380 African American T2DM cases and 271 African American population controls. Using ADMIXMAP, the estimate for the mean proportion of African ancestry was 0.804 (95% credible interval: 0.779-0.831) in cases, and 0.815 (0.789-0.840) in controls. SNPs rs11155818 and rs1033182 remained significantly associated with T2DM after adjusting for admixture. The allelic association p-values, based on 20,000 iterations, changed from 0.00004 (unadjusted) to 0.00016 for rs11155818, and 0.020 (unadjusted) to 0.022 for rs1033182. Haplotype analysis also indicated that the three haplotype blocks were still significantly associated with T2DM (P<0.001) after adjusting for admixture, and all 7 significantly associated individual haplotypes (P<0.05) within the three blocks remained significant at or below this level. These analyses suggest that admixture does not account for the observed single SNP and haplotype association results between this region of ESR1 and T2DM in our African American population sample.
Preliminary Test of Animal Gamma Knife Immobilization Device

Increased use of the Gamma Knife (GK) to perform stereotactic radiosurgery (SRS) in radiation oncology warrants investigation into its biological results. The addition of an animal 7T MRI provides an opportunity to perform GK treatments and examine their biological results. A novel animal restraint device is created allowing for imaging a rat brain in the 7T scanner and performing GK treatment. The goal of this study was to determine if an animal GK apparatus was able to accurately place a target for GK treatment. A phantom containing radiochromic film and a target was placed in the animal GK unit. The unit was imaged and the target was irradiated on the GK. Investigation of the target and radiochromic film showed that a dose was accurately delivered. We determined that the animal GK apparatus is capable of restraining a target throughout an imaging scan and accurately treating the target on the GK.

Association of the proprotein convertase subtilisin/kexin-type 2 (PCSK2) gene with type 2 diabetes in an African American population.

The proprotein convertase subtilisin/kexin-type 2 (PCSK2) gene, located on chromosome 20p11.2, is a strong functional candidate for type 2 diabetes (T2DM). PCSK2 cleaves the proinsulin molecule on the COOH-terminal side of Lys64-Arg65, which joins the C-peptide and the A-chain domains, and proinsulin levels have been reported as a predictor of T2DM. Additionally, a genome wide scan performed in 638 African American affected sibling pairs (ASP) from 247 families revealed modest evidence for linkage to T2DM age at diagnosis at 39 cM on chromosome 20p near microsatellite D20S470 (LOD 1.61; p=0.0075). Ordered subsets analysis also provided evidence for linkage to a T2DM subset with later age at diagnosis (max. LOD 2.50, p=0.027). The PCSK2 gene is within the LOD-1 interval of both linkage peaks. We genotyped 29 single nucleotide polymorphisms (SNPs) across this gene in 380 unrelated African American individuals with T2DM and end-stage renal disease (T2DM-ESRD) and 278 African American population controls without a known diabetes diagnosis. Four SNPs were found to be associated with T2DM: rs4814597 (p=0.047), rs1609659 (p=0.041), rs2021785 (p<0.001) and rs2269023 (p=0.040). Analysis with Haploview, extending the block if pairwise $D'>0.7$, revealed two blocks of high linkage disequilibrium (LD) containing 5 SNPs and 7 SNPs. Haplotype analyses using Dandelion showed the 7-SNP haplotype in the distal region of the gene was significantly associated with T2DM, with an overall haplotype $p$-value of 0.008. Within this block, there was a significant “risk” haplotype (6.8% in cases, 2.8% in controls; OR 2.46, p=0.022) counterbalanced by a “protective” haplotype (14.6% in cases, 22.9% in controls; OR 0.58, p=0.0066); rs2021785 distinguishes between these two haplotypes. The PCSK2 gene appears to play a role in susceptibility to T2DM in the African American population.
Engineered Heart Valve using Circulating Progenitor Cells Obtained from Patients with Vascular Disease

One of the continued problems of commercially available cardiac valve is the formation of thrombosis. Endothelial cell coverage of the valve surface is known to prevent the occurrence of thrombosis formation. In this study we investigated whether progenitor cells could be isolated, grown and differentiated from the peripheral blood of patients with vascular disease.

Circulating progenitor cells were isolated, grown and expanded from blood samples of patients with vascular disease. The cells were seeded onto collagen-based porcine derived valve matrix and placed under dynamic flow conditions that mimic normal circulation. The valve constructs were examined histologically, structurally and biomechanically over time.

The endothelial progenitor cell origin was confirmed using multiple cell specific markers. The cells seeded on valve matrices attached, proliferated and formed defined cell layers. The engineered valve tissue possessed similar biomechanical properties as normal valve tissues.

This study shows that progenitor cells can be isolated and grown from the peripheral blood of patients with vascular disease. The use of this technology may improve the outcome of heart valve surgery by minimizing the occurrence of thrombosis formation.
Meredith Lentz    Education
Advisor: Dr. Robert Evans

The extent to which primary sources in the biology classroom are a tool for teaching scientific literacy

Scientific literacy requires students to understand both the product and process of science. Primary sources, such as journal articles, offer students the opportunity to understand the process of science, whereas secondary sources, like textbooks, are typically product centered. The effect of reading primary and secondary sources was studied by assigning students a primary or secondary source article to read. The primary source was adapted to fit the students’ grade level and prior science knowledge. Both the primary and secondary source addressed the same content. After a set period for reading, students completed an attitude survey and posttest. The posttest was designed to test for both product and process knowledge through content knowledge, experimental design, and experiment interpretation. Results within classes showed some significant differences in favor of the primary source readers in both content knowledge and experiment interpretation. There was no significant difference in overall attitude between the two groups.

Nicole Levi    Biomedical Engineering
Advisor: Dr. David Carroll

Toxicity of Fullerene Clusters Within Human Cells

Unmodified fullerene clusters have been observed within multiple human cell lines. Visible confirmation of cell-fullerene interaction was made using confocal and optical microscopy. Determination of toxic effects of either the fullerenes or the dispersal solvent was made. No cytotoxic effects were found over an extended incubation time of C60 with any of three cell lines used. Optical sectioning allowed determination that fullerenes may permeate the cell membrane.
Electrospinning fabrication of Collagen-based Scaffold for vascular tissue engineering.

