

Yonas Abraham

Physics

Advisor: Dr. N.A.W. Holzwarth

A method for calculating surface electronic structures using semi-infinite boundary conditions

The SI-PAW "method is designed to solve the Kohn-Sham equations within the projector augmented wave PAW" formalism with boundary conditions appropriate for the semi-infinite geometry of material surfaces. This method, which directly distinguishes between bulk, surface, and defect states, is an extension of the very successful Appelbaum-Hamann method, modified to accommodate non-local potential terms in the PAW formalism. In the bulk region, the wave functions are composed of linear combinations of Bloch waves of the converged self-consistent periodic lattice. In the vacuum region, the wave functions are composed of functions which decay or propagate into the vacuum. In the interface region, the wavefunctions are composed of extensions of the Bloch wavefunctions or surface states which decay into the material. An efficient numerical integration scheme for determining the interface wavefunction is based on the GMRES algorithm.

Sallie Allgood

Biology

Advisor: Dr. Wayne Silver

THE EFFECT OF CAPSAICIN/VANILLOID RECEPTOR BLOCKERS ON PERIPHERAL TRIGEMINAL NERVE RESPONSES TO IRRITANTS

Vanilloid receptors (VR1), on peripheral trigeminal nerve (TN) fibers, are non-selective cation channels with high permeability for divalent cations. VR1 responds to heat, acids and capsaicin but its role in trigeminal irritation is not well known. Here we investigate the role of VR1 in TN responses using neural recordings from the ethmoid nerves of rats in response to solutions of capsaicin, propionic acid, cyclohexanone and nicotine delivered to the nasal cavity. In the presence of ruthenium red, an inhibitor of Ca²⁺ transport, the response to capsaicin and propionic acid decreased, to cyclohexanone increased, and nicotine stayed the same. In the presence of capsazepine, a competitive VR1 inhibitor, the same pattern was seen. Thus, while capsaicin and propionic acid may at least partially exert their effect through VR1, nicotine does not. In addition, cyclohexanone interacts in some way, but more work needs to be done to determine the exact interaction.

Lauren Anton

Molecular Medicine
Advisor: Dr. Bridget Brosnihan

Placental distribution of Ang-(1-7) and ACE2 in normal and compromised human pregnancies

Angiotensin-(1-7) [Ang-(1-7)] increases during normotensive pregnancy, attaining lower levels in preeclampsia. This study identified the expression of Ang-(1-7) and angiotensin converting enzyme 2 (ACE2) in the human placenta. Placental samples were obtained at the first-trimester or the third-trimester (normotensive and preeclamptic pregnancy). Immunohistochemistry was performed using an affinity purified polyclonal antibody to Ang-(1-7) or a monoclonal antibody to ACE-2. Ang-(1-7) and ACE2 staining showed a similar distribution in both maternal and fetal tissues, specifically, in syncytiotrophoblast, cytotrophoblast, invasive trophoblast, intraarterial trophoblast, endothelial cells of villi, vascular smooth muscle cells of stem villi, decidual cells, and glandular and luminal epithelium. The intensity of the Ang-(1-7) and ACE2 staining was decreased during preeclampsia as compared to first trimester and third trimester. The sites of expression of Ang-(1-7) and ACE2 in the human placenta support the hypothesis that Ang-(1-7) and ACE2 play a role in the control of placental blood flow.

Blythe Ashcraft

Chemistry
Advisor: Dr. Robert L. Swofford

CH OVERTONE ENERGIES CAN BE PREDICTED FROM AB INITIO POTENTIAL ENERGY SURFACES

The C-H stretching overtones of linear alkanes are found in the visible and near-IR regions. Our research specifically focused upon $\nu_{C-H} = 6$ using gas-phased photoacoustic spectroscopy. Using Grams/32 (Thermo Galactic), Lorentzian line shapes were fit to the energy peaks. It was seen that these energy peaks are sensitive to molecular conformers. We will show how the computed potential energy surfaces are fit with Morse potentials, leading to computed overtones. And finally, we will compare the computed absorption energies to the experimental results.

Allison Bagwell

Molecular Genetics
Advisor: Donald Bowden

Comparative Genomic Analysis of the HNF-4 α Transcription Factor Gene

A positional candidate gene in the type 2 diabetes mellitus (T2DM) linked region on chromosome 20q12-q13.1 is hepatocyte nuclear factor-4 alpha (HNF-4 α), the gene for the Maturity-Onset Diabetes of the Young type 1 (MODY1) sub-type of T2DM. Mutations in the coding region of HNF-4 α are rare in type 2 diabetes individuals. We hypothesized that altered regulation of HNF-4 α gene expression may contribute to susceptibility to T2DM. Comparative genomic analysis using PipMaker was performed with 13 kb of 5' promoter sequences of the human, mouse, and rat HNF-4 α . Three regions, located at -10.344 kb (295 bp in length), -6.476 kb (421 bp in length), and -5.472 kb (263 bp in length), were identified as having significant sequence identity between the 3 species with expect values of 1e-37, 1e-84, and 1e-79, respectively. Functional analysis of these three regions using transient transfection assays revealed that these sequences have weak ability to activate gene expression in pancreatic cells or dedifferentiated hepatoma cells, with expression being 1.0-2.5-fold over control vector. In differentiated hepatoma cells, the 295 bp region and the 263 bp region exhibit weak, though statistically significant, activity over control levels ($P \leq 0.001$). The construct containing the 421 bp sequence confers strong activity in the differentiated hepatoma cells, with a 13.71 +/- 1.95-fold increase in reporter gene activity over control vector ($P = 0.006$), suggesting that the 421 bp sequence is an enhancer of HNF-4 α gene expression that acts in a tissue-specific manner. The DNA of 259 Caucasian T2DM subjects was screened by denaturing high performance liquid chromatography to identify sequence variants in the three conserved regions. Only 2 SNPs were identified, both of which increased reporter gene activity 1.42-1.70-fold over wild type in the insulinoma cell lines ($P < 0.05$). These results suggest that functional regulatory elements of HNF-4 α , and likely other genes, can be successfully identified by comparative genomic analysis. Furthermore, the limited sequence variation within these regions suggests that these elements are likely of functional importance in humans.

Amber Barnes

Molecular Medicine
Advisor: Dr. Greg Kucera

Interaction of Hyperthermic Chemotherapy and Cyclooxygenase-2 Inhibition in Ovarian Cancer

Cisplatin resistance is a poor prognostic factor for ovarian cancer. Elevation of COX-2 is implicated in cisplatin resistance. Also, hyperthermia has been shown to enhance cytotoxicity; therefore, their combination could enhance response rates in ovarian cancer cells. Our study's objective is to determine the ability of hyperthermia and the inhibition of COX-2 to enhance the cytotoxicity of cisplatin in ovarian cancer cell lines. Our data demonstrate that the addition of NS-398 increases cytotoxicity in two ovarian cancer cell lines. This effect is enhanced with increased temperatures from 37 to 41 °C. At low doses of cisplatin, the addition of NS-398 to 2008 cells increases cytotoxicity at 37°C (1.8-fold) and 41°C (3.3-fold). In the C13 cell line, the addition of NS-398 to cisplatin causes an increase in cytotoxicity at 37°C (2.9-fold) and 41°C (3.4-fold). These results suggest that the combination of hyperthermic chemotherapy and COX-2 inhibition increases the cytotoxicity of cisplatin.

Hilary Beard

Psychology

Advisor: Dr. Christy Buchanan

The Link Between Pubertal Timing and Psychosocial Outcomes: Parent-Child Closeness as a Moderator

This study assessed the relation between the timing of pubertal development and various psychosocial outcomes in an attempt to determine whether parent-child closeness moderated the link between them. Previous research suggests that those who enter puberty early compared to their peers are at an increased risk for negative outcomes, including more internalizing and externalizing problems. In the past, research has emphasized this increased risk for early-maturing females to a greater degree than for early-maturing males. More recently however, researchers have identified negative outcomes associated with early maturation for both boys and girls, perhaps due to the stress of changes for which the child and family are not prepared. However, a good parent-child relationship has been shown to help buffer stressful situations for children. Thus, this study examined the degree of emotional closeness in the parent-child relationship, in order to see if the impact of early pubertal timing is reduced when there are high levels of parent-child closeness compared to when there are low levels of parent-child closeness.

The sample consisted of early adolescents (6th & 7th graders) and their parents. Results indicate that early pubertal timing was associated with higher levels of internalizing for both boys and girls. Significant interactions between parent-child closeness and pubertal timing emerged when predicting externalizing (for girls) and school performance (for boys), supporting the hypothesis that the link between early maturation and poor adjustment would be less strong among adolescents reporting close parent-child relationships.