The goal of this study is to create a biomimetic, small-diameter vascular graft using electrospinning technology. Vascular scaffolds have been fabricated by electrospinning polymer blends of collagen type I, elastin, and poly (D,L-lactide-co-glycolide) (50:50) at a total solution concentration of 12% (w/v). In this study, fiber sizes of 0.72±0.35 microns diameter were obtained from the electrospinning process. Collagen type I and elastin demonstrated uniform distribution by immunohistological staining. The mechanical testing for compliance showed a typical pressure-diameter curve for electrospun scaffolds. 82% of smooth muscle cells and 78% the endothelial cells can survive on the scaffold as analyzed by mitochondrial metabolic (MTT) activity assay.

This study shows that electrospun scaffolds exhibit the structure and mechanical behavior similar to native vessels. The results also indicate a favorable interaction between this synthetic nanofibrous scaffold with the two types of vascular wall cells. Electrospun vascular scaffolds possess ECM components and distribution similar to normal vessels. Collectively, this study demonstrates the promise of electrospinning as an effective fabrication process for cardiovascular grafts.

Properties of single fibrin fibers with a combined Atomic Force and fluorescence microscope

Fibrin fibers are the major structural component of blood clots, which perform the mechanical task of stemming the flow of blood. We have used a combined Atomic force microscopy (AFM) and fluorescent microscopy instrument to collect complete, calibrated stress-strain curves of different types of single fibrin fibers in aqueous conditions. We found the following mechanical properties of fibrin fibers. 1) Fibrin fibers have a very large extensibility. The breaking strain (strain at rupture) of crosslinked and uncrosslinked thrombin-induced fibers is 332%±71% and 226%±52%, respectively; and of crosslinked and uncrosslinked batroxobin-induced fibers 265±83% and 226%±71%, respectively. 2) Fibrin fibers show up to 85% hysteresis; hysteresis becomes larger with larger strains. 3) Fibrin fibers are elastic when the strain is lower than 60%. 4) At high strain, some permanent deformations occur and no recovery on a time scale of several minutes is observed. 5) The initial Young’s modulus is ~ 5 MPa and it increases with increasing strain (strain stiffening). 6) Fibrin fibers relax when stretched out and held at constant strain (stress decreases at constant strain.) Two distinct stress relaxation rates of 0.67 second\(^{-1}\) (fast), 0.03 second\(^{-1}\) (slow) were observed.
Zhidong Ma
Chemistry
Advisor: Ulrich Bierbach

Synthesis and Characterization of DNA-Targeted Acridinylguanidines

PT-ACRAMTU ([PtCl(en)(ACRAMTU-S)](NO3)2 (ACRAMTU = 1-[2-(acridin-9-y lamino)ethyl]-1,3-dimethylthiourea) is the prototype of a new class of metalating-intercalating cytotoxic hybrid agents that produce an array of DNA adducts previously unknown in platinum antitumor chemistry. To dissect the mechanism by which these agents damage double-stranded DNA and to investigate the kinetic and thermodynamic factors contributing to PT-ACRAMTU's unique sequence and groove specificity, we are making systematic changes to the drug prototype. Here we present novel synthetic strategies for the design of analogous acridinylguanidines as intercalating carrier ligands in platinum-acridine conjugates. Several methods of guanidylation are described. The acid-base chemistry of the novel compounds will be discussed with regards to the potential use of acridinylguanidines as DNA-affinic carrier ligands.

Masood Ahammed Machingal
Biomedical Engineering
Advisor: Dr. George Christ

Cellular activation, signal transduction and intercellular communication in smooth muscle cells.

Coordinated cellular responses are essential in homeostasis and synchronized functioning of smooth muscle tissues. Although smooth muscle activity is affected by local control mechanisms or innervation, signal transmission is largely impacted by gap junction channels. Gap junctions are intercellular channels that form an anatomical network for cell-to-cell communication by permitting the passage of small second messenger molecules and ions. We are exploring the role of intercellular communication in tissue (contractile) responses mediated by different types of vascular and nonvascular tissue such as the innervated and/or myogenic controlled arteries, sparsely innervated corpora, and the more highly innervated bladder. Interdisciplinary approaches including calcium imaging, contractile response measurements and mathematical modeling are utilized to evaluate cellular activation, signal transduction and intercellular communication. Understanding how these processes contribute to normal tissue responses in physiologically distinct tissues will provide important guidance to tissue engineering of, for example, the bladder, corpora and blood vessels.
Requirement of RunX1 for the Function of the Adenovirus E1B-55K–E4orf6 Protein Complex

During an adenovirus infection the E1B-55K–E4orf6 protein complex performs a variety of activities that are important for the production of progeny virus. These activities include the regulation of mRNA transport from nucleus to cytoplasm, the degradation of p53 and the disruption of double-stranded DNA break repair. Previous studies have suggested that some of these activities require the proper localization of E4orf6 and E1B-55K in the nucleus of infected cells at late times of infection. Previous studies have also shown that interaction of E1B-55K and E4orf6, as measured by their nuclear colocalization, occurs in primate cell lines but not in rodent cell lines. The nuclear localization of E1B-55K and E4orf6 in rodent cells can be restored by the addition of a portion of human chromosome 21 containing the \textit{RUNX1} locus. These nuclear matrix-associated proteins may function as a scaffold for the assembly of ancillary proteins that control gene expression. Analysis of human and mouse RunX1 proteins has indicated that a subset of human RunX1 proteins can promote the nuclear E1B-55K localization in rodent cells. Preliminary results suggest that \textit{RUNX1} is important for a productive viral infection in epithelial cells. These studies are consistent with the notion that RunX1 is a primate-specific factor that promotes a functional interaction of the adenovirus E1B-55K and E4orf6 oncoproteins during virus infection. Scrutiny of the role of RunX1 during an adenovirus infection will provide a greater understanding of this human pathogen.
Angiotensin-(1-7): A Novel Chemotherapeutic Agent for Lung Cancer

Angiotensin-(1-7) [Ang-(1-7)] is an endogenous peptide of the renin-angiotensin system which has vasodilator and anti-proliferative properties. Previous epidemiological studies suggest that patients receiving angiotensin converting enzyme (ACE) inhibitors had a reduced incidence of developing lung cancer. Since treatment of animals or humans with ACE inhibitors increases Ang-(1-7), the heptapeptide may have antigrowth properties. Previous studies in our laboratory showed that Ang-(1-7) reduced serum-stimulated growth of human lung cancer cells in vitro. The current study was initiated to determine whether Ang-(1-7) inhibits lung tumor growth in vivo, using a human A549 lung cancer xenograft model. A549 cells were injected subcutaneously into the lower flank region of athymic mice and tumor size was measured three times a week. When the tumors were approximately 100 mm\(^3\) in size, osmotic mini pumps were implanted for the intravenous delivery of either saline or Ang-(1-7). After 28 days of treatment, there was a 30\% reduction in tumor volume in the Ang-(1-7)-treated mice, whereas the tumor size in the saline-treated animals increased 2.5 fold when compared to tumor size prior to the treatment (84.3 ± 19.8 mm\(^3\) vs 326.1 ± 19.8 mm\(^3\), p < 0.05, n = 5). The Ang-(1-7)-infused tumors weighed 46\% less than the saline-infused tumors at the end of 28 days (0.128 ± 0.009 g vs 0.279 ± 0.03 g, p < 0.05, n = 5). These results correlate with a reduction in the proliferation marker Ki67 in the Ang-(1-7)-infused tumors when compared to the saline-infused tumor tissues. Ang-(1-7) reduced COX-2 mRNA by 57\%, suggesting that Ang-(1-7) may decrease COX-2 activity and proinflammatory prostaglandins (0.582 ± 0.078 vs 1.028 ± 0.137, p <0.05, n = 5). In addition, Ang-(1-7) up-regulated caspase-3 mRNA by 210\% in the A549 lung cancer xenografts, indicating that the heptapeptide may also reduce growth by inducing apoptosis (2.182 ±0.200 vs 1.038 ± 0.126, p < 0.05, n=5). These results suggest that Ang-(1-7) inhibits lung tumor growth in vivo and that Ang-(1-7) may be an effective treatment for lung cancer. (Supported by CA-10309; A04-126)
Minimal Lipidation of apoA-I by ABCA1 forms heterogeneous-sized pre-β HDL particles with reduced ability to interact with ABCA1

Plasma HDL particles exist as discrete-sized subfractions, but the mechanism of formation of these heterogeneous-sized particles is not understood. The initial step of nascent HDL formation requires transfer of cellular cholesterol (chol) and phospholipid (PL) by ABCA1 to lipid-free apolipoprotein A-I (LFA-I). To investigate nascent HDL subfraction formation, we incubated 125I-LFA-I with HEK293 ABCA1 or non-transfected control cells. Gel electrophoresis revealed multiple pre-β migrating HDL particles, ranging from <7.1-15.7 nm in diameter in the medium of ABCA1 cells, but not control cells. Each subpopulation of pre-β HDL was purified by FPLC into pre-β1 (<7.1 nm), pre-β2 (~7.5 nm), pre-β3 (~10 nm) and pre-β4 (~12 nm) HDL particles that decreasing in density and contained an increasing molar ratio of PL and chol to apoA-I, respectively. HDL subfraction formation over a 24 h time course revealed, unexpectedly, that pre-β2, 3, and 4 HDL were formed simultaneously. Pre-β HDL particles had remarkably reduced ability to bind to or efflux radiolabeled PL and chol from ABCA1 cells compared with LFA-I (<10.4% and <37.6% for PL and chol efflux, respectively). These results suggest a new paradigm for nascent HDL particle assembly in which interaction of LFA-I with ABCA1 results in variable addition of lipid to generate pre-particles of discrete sizes and lipid content, which are poor substrates for subsequent lipidation by ABCA1 and presumably require additional non-ABCA1 mediated lipidation for further maturation.
Mismatch Repair Defects and Human Prostate Cancer

Mismatch repair (MMR) defects are strongly associated with both hereditary and sporadic types of cancer. Our overall hypothesis states that MMR defects are associated with the development and progression of prostate cancer. Immunohistochemical analysis of clinical prostatectomies reveals that 64% of tumors have alterations in at least one MMR protein. Fifty percent of those tumors with MMR alterations show an increase in the levels of PMS2. These observations led us to hypothesize that elevated levels of PMS2 contribute to prostate tumorigenesis.

To investigate the effect of elevated PMS2 on genomic stability, we isolated normal and cancer DNA from patients with increased staining for PMS2 and performed microsatellite instability (MSI) analysis. Eighty percent of the prostate tumors with elevated PMS2 levels displayed MSI, suggesting that a phenotype for increased PMS2 is genomic instability. In vitro tissue culture analyses are ongoing to determine the effect of PMS2 overexpression on MMR mechanism and hprt mutation frequency. The data presented will document a novel discovery that an increase in this MMR protein contributes to genome instability.

A control algorithm to augment plantarflexion power using powered ankle-foot orthoses

Walking is an important component in maintaining independence. As we age, declines in lower extremity strength and power have been linked with reduced mobility. In particular, ankle plantarflexor weakness has been identified as a key determinant of reduced walking speed. In this study, we developed a control algorithm to actuate a pair of powered ankle-foot orthoses (PAFOs) to augment plantarflexor power. The PAFOs, which use pneumatic muscles to augment plantarflexion power, were designed based on those developed by Ferris, et al. (J. Appl. Biomech. 21, 189-197, 2005). Two young (21 & 23) and two older adults (70 & 75 years) completed overground gait analyses while wearing the PAFOs with pneumatic muscles (1) inactive and (2) active. When the PAFOs were active, peak plantarflexion power and positive work increased by 23% and 54%, respectively. The control algorithm and PAFOs will be useful for addressing how plantarflexor power influences physical function.
Lindsey Oliver    Chemistry
Advisor: Dr. Suzanne Tobey

Synthesis of Homopropargylic Amines through an Allenyl Imino-Ene Reaction

Homopropargylic amines are difficult to access with existing protocols despite their increasing importance in natural product synthesis. Reported methods require multiple steps, have poor yields, and are substrate-specific. This research investigates the imino-ene mechanism with an allene and an imine provides a one pot synthesis of a homopropargylic amine. This mechanism also has potential to produce a stereoselective and functionalized homopropargylic amine. Initially, Lewis acids such as MgBr₂, CuC₂H₃O₂·H₂O, and Yb(CF₃SO₂)₃ will be screened with several imines and a silyl allene. Extension of the methodology will include various alkyl and aryl 1-substituted allenes. Preliminary results with 1-dimethylphenylsilyl-1,2-butadiene as a substrate are reported.