Christopher Bennett

Education

Advisor: Dr. Robert Evans

The Relationship of Teacher Generated Lecture Questions, Lab Questions, Test Questions, and Student Achievement

The effect of teacher generated questions has been shown to affect the cognitive level of student thought processes. Test questions can identify the cognitive level that students are capable of operating on. Similarly, the product of those test questions, the student's answers, can also be analyzed to determine the cognitive level at which the student is answering the question on (Enger 1997). A natural study of the relationship between teacher generated lecture questions, lab questions, test questions and student achievement seems warranted. Three high school teachers were chosen, based upon their accessibility. The teachers were selected from two physical science disciplines, Chemistry and Physics, and a life science discipline, Anatomy. The cognitive level of all questions asked were grouped according to Bloom's Taxonomy. Percentages were computed for each of the teachers on each of the levels: lecture, lab, and tests. Each student test was analyzed, and a percentage of questions answered correctly on each cognitive level was also compiled for each teacher. Finally, each student's answers were analyzed to determine whether or not they were answered on, below, or above the cognitive level of each question. The relation of lab questions to student achievement was not shown by this study. The relationship of cognitive levels of test questions to correctness was not shown by this study. However, the negative relationship of test questions to cognitive level was shown. Teachers that wish to use high cognitive objectives must be aware that the higher the cognitive level of the question on a test, the more likely a student is to answer the question on a lower level.

Jennifer Bento

Biochemistry

Advisor: Dr. Donald Bowden

A SNP Map of Human Chromosome 20q12-13.1.

Human chromosome 20q12-13.1 is linked to type 2 diabetes mellitus (T2DM) in multiple studies. To identify T2DM susceptibility gene(s) in this region, a SNP fine map has been constructed across a 6 Mb region (41.6-47.5 Mb), containing the candidate diabetogenic genes, adenosine deaminase (ADA), hepatocyte nuclear factor 4 alpha (HNF-4 α) and glucose transporter 10 (GLUT-10). Verified SNPs from the NCBI dbSNP database, with minor allele frequency greater than 0.20, were placed on the map at an average density of 1 SNP per 25 kb. A total of 254 SNPs were genotyped on 310 Caucasian controls and 300 Caucasian cases with T2DM and end stage renal disease, using the Sequenom MassArray genotyping system. SnpAnalyzer, a web-based, enhanced version of the SnpAnalysis package (Kruglyak), was used to test each SNP for Hardy-Weinberg equilibrium, and to calculate inter-SNP linkage disequilibrium. Within regions of high LD ($D' \geq 0.70$), haplotypes were reconstructed using PHASE (Stephens *et al.*, 2001) and parametric and non-parametric tests for association with T2DM performed using Excel and Clump (Sham *et al.*, 1995).

Currently, 2.44 Mb of the region falls into 23 haplotype blocks of high ($D' > 0.70$) inter-SNP LD (range = 33-296 kb, mean = 93 kb) but there are also extensive regions that lie outside the blocks, the largest being 230 kb. Seven SNPs show evidence of allelic association with T2DM ($0.001 < p < 0.05$), with the strongest association centered on an intronic SNP in the gene cadherin-like 22 (CDH22, $p = 0.00146$). Each SNP was also genotyped on 40 CEPH trios, and showed similar LD results and haplotype structures to the Caucasian population of unrelates. These results indicate that the haplotype structure of the CEPH individuals is comparable to our Caucasian population, and therefore the CEPH trios offer a powerful independent method to confirm or predict block structure, with the benefit of inheritance-based ambiguous phase resolution. In conclusion, this SNP map will provide a framework for our on-going T2DM susceptibility gene association study, and for other diseases that map to this region.

Kimberly Blish

Molecular Medicine

With Jennifer Cottle, Udesh deSilva, Scott McGlone, Cody Smith, Ryan Smith

**Advisors: Dr. Jacquelyn Fetrow
Dr. Jennifer Burg
Dr. Timothy Miller**

Determining Significance in a Pair-wise Alignment

Decoding the genome is one of the central problems of bioinformatics. After the completion of the Human Genome Project, the objective becomes determining which regions of DNA encode proteins of vital significance in the cell. One method of finding important regions includes *in silico* translation of DNA regions into the hypothetical proteins encoded. Then, these proteins may be compared with other known proteins to look for similarities by which a function for the gene and resultant protein may be hypothesized.

In order to address this problem, we have produced a program that accepts an input nucleic acid sequence, translates it in 3 reading frames, and then completes pair-wise alignments of the translation with an input amino acid sequence of interest through a genetic algorithm. Our program produces alignments comparable to similar alignments fed into currently known programs available online.

Kelly D. Brooks

Education

Advisor: Dr. Bob Evans

An investigation of in-class occupational education and its effects on student perception and interest in the field of science.

The sciences penetrate almost every aspect of life in the United States, one of the world's most productive nations. This, in particular, is one reason for the great concern over the emerging statistics showing that U.S. students are losing interest and lagging behind in science achievement in comparison to their counterparts in many developed countries. The lack of involvement in science among U.S. students is leading to a shortage of native-born scientists and engineers (Gallagher, 1993). Some research indicates that occupational education may contribute to increased interest and retention in the science field (Mitchell 1977, Peterson, Long and Billups, 1999).

This anonymous survey study investigates in-class occupational education and its effects on student perception and interest in the field of science. One-hundred Winston-Salem Forsyth County high school science students were selected to participate. Both qualitative and quantitative data were collected from the surveys.

The results of this research support previous findings that suggest that in-class occupational education should be included as a vital part of the science curriculum. It is thought to assist students in drawing connections between education and career, science course registration, science concepts, increasing student understanding of science and thus increasing student interest, and possibly retention in the field of science.

Josh Buchanan

Computer Science

Advisor: Dr. David John

Creating a Robust Form of Steganography

Steganography is a relatively new and exciting field in the world of computer science. It involves embedding data into a medium in such a manner that it cannot be easily detected. This paper provides the reader with a basic overview of steganography. This overview includes the purpose, goals, and pre-digital history of steganography. The emphasis of my research is on hiding data within images, with a focus on the robustness of the hidden message. Current spatial embedding techniques are not robust to basic compression algorithms. I examine the 'least-significant-bit' paradigm which drives the spatial technique, and formulate a 'more-significant-bit' paradigm in order to produce a more-robust method. Following this paradigm leads to the idea of transform embedding, hiding data in the frequency domain. My research paper proposes a transform embedding method which uses existing ideas from digital watermarking, improving upon them with empirical data to make them suitable for steganography. This method is more robust than existing spatial embedding methods. Experimental results are presented which support this claim.

Stefanie E. Buckner

Education

Advisor: Dr. Leah P. McCoy

But Why?: Math Reasoning Skills with Technology

The National Council of Teachers of Mathematics takes a firm stance on students in grades K through 12 being able to reason and to use technology. This study of high school students looks at the relationship between using technology and being able to produce correct reasoning statements in Algebra II problems. Results were analyzed according to correct answers and whether or not technology was used. A Chi-Squared test of significance was performed. Although the results did not prove to be statistically significant, the data provided insight to students' diverse reasoning skills.

B.N. Carriere

Neurobiology & Anatomy

Advisor: Dr. Mark Wallace

Sensory Experience Shapes Multisensory Processing in Cortex and Superior Colliculus

Multisensory neurons are found in a number of cortical and subcortical structures. In cats, multisensory neurons in the cortex of the anterior ectosylvian sulcus (AES) and the midbrain superior colliculus (SC) are characterized by good spatial overlap in their different receptive fields. When multisensory stimuli are presented within these receptive fields, significant response enhancements are seen. We have shown that the development of normal multisensory processes in the SC is dependent upon sensory experience. Preliminary single-unit recordings from AES neurons of dark-reared animals suggest a similar experience-dependency. We have found in the SC that animals experiencing an environment with spatially disparate multisensory stimuli show changes in their multisensory processing abilities. Disparate spatial rearing changes the spatial organization of multisensory integration in a manner that follows receptive field changes. These results strongly underscore the importance of sensory experience in shaping the development of multisensory processes in both cortical and subcortical structures.

Crystal Chappell

Education

Advisor: Dr. Lean McCoy

The Effect of Content Based Writing on Students' Achievement in Pre-Calculus

In the wake of current accountability and assessment trends, it is important for mathematics teachers to find, and implement effective methods of instruction. Trends in mathematics education have varied over the years but recent research indicates that the use of writing within the content area may improve student understanding and achievement. Based upon previous findings on the positive effects of writing, talking and communication skills within mathematics instruction, it was hypothesized that the use of writing activities would have a positive effect on student achievement in Pre-Calculus. This study was undertaken to examine whether the use of writing in the mathematics classroom would affect the conceptual knowledge and understanding of eleventh and twelfth grade students enrolled in Pre-Calculus. Although the results of this study do not support this hypothesis, the value of such instructional techniques within the mathematics classroom cannot be dismissed.