Eric S. Oshige    Chemistry
Advisor: Dr. Paul B. Jones

Synthesis and investigation of photoactivated artificial metalloproteases

The synthesis and photochemical investigation of a number of photoisomerizable metal-binding ligands will be presented. This new class of molecule is designed to act as a photoactivated artificial metalloprotease. Trans to cis photoisomerization moves the carboxyl group of an ester or amide close to a metal-bound water molecule, leading to hydrolysis. Synthesis, photochemical characterization, hydrolysis kinetics and yields for reaction products will be reported. The scope of this reaction, potential for photolabile protection of alcohols and amines, and possible applications will be discussed.
Ramakrishna R. Pidaparthi  Chemistry
Advisor: Dr. Mark Welker

**Novel Synthesis of air stable, moisture resistant silyl dienes – Sequential / Tandem Diels-Alder and Hiyama Coupling reactions**

From the past 10 years, cross-coupling reactions of the aryl silicon compounds, Hiyama couplings have drawn much attention from the synthetic chemical community because of their economical, commercial availability in different forms or by their easy synthesis. But little attention was paid towards the synthesis of silyl dienes and their Diels-Alder reactions. We have not found any examples on the subsequent cross-coupling reactions of the resulting cycloadducts. Herein, we report easy, economical ways of synthesizing substituted and unsubstituted 2-silyldienes. Also we explain their synthetic applications by showing a couple of representative examples of the dienes prepared so far by using them in Diels-Alder and sequential / tandem cross-coupling reactions. From the studies, we have concluded that the reactivity and regio selectivity was enhanced by our dienes when compared with the reported literature.

Edward E. Pryor Jr.  Computer Science
Advisor: Dr. Jacquelyn S. Fetrow

**PASSS: Protein Active Site Structure Search**

Identification of protein function is very useful in structural genomics initiatives where the function of a protein structure is not always known in advance of solving the structure. Commonly, the overall protein sequences will be compared and, if similar, the proteins will be assumed to have a similar function. Proteins of similar sequence often exhibit similar functions; however, there are many documented examples where proteins have similar structure and function, but dissimilar sequences. In addition, sequence comparison does not provide information about the chemistry underlying the function. (2nd paragraph:) A method was developed to search the three dimensional structure of proteins for structural similarities within their active sites. Since this application compares the structure, and not sequence, two proteins with similar functional sites, but low overall sequence similarity, will be identified. The tool can be used to extrapolate function from known protein structures to unknown proteins.
Matthew Rave  
Physics  
Advisor: Dr. William Kerr

Berry curvature contributions to the density fluctuation spectrum of Bloch electrons

Recent work has shown that the equations of motion (EOM) for semiclassical Bloch electrons must be modified in the presence of a non-zero Berry curvature [1]. These corrections to the EOM have implications for many physical quantities: effective mass, electron orbits in a magnetic field, de Haas-van Alphen oscillations, etc. In addition the Boltzmann transport equation is also modified with possible ramifications for calculations of transport phenomena. We investigate these issues for a gas of spinless Bloch electrons in an external electric field. We find modifications to the traditional dispersion relation for density fluctuations; in particular we find damping due to the external electric field and an anisotropic sound velocity. [1] M.-C. Chang and Q. Niu, Phys. Rev. B 53, 7010 (1996)

Natallia Riddick  
Physiology & Pharmacology  
Advisor: Dr. Michael Nader

Effect of Menstrual Cycle Phase on Dopamine D2 Receptor Availability in Female Cynomolgus Monkeys

Numerous sex differences have been reported in clinical disorders such as Parkinson’s disease, Tourette’s syndrome and drug abuse. Many of these disorders involve dysfunctional dopamine (DA) neurotransmission. Within the DA system there are two superfamilies of receptors, D1- and D2-like. Sex differences exist in DA D2 receptor binding characteristics, in both animals and humans. The goal of the present study was to extend previous work on menstrual cycle and DA D2 receptors using high-resolution microPET imaging in drug-naïve female cynomolgus monkeys (n=7). Menstrual cycle phase was characterized by daily vaginal swabs and by blood draws to confirm progesterone levels. PET studies were conducted once during the luteal phase and once in the follicular phase using the DA D2 receptor ligand $[^{18}\text{F}]$fluoroclebopride (FCP). Regions of interest were drawn from MRIs around the caudate nucleus, putamen, anterior cingulate cortex and the cerebellum. Distribution volumes were assessed in each structure and the distribution volume ratio (DVR) for a brain region relative to the cerebellum was used to measure D2 receptor availability. D2 DVRs were significantly higher in luteal phase compared to follicular phase in both caudate and putamen. In contrast, low $[^{18}\text{F}]$FCP DVRs observed in the anterior cingulate cortex did not change across phases. These findings are in contrast to reports in humans that menstrual cycle does not affect D2 DVRs and suggest that DA receptor availability is significantly influenced by female hormone levels, which could have implications for the treatment of affective disorders in women. Supported by DA 017763 (MAN) and CBI pilot grant.
Patrick Rowe
Molecular Medicine
Advisor: Dr. Janice Wagner

The Effects of Hyperglycemia on Oxidative Stress in Diabetic Arteries

Numerous studies have shown that diabetes increases risk of cardiovascular disease. Hyperglycemia is thought to be responsible for many of the vascular complications of diabetes, possibly mediated through production of reactive oxygen species (ROS). Transition metals (iron, copper) are excellent catalysts for the production of damaging oxidants, and in previous studies we found evidence of enhanced arterial metal-catalyzed ROS in diabetic monkeys. The present study investigates the effects of hyperglycemia on systemic and arterial measures of iron regulation and oxidant stress. Twenty cynomolgus monkeys were randomized to either control or streptozotocin-induced diabetes (STZ-DM) and fed a moderately atherogenic diet for 1 month to investigate early effects of hyperglycemia. Results show increases in ferritin concentrations and measures of systemic (MDA, oxLDL) and arterial ROS (O$_2^-$) in STZ-DM monkeys with no compensatory increase in arterial heme oxygenase-1 protein (HO-1). Thus, a dysfunctional HO-1 response may allow heme-iron to accumulate in diabetic arteries.