Kejing Chen

Physics

Advisor: Dr. Daniel Kim-Shapiro

The Aggregation and Polymerization of Hemoglobin in High Phosphate Buffer System

We have observed an increase in the angular-dependence and intensity of light scattering from solutions of hemoglobin (Hb) in high concentration phosphate buffer compared to low phosphate buffer (PBS). In addition, we have found the decays of the autocorrelation function measured using dynamic light scattering from these solutions to be much slower than from solutions in PBS. These phenomena are due to either aggregation of Hb or the concentration fluctuations from liquid-liquid demixing (LLD). Using differential interference contrast microscopy we have now detected the presence of aggregates in the high concentration phosphate. Moreover, plots of the temperature dependences of the reciprocal of the light scattering intensity and mean particle size converge to two different temperature points, which is inconsistent with LLD prediction that they converge to a single point. We have also applied polarized light scattering (PLS) to the study of the hemoglobin polymerization in high phosphate buffer. A parallel program for PLS calculation that otherwise is significantly limited by computation time and memory size using a sequential method has been developed and applied to modeling hemoglobin polymerization. The results are compared with previous experimental measurements of PLS that suggested that polymerization is characterized by the formation of many nuclei, whose shape is non-spherical, followed by growth of these nuclei into polymers. This work is supported by NIH (HL 58091) and the Sickle Cell Program of the Commonwealth of Pennsylvania.

Daniel Cole

**With: Ryan Huff, Carleitta Paige,
Adam Reilly, Xiuli Xu**

Biochemistry & Molecular Medicine

**Advisors: Dr. Jennifer Burg
Dr. Jacquelyn Fetrow
Dr. Timothy Miller**

PKCYON: A Tool for Classifying Proteins

Authors: ¹Cole, Daniel; ²Huff, Ryan; ¹Paige, Carleitta; ²Reilly, Adam; and ³Xu, Xiuli; ¹Department of Biochemistry and Molecular Biology (715), ²Department of Computer Science (691), and ³Department of Physics (391).

The function of proteins is not always well defined. One essential tool that biologists need is a way to classify unknown proteins into protein families. We have devised a tool that will determine whether or not an arbitrary protein belongs to a protein family. More specifically, our tool will determine if an unknown protein is a member of the Protein Kinase C family. PKCYON will deduce the likelihood of an unknown protein to be in the PKC family by analyzing sequence identity and the presence of a “signature” sequence. Proteins that have a significant amount of sequence identity tend to have similar structural characteristics. Additionally, the presence of a “signature sequence” that is solely present in one family is a good starting point for placing unknown proteins into known protein families. PKCYON combines the Smith-Waterman dynamic programming algorithm with a regular expression search to automate this process.

Abbie Connoy

Molecular Medicine
Advisor: Dr. Kevin High

Increased NFκB Activation and Altered NFκB Dependent Gene Expression in Splenic Macrophages From Old Adult Mice

Abbie C Connoy, Liwu Li, Chad R. Marion, Kevin P. High, Program in Molecular Medicine, Wake Forest University Health Sciences, Winston Salem, NC, US, 27157.

Advanced age is associated with constitutive production of inflammatory cytokines, but waning immunity to specific stimuli. We demonstrate constitutive activation of NFκB in lymphocytes and macrophages of the spleen, that increases throughout the adult age spectrum (2-18 months) in DBA/2 mice. Protein expression levels of specific NFκB, and IκB subunits do not vary by age, however, p65 and c-Rel are present exclusively in the nucleus of resting splenic macrophages of older adult mice, and RelB is markedly increased in old mice. A cDNA array showed generally higher expression of mRNAs encoded by NFκB-responsive genes within splenic macrophages of older mice (vs. young adult). However, there is variability with some genes even demonstrating reduced expression. Real-time RT-PCR confirmed these results for mRNAs encoding two specific proteins. Markedly elevated nuclear localization of specific NFκB subunits (p65, c-Rel, and RelB) may play a role in immune senescence.

Jennifer Cottle
(see **Kim Blish**)

Computer Science

Determining Significance in a Pair-wise Alignment

Carol M. Curran

Education
Advisor: Dr. Robert Evans

The Relationship between Students' Educational Background and Environmental Attitude

This study examined the relationship between students' science educational background and environmental attitude. This research surveyed environmental attitudes of high school students and investigated relationships concerning science educational background and demographic features, including age, grade level and gender. Overall the surveys indicated a favorable environmental attitude from the sample group of freshmen and sophomore high school students consisting of a majority of women. Sixty-two percent of the students had taken two science courses including earth science and biology. No significant correlation was found between the number of science courses and environmental attitude. A correlation was found between mentors and factors that increased their environmental concern. The more factors students listed that increased their concern for the environment the more likely they were to have had a mentor that influenced their environmental concern. Therefore, mentors combined with outside environmental influences may have an impact on a student's environmental concern.

Amanda Davis

Chemistry
Advisor: Dr. Bradley Jones

Enantiomeric Separations of Amino Acids using HPLC coupled with ICP-Carbon Emission detection

Enantiomeric separations of amino acids generally require derivatization which can potentially introduce error. A derivatization step is unnecessary when using a chiral stationary phase (CSP) such as crown ether column. CSP columns resolve compounds with a primary amino group attached to the chiral center by forming a complex between the crown ether and the ammonium ion moiety of the sample. Seven underivatized amino acids were separated and detected using a crown ether column resulting in an average mass detection limit of 5 ng. The separation was accomplished by using a perchloric acid buffer as the mobile phase and carbon emission detection. The effluent from the HPLC was transported to an inductively coupled plasma atomic emission spectrometer. The carbon emission line at 193.09 nm was monitored by the detector. Carbon emission in the ICP is independent of amino acid structure; therefore a single, universal set of standards was used. Results were quantified by using an internal standard as opposed to a calibration curve. The summation of the D- and L-amino acid yielded an average error of approximately 1.0 % when comparing the values to a solution of known concentration.

Subhasis De

Chemistry
Advisor: Dr. Mark E. Welker

PREPARATION OF A BF_3 SUBSTITUTED 1,3 - DIENE AND ITS TANDEM DIELS – ALDER / CROSS COUPLING REACTIONS.

The preparation and characterization of potassium organotrifluoroborate substituted 1,3 diene will be described. This air stable salt is found to be very efficient in cycloaddition with common dienophiles and subsequent palladium-catalyzed cross-coupling reactions with aryl and heteroaryl halides. A schematic of the reaction is shown below. Preliminary results indicate preference for the para over meta isomer ranging from 3 to 4 : 1. We have also prepared the tetra n-butylammonium (TBA) salt of the BF_3 substituted diene and are hoping to attain better regioselectivity in Diels-Alder reaction. Future work will be directed towards a catalytic exo and enantioselective version of the cycloaddition. This methodology can be used to access biologically important cis fused bicyclic compounds related to known diterpenes.

Victoria Del Gaizo Moore

Molecular Medicine

Advisor: Dr. R. Mark Payne

Localization of TAT Fusion Proteins to Mitochondria *In Vitro*, *In Vivo*, and Across the Placenta

Defects in mitochondrial function are responsible for many human diseases. Two major problems have hindered gene therapy of mitochondria defects: 1) Mitochondria are in all tissues of the body so a gene therapy must be capable of reaching all tissues. 2) The therapy must localize specifically to mitochondria. We hypothesized that TAT fusion proteins would cross both mitochondrial membranes and incorporation of a mitochondrial signal sequence into a TAT fusion protein would allow processing and localization of exogenous proteins in mitochondria. Furthermore, TAT fusion proteins interact specifically with membrane phospholipids. We compared a TAT-mitochondrial malate dehydrogenase signal sequence (mMDH)-enhanced green fluorescent protein (eGFP) fusion protein to TAT-GFP using isolated mitochondria, cultured cells, animals, and large unilamellar vesicles. Results from this comprehensive study support our hypothesis and offer insight into the mechanism of TAT protein transduction. Furthermore, we show that TAT fusion proteins may have the potential to treat mitochondrial diseases.