Alexander M. Schoemann
Psychology
Advisor: Dr. Catherine Seta

How do we pick our leaders? Similarity and qualification as determinates of leader selection.

The social identity theory of leadership has demonstrated that when group salience is high people will prefer a leader who is a prototypical in-group member and they will rate a prototypical in-group member as a more effective leader (Hains, Hogg, & Duck, 1997). Does preference for an in-group leader hold across performance based (solving logic problems) and attitude based (group discussions) tasks? Participants (N=99) were randomly placed into groups. Participants were given a performance or attitude based group task and chose between a leader who was a prototypical in-group member and a leader who held stereotypical leader traits. Results: Males strongly preferred the stereotypical leader in both situations ($\chi^2=0.01$, p=.925). Females strongly preferred stereotypical leaders for performance based tasks, but showed equal preference in an attitude based task ($\chi^2=3.13$, p=.039). The gender difference may be drive by females viewing leader selection as more important than males (t=2.62, p=.026).
Neural Tissue Engineering Scaffolds from Self-Assembled Human Hair Keratins

Current treatments for peripheral nerve injury consist of surgical reconnection of the damaged nerve ends, the use of an autograft, or the insertion of guidance conduits. Clinically, the use of nerve conduits has been restricted to smaller defects because of limited functional recovery with increased nerve gaps. We hypothesize that a tissue engineering approach that employs a nerve guide filled with an optimized keratin scaffold can accelerate regeneration beyond current clinical limits. Keratins extracted from human hair fiber are a novel group of biomaterials with superior biocompatibility and growth factor activity. Recently, we have also discovered a remarkable ability for certain keratin preparations to self-assemble into porous, fibrous morphologies that are amenable to cell infiltration. In this study, we employed a tibial nerve injury mouse model to determine whether insertion of a keratin hydrogel into the conduit would accelerate functional nerve regeneration in vivo. After 6 weeks, the extent of regeneration was evaluated using electromyography (EMG). Functional testing showed that keratin filled conduits significantly enhanced the nerve regeneration process in comparison to empty conduit controls. This data demonstrates that keratin hydrogels serve as effective scaffolds for neural tissue engineering and facilitate functional recovery of damaged nerve. Therefore, we believe keratin filled conduits show great promise clinically and may allow for correction of larger nerve defects.
Protein Labeling with Red Squarylium Dyes for Analysis by Capillary Electrophoresis and Laser-Induced Fluorescence Detection.

The use of fluorescent probes enables increased sensitivity for detection of biomolecules over UV-visible detection. Squarylium dyes are a class of compounds which non-covalently label proteins and fluoresce in the NIR region. Absorption in the NIR is of particular interest in fluorescent labeling because it offers lower background signal and less scattering than the visible and ultraviolet regions when analyzing biological samples. In addition, lesser expensive, longer lasting, diode lasers can be used for excitation. The stability, along with their ability to form non-covalent bonds with proteins makes Squarylium Red-1c and Red-3 ideal probes for on-column fluorescence labeling thereby resulting in less sample handling and increased the speed of analysis.

The Effectiveness of Writing Across the Curriculum.

The purpose of this study was to gauge the effectiveness of writing across the curriculum in a high school biology classroom. Several classes of regular and honors students were used to gather data. The classrooms were split in half with half of the class completing higher order writing assignments and the other half lower order worksheets. The classes were then tested for understanding of the material taught. It was found that the students who completed the worksheets did not have significantly better scores on the tests. Therefore, this study does not support previous research that writing across the curriculum promotes better grades and understanding due to thinking at higher levels on Bloom's taxonomy.
**Defects in gravitropic response and lateral root development in hy5 are flavonoid independent**

Plants respond to gravity by differential growth mediated by changes in distribution of the hormone auxin. Auxin transport is regulated by flavonoids, which act as endogenous transport inhibitors. We have tested the role of flavonoids in root gravitropism by examining gravitropic response in the tt4 mutant, which is deficient in a flavonoid biosynthetic enzyme, and the hy5 mutant, which has defects in transcription of multiple genes including those encoding flavonoid biosynthetic proteins. Multiple tt4 alleles have reduced root gravitropism indicating that flavonoids are required for maximal gravity response. hy5 also has defects in root gravitropism, so we asked whether these defects were due to defective flavonoid biosynthesis. We treated hy5 with flavonoid precursor and quantified flavonoid accumulation, and gravity response. Our results indicate that flavonoid biosynthesis is restored in hy5, but gravity response is still reduced due to altered expression of genes beyond those of flavonoid synthesis.

**Contributions of L7Ae Loop 9 Residues to RNA-Binding Specificity**

Archaeal ribosomal protein L7Ae is a multifunctional RNA-binding protein that recognizes K-turn motifs in ribosomal, box C/D, and box H/ACA snRNAs. In eukaryotes, the 15.5kD/snu13p homologs are the functional counterparts that interact with box C/D snoRNAs and spliceosomal snRNAs. These proteins bind box C/D s(no)RNAs and are required for subsequent interactions with the Nop56/58 and fibrillarin core proteins for roles in 2′-O methylation of ribosomal and other RNAs.