Udesh deSilva

Biochemistry & Molecular Biology

(see Kim Blish)

Determining Significance in a Pair-wise Alignment

Molly DuBray

Psychology

Advisor: Dr. Janine M. Jennings

Functional Neuroimaging of Familiarity and Recollection

Molly B. DuBray, Janine M. Jennings, Paul J. Laurienti, & Joseph Maldjian

Participants underwent event-related fMRI while performing a continuous recognition task in which they were asked to identify words from a prior study list and new words (unstudied) that were presented twice during the test phase. The second presentation of these new words, which occurred at one of two different lag intervals, was of particular interest as participants had to recollect the first occurrence of these items in order to distinguish them from the previously studied words that were relatively comparable in familiarity. Accurate responding to repeated items was associated with activation in the bilateral inferior parietal gyrus (BA 40), right precuneus (BA 7), left medial frontal gyrus (BA 9), and bilateral superior frontal gyrus (BA 8, right BA6). Implications regarding the neural underpinnings of familiarity (automatic memory processing) and recollection (consciously controlled memory) will be discussed.

Emily Farrar

Education

Advisor: Dr. Robert H. Evans

The Effect of Ability Grouping on Student Attitude and Achievement in Science Labs

The purpose of this study was to determine which grouping method produces the highest achievement for the greatest number of students in the laboratory setting while also examining the emotional and social aspects of grouping. Among other things, results showed that high ability students had a significant preference to work with members of their same ability level. High ability students do not appear to mind helping lower ability students, but they just want an equal opportunity to learn more as well. The primary question of this research was the effect of ability grouping on students' achievement and their attitude towards group work. Because the results showed that neither homogeneous nor heterogeneous ability grouping is uniformly superior for promoting the achievement of all students, it may be more important to consider the social and emotional effects of different types of grouping.

Melissa Fox

Psychology

Advisor: Dr. James Schirillo

A Gender Difference in Portraits by Rembrandt

The psychological literature reports that a face's left-side emits negative emotions, while its right-side emits positive emotions. We also avoid left-cheek images and approach right-cheek images. Interestingly, the Western art literature reports that ~68% of female portraits turn their left-cheek toward the viewer, while only ~54% of male portraits expose their left-cheek. We tested if left-cheeked portraits elicit more avoidance than right-cheeked portraits by having 73 participants rate all 373 of Rembrandt's portraits on a 5-point approach/avoidance Likert scale. Participants reported that they would rather approach left-cheeked females, unlike the psychological literature prediction, but agreeing with Rembrandt's larger proportion of left-cheeked females (64%) compared to left-cheeked males (33%). Moreover, rotating female portraits from right- to left-cheek shifted their reports from neutral to approachable. Participants would rather avoid all males portraits (i.e., either cheek), but only when males turn from straight ahead to exposing more left-cheek were they judged as increasingly more avoidable, corresponding with the existing psychology literature.

Samuel Franklin

Neurobiology & Anatomy

Advisor: Dr. Craig K. Henkel

Bilateral Cochlea Ablation Disrupts the Development of Banded DNLL Afferent Projections in the Rat Inferior Colliculus

The central nucleus of the inferior colliculus (CNIC) is a site of convergence for ascending auditory projections. Within the CNIC, some excitatory and inhibitory afferents are organized in a laminar pattern of interdigitating bands. For example, inhibitory GABAergic projections from the dorsal nucleus of the lateral lemniscus (DNLL) decussate in the commissure of Probst and end in a banded pattern in the contralateral CNIC. Previous studies in our laboratory (Gabriele et al 2000) showed that DNLL afferents in the neonatal rodent CNIC are present at birth, but not banded. Moreover, unilateral cochlear ablation at P2 disrupted the development of bands within the CNIC. To determine if the overall spontaneous activity generated by the cochlea, rather than an imbalance of activity due to unilateral cochlea removal, is the critical factor in the disruption of band development within the CNIC, both cochleas were ablated in P2 rat pups. Pups were reared to P12, anesthetized, and sacrificed by transcardial perfusion of 4% paraformaldehyde. Glass pins coated in DiI (1, 1'-dioctodecyl-3,3,3',3'-tetramethylindocarbocyanine perchlorate) were placed in the commissure of Probst in order to visualize contralateral DNLL afferent projections. In the CNIC of ablated animals, fluorescent label from DNLL afferents appeared less intense bilaterally, compared to control animals. Furthermore, in ablated animals, DNLL afferents failed to segregate into a refined pattern of bands compared with age-matched control animals. These results indicate that bilateral cochlear ablation disrupts the normal development of DNLL bands observed in the CNIC.

Carla J. (Colicigno) Gallagher

Molecular Medicine

Advisor: Donald W. Bowden

Linkage of diabetic nephropathy to chromosome 18 in African Americans

We have conducted a genome-wide search for linkage to T2DN in 214 affected sib pairs from 171 African American (AA) families (361 total subjects). Among the sibs with DN, 49 had overt DN (serum creatinine concentration ≥ 2 mg/dl or urine albumin:creatinine ratio ≥ 300 mg/g), and 312 had end-stage renal disease (ESRD). Median age of onset of ESRD was 17 ± 9.4 years after diagnosis of diabetes. The AA diabetic subjects had a mean \pm SD (median) age of 59.4 ± 9.1 (60) years, mean age at diabetes onset 39.2 ± 10.9 (39) years, mean body mass index 30.5 ± 6.9 (29.4) kg/m². We tested for genetic linkage between T2DN and 369 polymorphic markers spanning all autosomes using GENEHUNTER-PLUS with ASM (allele sharing model). Genotyping was performed at the Center for Inherited Disease Research.

In our genome scan, strong or suggestive (LOD score > 1.0) evidence for linkage was not detected in the entire set of T2DN affected sib pairs. Subsequent analysis, stratifying on age of onset of diabetes and BMI were performed. Mean age at onset of diabetes was calculated for each sib pair. Analyses were performed by dichotomizing the data into early (below the population median of 39 years) versus late (above the median) age at diabetes onset. In the early age at diabetes-onset sib pairs, the maximum LOD score observed was 2.35 between markers D18S862 and D18S1364, in contrast to a LOD score of 0.00 in the same region for the late age at diabetes-onset group. Stratification for BMI did not reveal additional evidence of linkage.

The 18q22.3-23 region has previously been implicated as harboring type 2 diabetes associated nephropathy (T2DN) susceptibility genes in Turkish and Pima Indian families (Vardarli et al. *Kidney Int* 62:2176-83, 2002). Our results in African Americans replicate evidence for a DN locus in this region. Our results in AAs with T2DN and an early age at diabetes onset suggest that the susceptibility locus in this region may be more frequently involved in progression to ESRD in younger diabetics.

James Jason Galvez

Physiology and Pharmacology
Advisor: Dr. R. Mark Payne

O₂⁻ Damages Mitochondrial Function During I/R

Superoxide (O₂⁻) is an important and ubiquitous free radical formed under normal conditions and during ischemia and reperfusion (I/R). Recently a class of metal-based (Mn²⁺) low molecular weight synthetic enzymes has been developed possessing antioxidant activity specific only for O₂⁻, termed superoxide dismutase (SOD) mimetics. *M40401*, a Mn²⁺ based SOD mimetic, is highly selective for the dismutation of O₂⁻ and was utilized as an experimental tool to dissect the role and specific targets of O₂⁻ during I/R. In this study we examined the effects of *M40401* during I/R in the heart and more specifically, we investigated mitochondrial damage following I/R. *M40401* protection against I/R was tested *ex vivo* in the isolated and perfused heart. Mitochondrial protection following I/R was evaluated by measuring O₂ consumption in left ventricular tissue homogenates. Results obtained in this study exhibit *M40401* is able to directly reduce O₂⁻ during I/R resulting in significant protection of heart function, as shown by a reduction in left ventricular end-diastolic pressure (LVEDP) elevation. In addition, mitochondrial function assays revealed a decline in stimulated respiration following I/R, an observation that was totally inhibited in the presence of *M40401*. Overall, these results demonstrate that reducing O₂⁻ during I/R is protective and that mitochondria are significant targets leading to decreased functional recovery following I/R.

Joshua Grill

Neuroscience
Advisor: Dr. David Riddle

DENDRITIC REGULATION IN A MODEL OF ADULT-ONSET IGF-1 DEFICIENCY.