The amino acid sequences and structures of the archaeal L7Ae and eukaryotic 15.5 kD / snu13p proteins are remarkably similar. Studies from several labs have shown that L7Ae interacts with both the box C/D and box C′/D′ motifs in archaean and eukaryotic s(no)RNAs, while the 15.5kD/snu13p protein can only interact with the box C/D motif. We present site-directed mutagenesis and biochemical analyses which examine the basis of the differential RNA-binding activities of the *Methanocaldococcus jannaschii* and mouse 15.5kD box C/D core proteins.
Do People Know How They Are Acting?

The area of personality agreement and person-perception has investigated the factors that influence agreement between target self-ratings of behavior and observer ratings of target behavior. Research suggests that targets and observers show only moderate to weak agreement on behavior ratings, calling into question the accuracy of self reports of behavior. This study specifically examined (i) whether targets and observers agree about how the target is acting in brief activities, and (ii) how familiarity, or the increased observation of a target individual over time, affects the level of agreement between observers and targets. Targets interacted in groups for 10 weeks, resulting in 20 behavioral ratings for each target-observer pair. There were significant levels of agreement for the typical target-observer pair on 18 of the 20 behaviors and agreement increased from the 1st to the 10th session for about half of the behaviors, demonstrating a strong familiarity effect.

Target-observer agreement was significant for almost all behaviors and agreement increased over time.
New Prussian Blue analogues based on cluster [Nb6Cl12(CN)6]4−: Synthesis and characterization

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The Prussian Blue analogues based on hexacyanometalate compound [M(CN)6]n− are among the earliest known coordination compounds and their diverse magnetic and electronic properties have been studied extensively.[1-3] Recently they have provoked much interest because of their interesting absorption properties.[4,5] In our quest for cluster-based hybrid materials we investigated the preparation and the properties of a new family of Prussian Blue analogues with a formula (MeN)2 [ANb6Cl12(CN)6]nH2O (A = Mg, Co,…) in which the octahedral [Nb6Cl12(CN)6]4− cyanochloride metal cluster is used as an expanded analogue of the mononuclear complex [M(CN)6]4−. Powder X Ray diffraction patterns of prepared compounds can be indexed in f.c.c unit cell with unit cell parameter varying from 15.1 to 16.0 Å. The shift of $\nu$(CN) band to high wavenumber values in IR spectra shows the coordination of N of the CN group in [Nb6(CN)6]4− to the metal A. Thermogravimetric study shows thermal stability up to 250 °C. Gas adsorption investigations were carried out and indicate that the adsorption isotherms are type I isotherm characteristic of microporous materials with homogeneous pores. The Langmuir surface was estimated to be 258m2/g. This surface area is comparable to inorganic zeolites where the highest surface area is around 500m2/g.
Active Site Profile Scoring With Protein Features

The active site structure of a protein is a key determinant for the protein function. Active site profiling is a method used to represent active site structural characteristics of proteins with similar functional sites. A sequence identity-based scoring method for the active site profile was previously developed to discriminate between true functional sites and those of similar structure but not similar function [1]. The scoring method clearly delineates sequentially conserved protein families. However, its performance significantly decreases with larger and more complex superfamilies. New scoring methods are being developed to solve this problem. These methods incorporate amino acid physicochemical properties, such as hydrophobicity, conformational reference, and charge into the scoring function. Each property is first preprocessed using a normalization method and then encoded into the active site profile. Various quantitative and statistical methods are implemented as part of the new scoring methods. The goal for the new scoring methods is to separate out the true positive from the false positive profiles for all families, as well as providing additional information within each profile to predict properties that contain the most information about the active site.

Self-compassionate Reactions to Negative Events: Cognitive and Motivational Processes

Self-compassion involves three components: (a) self-kindness – forgiveness and acceptance of one’s failures and flaws, (b) mindfulness – maintaining a balanced view of one’s emotions, and (c) common humanity – viewing shortcomings and setbacks as a normal part of experience. Recent research indicates that self-compassionate people have greater psychological well-being and resilience (Neff, 2003; Leary et al., 2006). However, because high self-compassion correlates highly with high self-esteem and low neuroticism, the relationship between self-compassion and well-being may reflect the influence of these other variables rather than self-compassion per se. We investigated four cognitive and motivational concomitants of self-compassion’s while controlling for neuroticism and self-esteem. Multiple regression analyses revealed that self-compassionate people worry less, have fewer egoic beliefs, are motivated by growth rather than validation, and have fewer catastrophic thoughts following negative events, which leads to less volatile emotional reactivity.
Teachers’ Use of the First and Last Five Minutes of Class

From the first bell of the day to the final ‘ring’ that releases students to buses, parents and extra-curricular activities, teachers’ responsibilities extend far beyond instruction. The function of classroom time has been expanded to include certain administrative roles, including taking attendance, making announcements and general class organization. While this expansion of duties has streamlined many school processes and ensured all students receive important information (a presentation on the new SAT, for example) it has represented a decrease in instructional time as well as a change in the classroom order of events.

This study focused on four teachers’ use of the first and last five minutes of class time; their actions were coded and analyzed and conclusions drawn about the effectiveness and efficiency of those critical ten minutes. The results suggest that overall, 2/3 of the first five minutes are spent in non-instructional activities, while only 1/3 of the last five minutes are non-instructional.

Preferential translation of vesicular stomatitis virus mRNA is conferred by transcription from the viral genome.

Translation of host mRNAs is inhibited in cells infected with vesicular stomatitis virus (VSV). It has been proposed that viral mRNAs are subjected to the same inhibition, but are predominantly translated because of their abundance. To compare translation efficiencies of viral and host mRNA during infection we used an EGFP reporter expressed from a recombinant virus or from the host nucleus in stably-transfected cells. Relative translation efficiencies were determined by the ratios of the rates of protein synthesis to mRNA levels. Translation efficiency of host-derived mRNA was reduced more than three fold at eight hours post-infection while viral-derived mRNA was translated over two-fold more efficiently than host mRNA in uninfected cells and around seven-fold more efficiently than host mRNA in wtVSV-infected cells. To determine if cis-acting sequences in untranslated regions (UTRs) are involved in preferential translation, we constructed EGFP reporters with VSV or control UTRs and measured the translation efficiency in mock-infected and VSV-infected cells. The presence of VSV UTRs did not affect mRNA translation efficiency. Therefore, we conclude that the source of VSV mRNA distinguishes it from host mRNA allowing preferential translation.
Challenges and Trends in North Carolina College and University Career Centers

This poster describes the results of research conducted by contacting all multidisciplinary four-year colleges and universities which have on-campus career centers in North Carolina which was funded by a grant from the North Carolina Career Development Association. A 49-item online survey and 5-item follow-up survey were distributed to directors of each career center in order to gather information on trends in staffing, methods of counseling used, the future of the profession, and best practices used at each higher education institution. Highlights of survey results include strategies to maximize budgetary constraints and innovations developed which increase student and recruiter investment in the college or university. Implications for further research are noted.