J.D. Grill¹, W.E. Sonntag^{1,2} & D.R. Riddle^{1,3}. Prog. in Neuroscience¹, Dept. of Phys. & Pharm.² and Dept. of Neurobiol. & Anat.³

The dendrites of some cortical neurons regress with age and this change may result, at least in part, from the aging-related decline in insulin-like growth factor-1 (IGF-1). To understand how IGF-1 influences dendritic changes, we have tested whether a decline in plasma IGF-1 is sufficient to alter dendritic morphology. Dwarf rats of the Lewis strain have a reduction in growth hormone (GH) production and, consequently, a significant decline in plasma IGF-1 levels. GH/IGF-1 levels in dwarf rats were maintained through the developmental period by administering GH. Control animals continued to receive GH (GH/IGF-1 replete), whereas experimental animals received only saline as adults (GH/IGF-1 deficient). The dendritic arbors of over 600 pyramidal neurons were reconstructed and quantified. Though body weight was significantly reduced in deficient animals, dendritic analyses showed no differences between groups. Thus, a decreased plasma level of IGF-1 alone is not sufficient to induce dendritic changes.

Brian Grimberg

Biology

Advisor: Dr. Clifford Zeyl

Sex is good

Out of the three billion species of microorganisms on planet Earth, less than one thousand have adapted to human beings and become infectious. However, despite our long history together, there are an ever-increasing number of emerging pathogens due to increased human interaction with each other as well as with their environments. Thanks to many advances in modern medicine immunocompromised patients, such as those with HIV or cancer, are living longer than ever before and have therefore created additional environments for previously non-infectious organisms to become pathogenic. *Saccharomyces cerevisiae*, a well-studied organism in its better known role as beer and bread yeast, is one such emerging pathogen. The overall goal of this project was to explore how *S. cerevisiae* evolved to become a pathogen and explore the benefits of sexual reproduction on this process of pathogenesis and evolution in a host organism.

It has been theorized that an increase in variation, brought about through sex or an increase in the mutation rate, may accelerate the adaptation to a variable environment such as a host. Asexual and sexual strains were mixed together in equal proportions and allowed to evolve in both a "host" (mouse) and "laboratory" (test tube) environment. The sexual strain was more successful than its asexual counterpart when allowed to reproduce sexually in a host. No advantage of sexual reproduction was observed in a test tube experiments.

Beth Cauble Gross

Education

Advisor: Dr. Robert H. Evans

A Study of the Relationship between Religious Beliefs and Confidence in the Theory of Evolution in High School Students and Their Science Teachers' Culturally Sensitive Instructional Responses

This research examined the attitudes and beliefs of high school students towards evolution, and specifically, the strength of their adherence to religious teachings, their knowledge and beliefs about evolutionary theory, and their opinions concerning evolution instruction in public schools based on their religion. Overall, the study found misconceptions about the nature of science, and mainly that students do not understand the difference between the nature of a scientific theory and a religious belief. However, it also showed that students are perceptive about some aspects of the nature of science, such as its lack of association with larger world-views and its ability to coexist with religious beliefs. The study reported a great deal of controversy surrounding the issue of evolution. It can be concluded that there is a lack of knowledge of the theory of evolution among high school students, and this may or may not be due to their teachers' presentations.

Anne Haase

Microbiology & Immunology
Advisor: Dr. Daniel Wozniak

Negative Regulation of Flagellar Motility in *Pseudomonas aeruginosa* by the Alternative Sigma Factor AlgT

Haase, A.¹; Wolfgang, M. C.²; and Wozniak, D. J.¹

¹Wake Forest University School of Medicine; Winston-Salem, NC 27157; ²University of North Carolina at Chapel Hill, Chapel Hill, NC 27599

Pseudomonas aeruginosa is the terminal pathogen in individuals suffering from cystic fibrosis (CF). Strains that initially colonize the CF lung generally have a non-mucoid, motile phenotype. During the course of infection, many of these strains undergo a conversion to a mucoid and/or non-motile phenotype, which provides the bacterium with a selective advantage in the CF lung by allowing it to evade host defenses. We observed that in CF isolates, the mucoid and the non-motile phenotype occur predominantly together, which suggested the involvement of a common regulator. Studies in our laboratory have shown that both alginate and flagellum biosynthesis are inversely controlled by the alternative sigma factor AlgT. While the role of AlgT as key regulator in the expression of the polysaccharide alginate is well understood, the negative control of flagellar motility by AlgT remains unclear. The purpose of the current study is to identify the target of AlgT within the complex flagellar hierarchy and to determine the AlgT-mediated regulatory mechanism involved in the inhibition of flagellum biosynthesis. Using promoter fusion assays, we showed that AlgT exerts its negative effect downstream of *rpoN* and upstream of *fliC*, which is the major structural component of the flagellar filament. Microarray analysis comparing mRNA levels of flagellar genes in AlgT⁺ and AlgT⁻ strains of *P. aeruginosa* was performed to further narrow down possible AlgT targets within the complex flagellar hierarchy. The results of this analysis revealed that the vast majority of flagellar genes were significantly (at least threefold) downregulated in the presence of AlgT. A pronounced AlgT-effect was observed in a number of genes shown to be crucial for the transcriptional regulation of flagellum expression, including the “flagellar master switch” FleQ and the two-component system FleSR. Promoter fusion assays confirmed the negative effect of AlgT on *fleQ* transcription. Together, these studies indicate that AlgT mediates the negative control of flagellum biosynthesis by inhibiting the expression of critical regulators in the flagellar biosynthetic pathway.

ASM Meeting 2004
Under Review

W. David Hairston

**Neurobiology & Anatomy
Advisor: Dr. Mark Wallace**

Cross-modal temporal integration in developmental dyslexia

Dyslexia is generally ascribed to disrupted phonological processing; however, recent research suggests that the difficulties seen in dyslexia may not be limited to the linguistic realm, and may be associated with temporal problems within multiple sensory modalities. To test whether cross-modality timing deficits, which would be detrimental to linguistic development, occurs in these individuals, normal control and dyslexic subjects first performed a staircase-mediated visual temporal order judgment (TOJ) task to determine a threshold visual stimulus onset asynchronies (SOAs). Next, the visual targets were presented at this SOA accompanied by task-irrelevant sounds on most trials, with the first sound always synchronous with the first light. The second sound was either synchronous or lagged behind the second light by a variable time. Visual TOJ performance differed in dyslexics, in that longer SOAs were needed to reach performance equivalent to controls. For both groups, the auditory delay enhanced performance, suggesting temporal auditory capture of the visual stimulus. However, dyslexics showed a higher performance gain than control subjects, and across a larger range of temporal delays. Taken together, these results support the concept of pre-linguistic alterations in cross-modal temporal processing in dyslexia, wherein these subjects integrate cross-modal stimuli over a larger temporal “window” than normal.

Lori Hart

**Cancer Biology
Advisor: Dr Costas Koumenis**

Adenovirus E4orf6 protein inhibits DNA repair and radiosensitizes human tumor cells.

The adenoviral protein E4orf6 was previously reported to inhibit both *in vitro* V(D)J recombination and adenoviral DNA concatenation, two processes that rely on cellular double strand break repair (DSBR) proteins. The known biochemical functions of E4orf6 in the context of adenoviral infection require its interaction with E1B-55K. Here we report that E4orf6, stably expressed in RKO human colorectal carcinoma cells or transiently expressed by adenoviral vector in U251 human glioblastoma cells, significantly radiosensitizes the cells compared to respective empty vector. Expression of a mutant form of E4orf6 failed to radiosensitize RKO cells. E4orf6 reduced DSBR capacity in transfected and infected cells as measured by sublethal DNA damage repair assay and phosphorylated H2AX (γ -H2AX) levels, although the kinase activity of DNA-PK towards heterologous substrates remains unaltered. These results demonstrate for the first time that E4orf6 expression hinders the cellular DNA repair process in mammalian cells in the absence of E1B-55K or other adenoviral genes, and suggest that viral-mediated delivery of E4orf6 could be a useful approach for the treatment of radioresistant solid tumors such as glioblastomas.

Jessica Hatz

Psychology
Advisor: Dr. Cathy Seta

Exploring opposing views of regret: Consistency and desirability versus counterfactual generation as causal indicators of regret feelings

Goals: Norm theory predicts that decisions to act will induce more regret than inactions because they are more mutable. Recent research (Seta et al., 2001) demonstrated that counterfactual thinking was not necessary for the experience of regret, but that consistency (between the person's original orientation and latter behavior) and decision desirability mediated the influence of decisions to act or not act on feelings of regret. The current study was conducted to further contrast predictions of norm theory and the Seta et al. model.

Method: Participants in happy moods retrospectively reported on situations in which they made poor decisions to go out or to stay home. Participants indicated felt regret either prior or subsequent to counterfactual-generation.

Results: ANOVA indicated main effects of decision-type and timing of regret judgments: Participants felt more regret about decisions to stay home, and felt more regret after counterfactual generation.

Mediation analyses revealed that consistency and desirability mediated the decision-type effect. Although counterfactuals did not mediate this effect, it did serve as a significant predictor of overall regret.

Conclusions: These findings are supportive of the Seta et al. model and support their emphasis on the relationship between an individual's decision and his/her action-orientation as a determinant of regret. In addition, the results suggest that counterfactuals do play a role in producing regret, although this effect is not the one expected from norm theory. Possibilities for mediating and moderating roles of counterfactuals are discussed.

Steven Howell

Chemistry
Advisor: Dr. R.E. Nofle

Towards a Synthesis of Thiophene-based Conducting Polymers Bearing Hemi-labile Ligands.

We are interested in the synthesis of thiophene-based conducting polymers having side chains, which can chelate metal ions and act as potential catalysts. Our strategy is to incorporate a hemilabile ligand, which coordinates strongly at one metal site and weakly at another. In this report, seven novel precursors to conductive polymers have been synthesized and characterized. These precursors each contain an amide functional group with a pyridine moiety. Each precursor varies according to the type of pyridine moiety attached and the spacing between the thiophene group and the amide functional group. The compounds were characterized using ^1H and ^{13}C NMR, IR spectroscopy, GC-MS, X-ray diffraction and elemental analysis, while their electrochemical properties were studied using cyclic voltammetry and double potential step chronoamperometry. Chelation of metals (copper and zinc) by several monomers was successfully demonstrated and the complexes were characterized by X-ray diffraction, cyclic voltammetry and/or ^1H NMR.

Ryan Huff
(see Daniel Cole)

Computer Science

PKCYON: A Tool for Classifying Proteins

Kris Huang

Biomedical Engineering
Advisor: Dr. Dan Kim Shapiro

Nitrite and Deoxygenated Hemoglobin: A Source of Nitric Oxide

Kris Huang; Xiuli Xu; Howard Shields; Anne Jeffers; Man Cho; Jinming Huang; S. Bruce King, Ph.D; Mark Gladwin; Rakesh Patel; Daniel Kim-Shapiro.

It was shown recently that intra-arterial infusion of nitrite results in vascular dilation and increased local blood flow . Consistent with these in vivo observations, in vitro studies show that nitrite-dependent vasodilation is enhanced by the presence of hemoglobin in a manner that is inversely proportional to oxygen pressure. These findings suggest that reduction of nitrite by deoxygenated hemoglobin (deoxyHb) may serve as a reservoir for in vivo nitric oxide (NO) that is available for use under hypoxic conditions. We performed in vitro kinetic measurements of nitrite reacting with deoxygenated whole venous blood and pure deoxyHb under various temperatures and concentrations of hemoglobin and nitrite. The reactions in blood yielded bimolecular rates consistent with the iron nitrosyl hemoglobin (HbNO) and vasodilation seen during in vivo infusions of nitrite. It has been suggested recently that NO formed from nitrite reduction is mainly bound to Fe(III)Hb , but we present data contrary to this. We also present data from studies aimed at determining whether NO produced from nitrite reduction by deoxyHb in the red blood cell (RBC) can be exported. We realize the difficulty of NO export from the RBC that results from hemoglobin's excellent scavenging ability; therefore, the observed in vivo vasodilation may be a result of other mechanisms, but more work must be done to determine whether the nitrite-deoxyHb reaction is indeed responsible.

Leslie Hunter

Health & Exercise Science
Advisor: Dr. Shannon Mihalko

Improving Adherence To The Diabetes Self-Care Regimen: A Pilot Study

Diagnosis of diabetes mellitus has increased 61% since 1991 and is currently estimated at 17 million. Although diabetes can be managed through a self-care regimen that addresses physical activity, diet and medication, adherence to the diabetes regimen is the greatest obstacle toward diabetes control. The purpose of the BRIDGE (Bringing Diabetes General Education to Life) study was to pilot test a behavioral intervention based on Social Cognitive Theory (SCT) that encourages the necessary lifestyle changes for adherence to the diabetes self-care regimen. This longitudinal pilot included 12 older adults (M age=66.2 ± 8.1 years) diagnosed with type 2 diabetes who had recently completed a general diabetes education program. Assessments at the 3 month midpoint demonstrated that those participants randomized to the intervention group improved their self-reported physical activity (ES=1.25) as determined by the Physical Activity Scale for the Elderly (PASE) to a greater extent than those in the control group (ES=0.45). Participants in the intervention group reported an increase in self-efficacy for physical activity (ES=0.81) as compared to no change in the control group (ES=0.04). Regimen adherence was further confirmed by glucose control using HbA1c levels, inasmuch as HbA1c levels declined in the intervention group (ES=-0.55) while increasing in the control group (ES=0.78) over time. These findings have important implications for public health as they suggest that a behavioral intervention beyond the usual care diabetes education program improves adherence to the diabetes self-care regimen.

Anne Jeffers
(see Kris Huang)

Physics

Nitrite and Deoxygenated Hemoglobin: A Source of Nitric Oxide

Felysha Jenkins

Psychology
Advisor: Dr. Charles Richman

Interracial Dating: The Openness of White Women Versus White Men

Many have hypothesized that as diverse ethnic groups become the norm (Moore, 2000), ethnic relations will improve. Although strides have been made in this area, interracial dating remains taboo for many people. More specifically, interracial dating between European Americans and African Americans carries the greatest stigma in our culture (Lewandowski & Jackson, 2001). European American undergraduate men and women were surveyed on their attitudes toward dating African Americans. They completed the following scales: racial identity, relationship fulfillment, and interracial dating attitudes. The results indicate that women are more open to interracial dating than men. These findings were discussed in relation to several relationship models.

George Chih-Thai Jiang

Physiology and Pharmacology

Advisor: Dr. Kent E. Vrana.

FUNCTIONAL ANALYSIS OF THE V177I CODING REGION POLYMORPHISM OF HUMAN TRYPTOPHAN HYDROXYLASE (hTPH1).

Tryptophan hydroxylase (TPH) is the rate-limiting enzyme in the biosynthesis of the neurotransmitter serotonin (5-HT). Recently, Ramaekers *et al.* (2001) have reported the first coding region polymorphism of human tryptophan hydroxylase, a valine to isoleucine substitution at residue 177 (V177I). A hypothetical model of human TPH and the crystal structure of the catalytic domain suggest that the V177 residue points into the active site and may direct interactions with the tryptophan substrate. In an attempt to elucidate the functional effect of the valine to isoleucine substitution at residue 177, site-directed mutagenesis was employed to generate a number of mutants for analysis. Mutation of V177 to isoleucine and alanine (V177I and V177A, respectively) resulted in no significant changes in TPH activity. Substitutions of V177 with leucine, phenylalanine, arginine, glutamate, glycine, serine and threonine resulted in severely reduced enzyme activity. Steady-state kinetic analyses were performed for wild-type TPH, V177A and V177I. The K_m of V177A for tryptophan ($31.6 \mu\text{M} \pm 1.4$) was not significantly different from that of wild-type ($26.4 \mu\text{M} \pm 3.3$). However, V177I exhibited a significant 55% increase in the K_m for tryptophan ($41.1 \mu\text{M} \pm 6.5$). No changes were observed in the Michaelis constant of BH_4 for all proteins tested. Due to insufficient enzyme activity, steady-state kinetic analyses were not performed on the V177G, V177S, V177T, V177L, V177F, V177R, and V177E mutants. These findings suggest that the identity of the residue at position 177 is critical for the proper formation of the substrate pocket. In the case of the naturally-occurring polymorphism, it seems likely that enzyme activity would only be compromised under conditions of reduced amino acid substrate concentrations.

This work was supported by NIH grant GM38931.

Carrie John

Physiology & Pharmacology

Advisor: Dr. Sara R. Jones

Effect of monoamine transporter uptake inhibitors and releasers on dopamine and serotonin dynamics in mouse brain

Abuse of psychostimulants is a major public health problem. While cocaine and other pure uptake inhibitors compete with monoamines at their transporter, amphetamine and its derivatives (AMPHs) also cause reversal of the transporter, resulting in monoamine release. This difference in the mechanism of action of these two classes of psychostimulants results in characteristically different pharmacological and kinetic profiles. Characterization of electrically evoked release in mouse midbrain reveals that fast scan cyclic voltammetry (FSCV) records dopamine (DA) in the caudate-putamen (CPu) and serotonin (5-HT) in the substantia nigra pars reticulata (SNr). The effects of cocaine, methylphenidate, PTT, amphetamine, methamphetamine, and MDMA on electrically evoked DA or 5-HT release and uptake in mouse CPu and SNr slices were compared using FSCV. The results show that the rank order of uptake inhibition at the dopamine transporter is PTT>methylphenidate>MDMA>cocaine>methamphetamine; the rank order of uptake inhibition at the serotonin transporter is MDMA>methamphetamine>cocaine=PTT>methylphenidate.