Authenticity is Related to Within-Person Variations and Between-Person Variations in Behavior

This study investigated whether variations in felt authenticity are correlated with certain within-person variations in behavior (states) and between-person variations in behavior (traits). Targets participated in different activities while being observed; twice during each activity, self-reports and observer-reports of a target’s behavior and authenticity were made. It was determined that, consistent with Humanistic theories of authenticity and contrary to a trait-consistency theory of authenticity, (a) increases in felt authenticity correlated with within-person increases in state agreeableness, state emotional stability, state extraversion, and state openness, regardless of trait levels; and (b) increases in felt authenticity correlated with higher between-person variations in levels of trait agreeableness, trait conscientiousness, trait extraversion, and trait self-concept clarity. It was also determined that an observer’s perception of target authenticity was not correlated with within-person variations in behavior and between-person variations in behavior, indicating that self-perceptions of behavior might not correlate with observer perceptions of behavioral authenticity.
The EphA2 Receptor and EphrinA1 Ligand: Differential Expression and Function in Glioblastoma Multiforme

Glioblastoma multiforme (GBM) is the most common and lethal primary malignant brain tumor. We have previously shown that EphA2, a member of the Eph receptor tyrosine kinases, is a molecular marker and potential therapeutic target in GBM.

We have now examined the expression of EphA2 together with its membrane-bound ligand, ephrinA1. We have also begun to investigate a potential functional role for the receptor and ligand in the highly invasive and malignant GBM phenotype. Western blot analyses revealed a pattern of differential expression of EphA2 and ephrinA1 in GBM cell lines and tissues. High levels of EphA2 were consistently associated with low levels of ephrinA1, and vice versa. In addition, the failure of a phospho-tyrosine specific antibody to recognize phosphorylated EphA2 in GBM cells and tissues indicated the presence of unactivated, non-tyrosine phosphorylated receptor. Notably, EphA2 became phosphorylated upon stimulation of GBM cells with a soluble form of ephrinA1. Thus, low levels of ephrinA1 may favor the presence of unactivated EphA2, which in turn has an impact on the malignant properties of GBM. In support of this notion, high EphA2-expressing cell lines treated with ephrinA1 exhibited a significant dose-dependent decrease in anchorage independent growth and invasion, and a temporary decrease in EphA2 protein. Furthermore, the shape of GBM cells dramatically changed in response to ephrinA1, resulting in the shortening of processes and loss of polarity.

Thus, the EphA2/ephrinA1 system may play a dual role in GBM, with EphA2 potentially serving as an oncogene, and ephrinA1 as a tumor suppressor. This scenario will be exploited for the specific therapeutic targeting of GBM.
Saami Yazdani         Biomedical Engineering
Advisor: Dr. Joel Berry

Natural collagen scaffolds for tissue engineered blood vessels.

Small caliber synthetic grafts used for CABG are compromised by thrombogenicity and accelerated intimal thickening, resulting in early graft occlusion. Synthetic grafts do not possess the mechanical and biological properties of native artery. Tissue engineered blood vessels (TEBV) represents a new approach to alleviate problems associated with synthetic grafts. Endothelialization of small-caliber TEBV is essential in maintaining lumen patency. The purpose of this study was to characterize the structure; both mechanically and morphologically, of an endothelialized small-caliber TEBV. Porcine carotid arteries were decellularized and the mechanical properties were measured to ensure the conduit behaved similar to the native tissue. The TEBV were seeded with endothelial cells (EC) in a bioreactor where they were subjected to physiological conditions for 1 week. The results of the mechanical properties illustrated that the TEBV performs similar to the native artery with regards to stress, strain, and burst pressure. Hematoxylin and Eosin staining and Scanning Electron Microscope illustrated that Bovine EC, seeded on the luminal side, adhered to the matrix and formed a uniform monolayer. These results reveal that preconditioning of the cells in a bioreactor is important when forming a monolayer of EC. TEBV coated with EC posses many morphologic and functional characteristics and may potentially be useful clinically as vascular grafts.

Ye Yuan             Physics
Advisor: Freddie Salsbury

Title of Poster: Electrostatic study of TryP’s local conformational change.

Tryparedoxin peroxidase (TryP) from Crithidia fasciculate is a member of peroxiredoxin (Prx) superfamily which utilizes redox-active cysteines in the active site in the reduction of peroxides, which is implicated in signalling processes. As cysteine activation requires the deprotonation of an active site cysteine, the lowering of the pKa of this residue is especially important for function. During the course of the catalytic cycle, TryP undergoes active site conformation changes during which the environment of the cysteine changes. Structures representing these changes have been obtained via x-ray crystallography. In order to ascertain the effect of these local conformation changes on the molecular function, 8 monomers of TryP in three different active site conformations are analyzed dynamically and through electrostatics. The pKa of active site CYS varies between the different conformations. However, different monomers in the same local conformation exhibit similar electrostatic behavior as measured by both the cysteine pKa and the nature of the residues giving rise to the cysteine pKa. This work provides insight into the catalytic mechanism of TryP.
Assembly of Neutral cluster-based supramolecular nano-rod \([\{\text{Mn(salen)}\}(4,4'\text{-bpe})\text{[Mn(salen)](H2O)}]\)\(_2\text{[Nb6Cl12(CN)6].8H2O}\)

The preparation of supramolecular assemblies built of functional molecular building blocks with well-defined structures is an important topic in material chemistry. Our work in recent years has concentrated on the preparation and characterization of structures built of octahedral metal clusters and molecular metal complexes. Here we report the preparation and structure of a 4.4 nm nano-rod built of [Mn(salen)]\(^+\) metal complex and octahedral cluster [Nb6Cl12(CN)6]\(^-\) and a conjugated linker, 4,4'-bpe (trans-1,2-Bis(4-pyridyl)ethylene).