Stephanie Jolley

Psychology

Advisor: Dr. William Fleeson

Explaining Within-Person Variability: Extending the Chameleon Effect to Trait Behavior

The current research attempted to explain why persons demonstrate large variability in their trait relevant behaviors. Our main hypothesis was that an individual's trait relevant behavior is related to the trait behaviors of the person he or she is with, such that the individual mimics the other person's trait behaviors. We also predicted that the three traits studied will vary in how much they are mimicked.

The experience sampling method was used in this study. Undergraduate students carried Palm Pilots for 15 days and responded to questionnaires five times per day. The average correlation between the participant's behavior and the participant-reported behavior of another person he/she was with were significant for all three traits. Openness and neuroticism appeared to be mimicked more than extraversion. The findings suggest that a person's trait relevant behaviors may be different across situations because he/she is interacting with and mimicking different people in each setting.

JaNae Joyner

Molecular Medicine

Advisor: Dr. Bridget Brosnihan

Enhanced Renal Distribution of Ang-(1-7) and ACE-2 during Pregnancy

Pregnancy is characterized by an activation of the renin-angiotensin-aldosterone system serving as an endocrine circulating system involved in blood pressure regulation. Urinary levels of Angiotensin-(1-7) have been shown to be increased in humans and rats, suggesting an increase in the local kidney tissue production of Ang-(1-7). Therefore, assessment of the immunocytochemical distribution of Ang-(1-7) and its processing enzyme, angiotensin converting enzyme 2 (ACE2), was determined in kidneys of pregnant Sprague Dawley rats and virgin females. Ang-(1-7) and ACE2 staining was present in the tubules of the inner cortex and outer medulla of both groups. The intensity of ACE2 staining appeared to be significantly greater in pregnant rats as compared to the virgin females. This is the first demonstration of immunocytochemical distribution of Ang-(1-7) in association with ACE2 in the kidney and show that pregnancy causes an upregulation of ACE2 that may lead to increased production of Ang-(1-7) during pregnancy.

Robin Kester

Computer Science
Advisor: Dr. Errin Fulp

Service Differentiation Using p-Persistent CSMA/CD

The popularity of networking technology has led to an increase in the number of users and a growth in traffic produced by each user. As a result, the demands for increasing the speed and efficiency of networks must be met so that networks can continue to be used in the future. This becomes increasingly difficult, given that the diverse nature of applications require different types of network support. This research focuses on providing differentiated Quality of Service (QoS).

One of the most popular local area network (LAN) standards is IEEE 802.3, Ethernet. Ethernet networks use the Carrier Sense Medium Access with Collision Detection (CSMA/CD) protocol for determining which stations on the network will get to transmit next. These networks have been known to exhibit poor throughput performance as network traffic increases. More collisions will occur as more stations attempt to transmit data, resulting in few successful transmissions. Furthermore, there is no differentiation among the stations, since all stations are treated equally.

A common alternative to CSMA/CD is p-persistent CSMA/CD. This protocol gives each station a probability of being able to transmit. Ethernet can be viewed as a 1 persistent CSMA/CD protocol, because all stations on a given network have equal probability (probability of 1) for accessing the medium for transmission which has poor performance.

It has been proven that the optimal probability value should be based on the number of stations wishing to transmit on the network. However, given the dynamic nature of networks, knowing this value a priori is not feasible. This research introduces a new persistence CSMA/CD system which dynamically changes the persistence value based on the network's current traffic load. Our results show that this system easily outperforms other CSMA/CD systems in terms of efficiency and QoS. Also, the new p-persistence CSMA/CD protocol requires few modifications for implementation.

Sadie Leder

Psychology
Advisor: Dr. Mark R. Leary

Relationship Involvement and Trait Self-Esteem as Predictors of Hurt and Anger in Ongoing Romantic Relationships

Hurt feelings and anger are common emotional responses to partner misbehaviors. In order to examine the moderating effects of relationship involvement and trait self-esteem on both hurt and anger, 127 participants completed measures of self-esteem and relationship involvement, as well as rated how hurt and how angry they would be if their romantic partner behaved in each of 30 aversive ways. Results indicated that participants who were more involved in their relationships had stronger reactions to partner misbehaviors. Specifically, higher relationship importance, exclusivity, satisfaction, love, and expectancy were associated with greater hurt and anger. However, patterns for hurt and anger differed notably, suggesting that they are not determined by precisely the same factors. Furthermore, self-esteem had a moderating effect, especially on ratings of anger. The trend was for high self-esteem participants to report greater hurt and anger when relationship involvement was low, but for low self-esteem participants to show greater hurt and anger when relationship involvement was high.

Hong Li

Biomedical Engineering
Advisor: Dr. Pete Santiago

A practical automated polyp detection scheme for CT Colonography

Colorectal carcinoma is the leading cause of cancer-related death in the nonsmoking population with about 60,000 people dying from colorectal cancer each year. Although the high accuracy screening procedure, i.e. optical colonoscopy (OC), at regular intervals would substantially decrease the mortality, its discomfort, perforation risk, high cost, and high negative statistic are not readily accepted by potential patients. Computerized polyp detection (CPD) is promising to improve the screening accuracy and to reduce the reading cost of CT colonography (CTC), which provides an alternative full-colon screening scheme and overcomes some of the disadvantages of OC. In this paper, a fully automated CPD system is presented, which takes DICOM images from CT scanners and provides a list of detected polyps. The system comprises three stages, segmentation, polyp candidate generation, and false positive (FP) reduction. Both supine and prone scans are used for improving detection sensitivity. Major shape features, mean curvature, and Gaussian curvature with a connectivity test efficiently produce polyp candidates. Six shape features and a multi-plane linear discriminant function (MLDF) are used for the FP reduction. We have tested the system on 68 real subjects (20 positive and 48 negative for 6 mm and larger polyps from colonoscopy results). 95% accuracy and 33% specificity at patient level were achieved, indicating that 16 out of 48 health subjects could avoid OC. One 11 mm polyp missed by CPD but was also not reported by the radiologist. We anticipate that an MAP classifier tuned by supervised training may improve the detection performance. The execution time for both scans is about 10-15 minutes using a 1 GHz PC running Linux.

Xi Li

Biomedical Engineering
Advisor: Dr. Jianming Zhu

Determination of Neuron Fiber Structure with High Angular Resolved Diffusion Attenuated Imaging

Xi Li, Jianming Zhu, Hong Li, Miaohua Jiang

The conventional DTI method has limitation on resolving the fiber orientations for voxels with multiple crossings. In our work, we proposed a new method to determine the neuron fiber structure based on high angular resolved diffusion attenuated imaging (DAI).

A series of diffusion attenuated images are acquired along a large number of diffusion encoding gradient directions (25, 55, 99 directions are used in our experiments). These encoding directions are evenly distributed on a 3D sphere. The MR signal along each direction can be written as $\ln(S_0/S_i) = b \cdot g_i^T \cdot D \cdot g_i$, where S_0 and S_i are the intensity without and with diffusion-weighting respectively, g_i is the diffusion-encoding direction, and D is apparent diffusion coefficient. The true diffusion directions can be related to one or more of the diffusion-encoding directions via a rotational operator. This equation also states that the signal attenuation is proportional to the projection of the diffusibility along each direction. If we map the diffusibilities along all diffusion-encoding directions, the directions with highest diffusibilities will indicate the principal diffusion directions for voxels contain multi-fiber crossings.

Figure 1 shows the comparison between the derived fiber orientation maps using DAI and DTI. With 98% confidence level, the orientation differences were less than 10 degree for voxels where only one dominating diffusion direction is determined.

The accuracy of the fiber orientation determination using DAI increases as the number of diffusion encoding directions increases. This method could be useful for generating more accurate fiber tractograms.

Wenhua Liu

Physics
Advisor: Dr. Martin Guthold

Mechanical Properties of Individual Fibrin Fibers

Fibrin fibers are the major structural component of blood clots. Thus, determining the strength and mechanical properties of blood clots will provide new insights into the wound healing process and will advance our understanding of heart attacks and strokes.

In the study described here, the rupture force and mechanical properties of individual fibrin fibers are being measured. The rupture force, F_R , of human fibrin was determined as a function of the diameter, D , and found to follow a $F \sim D^{1.4}$ dependence. Assuming a simple model where the rupture force is proportional to the cross section of the fiber, the data suggest that the fiber is inhomogeneous or porous. Some modifications show that the deformations are elastic. The Young's modules of the fibers is estimated to be about 0.8 MPa.