The one-pot reaction between [Mn(salen)]ClO\(_4\)\(\cdot\)2H\(_2\)O, (Me\(_4\)N)\(_4\)[Nb6Cl12(CN)6]\(\cdot\)2MeOH and 4,4'-bpe leads to the formation of the title neutral compound whose structure consists of an [Nb6Cl12(CN)6]\(^-\) cluster that connect to two dimeric [(Mn(salen))(4,4'-bpe)(Mn(salen))] through two cyanide ligands located in Trans positions. The dimers are formed of two [Mn(salen)]\(^+\) metal complexes bridged by a 4,4'-bpe linker. The most striking feature of the compound is its length (about 4.47nm) and its neutral charge, both of which are rather rare in metal clusters chemistry.

Yue Zhao

Structural Complexity and Dimensional Flexibility in Template Controlled Molecular Assembly of Metal Dialkylphosphonate Polymers

Two novel gallium dialkylphosphonates were prepared by solvothermal reactions and characterized by single crystal X-ray diffraction. Ga2O3, HCl, (H2PO3)\(_2\)CH\(_2\), and different organic templates were mixed in ethanol and the mixtures were sealed in Teflon pouches and heated in 150 ml capacity Teflon-lined stainless steel Parr autoclave at 150°C for 3 days.

The compound Ga[(PO3CH2PO3H)(HPO3CH2PO3H)(H2en) (I)] crystallizes in the triclinic system (space group P-1 (No.2), a = 6.336(2) Å, b = 9.910(3) Å, c = 12.347(4) Å, \(\alpha = 79.626(5)°\), \(\beta = 85.785(5)°\), \(\gamma = 80.396(5)°\), \(V = 751.2(4)\) Å\(^3\)). It has 1D anionic framework. Each (GaO\(_6\)) octahedra is linked through three (PO3CH2PO3)\(^-\) anions to form chains running along the a axis. The (HPO3CH2PO3H)\(^2\)- unit acts as chelating ligand of the gallium atom.

Compound Ga(PO3CH2PO3)(H2O)(H2DABCO)0.5 (II) crystallizes in the monoclinic system (space group C2/c (No.15), a =24.344(3)Å, b =8.1838(9)Å, c =9.566(1)Å, \(\beta =96.003(2)°\), \(V =1895.2(4)\) Å\(^3\)). It has 2D anionic framework. Each layer is built of (GaO\(_6\)) octahedra linked through (PO3CH2PO3)\(^-\) anions.
Hybrid Inorganic-organic Frameworks Built of Octahedral Metal clusters \( [\text{Nb}_6\text{Cl}_{12}(\text{CN})_6]^4^- \) and Manganese Schiff-Base Complexes

Reactions between \( \text{R}_4[\text{Nb}_6\text{Cl}_{12}(\text{CN})_6] \) (\( \text{R} = [\text{Me}_4\text{N}]^+, [\text{Et}_4\text{N}]^+ \)) and \([\text{Mn}_2(L)_2(\text{OAc})](\text{ClO}_4)\) (\( L = 7\)-Me-salen) were investigated in order to prepare frameworks built from the octahedral cyanochloride cluster \( [\text{Nb}_6\text{Cl}_{12}(\text{CN})_6]^4^- \) and the phenoxo-bridged dimer \( [\text{Mn}_2(L)_2]^2^+ \). Depending on the starting materials and solvent systems, three different compounds were obtained: \([\text{Me}_4\text{N}]_2[[\text{Mn}(L)_2][\text{Nb}_6\text{Cl}_{12}(\text{CN})_6]]\cdot2\text{MeOH} \) (1); \( [[\text{Mn}(L)(S)]_4[\text{Nb}_6\text{Cl}_{12}(\text{CN})_6]]\cdot2\text{MeOH}•2\text{H}_2\text{O} \) (S = MeOH, \( \text{H}_2\text{O} \) ) (2) and \([\text{Mn}(L)(\text{EtOH})_2][[\text{Mn}_2(L)_2][\text{Nb}_6\text{Cl}_{12}(\text{CN})_6]]\cdot2\text{MeCN} \) (3). In 1, each cluster is linked to four monomeric complexes \([\text{Mn}(L)]^+ \) and each monomer links two cluster units to give anionic layers parallel to the crystallographic \( ab \) plane; In 2, each cluster is coordinated by four solvated monomers \([\text{Mn}(L)(S)] \) to form pentameric units that are hydrogen bonded to each other to form chains along the crystallographic \( a \) axis. In 3, \([\text{Nb}_6\text{Cl}_{12}(\text{CN})_6]^4^- \) and dimeric units \([\text{Mn}_2(L)_2]^2^+ \) connect to each other via \( \text{CN}^- \) ligand to form neutral chains extending along the crystallographic (110) axis. For comparison purposes, reactions between the anion \([\text{Fe}(\text{CN})_6]^4^- \) and \([\text{Mn}_2(7\text{-Me-salen})_2(\text{OAc})](\text{ClO}_4)\) in MeOH/H\( _2\text{O} \) were investigated leading to formation of a neutral 2D framework \([[[\text{Mn}_2(7\text{-Me-salen})_2][\text{Fe}(\text{CN})_6]]_4•4.5\text{MeOH}•4\text{H}_2\text{O} \) (4), in which each \([\text{Fe}(\text{CN})_6]^4^- \) is coordinated by four dimers and each dimer links two \([\text{Fe}(\text{CN})_6]^4^- \) to form layers that stack on top of each other along the crystallographic \( c \) axis. 1 is paramagnetic. In 3 an antiferromagnetic transition is observed below 70K while in 4 a ferromagnetic transition is observed below 50 K. Details of synthesis, crystal structures, magnetic properties and thermal behavior of these materials will be presented.