Yu Liu

Neuroscience

**Advisors: Dr. Drake Morgan
David C. S. Roberts**

Cocaine-like discriminative stimulus effects of novel methylphenidate analogs

There is a growing interest in the potential use of monoaminergic reuptake blockers as pharmacotherapeutics for cocaine abuse. A series of cocaine and methylphenidate analogs have been synthesized that show a wide range of binding characteristics for the dopamine (DAT), serotonin (SERT), and norepinephrine (NET) transporters. The current study characterized the discriminative stimulus effects of novel methylphenidate (including HDMP27, 28 and 29) analogs, and compared them to previously characterized tropane (including PTT, HD23 and HD60) analogs and a reference DAT (GBR12909), SERT (fluoxetine) and NET (desipramine) blocker. Male, Sprague-Dawley rats were trained to discriminate saline from 10 mg/kg (i.p.) cocaine in a standard two-lever, food-reinforced drug discrimination procedure. In general, it appears that activity at the DAT is necessary to produce cocaine-like discriminative stimulus effects. Greater affinity for SERT decreases the potency for substitution, whereas increased affinity for NET enhanced the potency of the drug. In combination tests, compounds with higher DAT affinity tended to interact with cocaine in a supra-additive manner, whereas drugs with higher SERT affinity interacted in a sub-additive manner. These results suggest differing contributions of serotonin and norepinephrine to cocaine-like discriminative stimulus effects.

Virginia L. Lockamy

Physics

Advisor: Dr. Daniel B. Kim-Shapiro

The search for the mechanism of NO Release in Hydroxyurea Therapy

Hydroxyurea (HU) is an FDA approved drug used to treat sickle cell disease patients. Some of the beneficial effects of the drug may be due to its ability to be converted into nitric oxide (NO). We have found that HU liberates NO in the presence of oxyhemoglobin (oxyHb) or deoxyhemoglobin (deoxyHb) but these reactions are too slow to account for observed in vivo NO formation. We will show that the HU reaction with methemoglobin (metHb) is also too slow to account for in vivo NO formation. We have hypothesized that, in vivo, HU is metabolized to hydroxylamine (HA), which then reacts quickly with hemoglobin to produce NO. Here we examine the reaction of HA with oxyHb, deoxyHb, and metHb. The formation of metHb and nitrosyl hemoglobin (HbNO) is observed using absorption spectroscopy and electron paramagnetic resonance (EPR) spectroscopy. We are also currently searching for in vivo evidence of the hydrolysis of HU to HA.

Scott McGlone

(see Kim Blish)

Computer Science

Determining Significance in a Pair-wise Alignment

Brian Moore

**Health & Exercise Science
Advisor: Dr. Michael Berry**

Relationship between dyspnea and oxygen consumption among COPD patients after exercise training.

The purpose of this study was to examine the relationship between dyspnea ratings and oxygen consumption (VO_2) before and after three months of exercise training in patients with mild and moderate chronic obstructive pulmonary disease (COPD). Methods: Maximal graded exercise tests were performed by 99 COPD patients (14 mild, 85 moderate) before and after three months of exercise training. Dyspnea was recorded every minute of the exercise test and VO_2 was measured using expired gases and reported as a percent of $\text{VO}_{2\text{peak}}$. Individual regression equations were developed to predict dyspnea from VO_2 prior to and following exercise training. Two-way ANOVA was used to compare slopes and intercepts between mild and moderate COPD patients before and after training. Results: Slopes of the regression lines were significantly different for moderate COPD patients between 0 and 3 months (0.14 ± 0.10 vs. 0.10 ± 0.05 , $p=0.001$). Intercepts of the regression lines were also significantly different for moderate COPD patients between 0 and 3 months (-6.83 ± 6.55 vs -4.39 ± 4.22 , $p=0.017$). However, in mild COPD patients, no significant changes were seen from 0 to 3 months in slopes (0.11 ± 0.03 vs. 0.10 ± 0.03 , $p=0.256$) or intercepts (-4.76 ± 2.14 vs -4.24 ± 2.30 , $p=0.545$). Conclusion: Following exercise training, moderate COPD patients reported a lower slope and greater intercept in the regression equation predicting dyspnea from VO_2 . These results suggest that exercise training allows patients with moderate COPD to perform physical activity at a given level of VO_2 with less dyspnea.

Yvonne Mortensen

**Psychology
Advisor: Dr. Christy M. Buchanan**

Two Sides to Every Story: Mothers' and Adolescents' Views of Parenting and the Parent-child Relationship

Associations between parent-adolescent discrepancies and perceptions of parenting and the parent-child relationship over a one year period were explored in a sample of early adolescents and their mothers. Results indicate support for the expectancy realignment model in regard to discrepancies, with higher rates of discrepancies at one point in time being correlated with more positive views of parenting and the parent-child relationship at a later point in time.

Lanay Mudd

Health & Exercise Science
Advisor: Dr. Patricia A. Nixon

Follow-up of a Randomized Controlled Trial of Postnatal Dexamethasone Treatment in 8-10 year old Children Born Prematurely with Very Low Birth Weight

Postnatal dexamethasone treatment has been shown to have short-term benefits on pulmonary function in premature infants as indicated by fewer days on mechanical ventilation and supplemental oxygen; however, the long-term effects have yet to be determined. The purpose of this study was to compare ventilatory responses during exercise in children born with very low birth weight (VLBW), $\leq 1500\text{g}$, who were treated with a 42-day tapering course of IV dexamethasone postnatally (DEX), with those VLBW children who were given a placebo (CON). The DEX group consisted of 20 children (9 male) and the CON group consisted of 18 children (9 male). Each child performed standard spirometry according to ATS guidelines at rest as well as a progressive exercise test on a cycle ergometer. From spirometry, forced expired volume in 1 second (FEV1) and maximum voluntary ventilation (MVV) at rest were determined. From exercise testing, aerobic fitness ($\text{VO}_{2\text{peak}}$), and ventilatory responses during exercise including minute ventilation (VE), tidal volume (VT), respiratory rate (RR), the ventilatory equivalents for oxygen (VE/VO_2), and for carbon dioxide (VE/VCO_2) were determined. The groups did not differ significantly by age, height, or weight. Mean $\text{FEV1}\%$ predicted did not differ between the two groups (82 v. 83% for DEX and CON respectively). Mean $\text{VO}_{2\text{peak}}$ was also similar for DEX (40.0 ml/kg/min) and CON (38.9 ml/kg/min) groups. VE, VT, and RR at peak exercise did not differ significantly between the groups ($P>.50$). However, the DEX group exhibited a lower VE/MVV at peak exercise (90% v. 108% for DEX and CON), and lower VE/VO_2 (31.95 v. 35.43) and VE/VCO_2 (30.50 v. 34.18) responses to exercise ($p<.05$). These results suggest that 8-10 year-old children, born prematurely with VLBW and treated with dexamethasone postnatally, used less of their breathing reserve and had more efficient ventilatory responses to exercise than VLBW children who received placebo. These results may have implications for more efficient ventilatory responses to and better tolerance of everyday activities in VLBW children.

Jessica Munley

Education
Advisor: Dr. Leah McCoy

Hands-On Materials in a Geometry Classroom

Attitudes toward mathematics play a major role in deciding a student's mathematics journey. Research has shown that use of instructional activities with hands-on manipulative models is positively related to students' attitudes toward mathematics. However, it is the teacher's decision to determine how these activities are implemented in their classroom. This study explored teacher's implementation of manipulative and hands-on activities in high school Geometry classes.

Michael Murray

Biochemistry
Advisor: Dr. Jacquelyn Fetrow

Comparison of the unfolding pathways of two homologous proteins

Explicit solvent molecular dynamic simulations are able to realistically simulate the pathways of protein unfolding. Traditionally, these simulations have been done at elevated temperatures (498K) to allow unfolding on a feasible timescale. Advances in computer hardware have allowed researchers to study thermal unfolding at lower temperatures. Here we compare the unfolding of chymotrypsin inhibitor 2 and eglin c (homologous protease inhibitors, thirty-two percent identity) at seven temperatures ranging from 298K to 498K. At 298K both proteins maintain their native structure through the course of the simulations. In simulations below the proteins' melting temperature the trajectories are characterized by general expansion and contraction in the surface and active site loops. Above the melting temperature, thermal denaturation of eglin c is characterized by breathing and expansion of the hydrophobic core and secondary structures followed by general unfolding. Shorter simulations of CI2 indicate a similar thermal unfolding pathway.

KerryAnn O'Connor

Physiology & Pharmacology
Advisor: Dr. Steve Childers

CHRONIC BLOCKADE OF BIOGENIC AMINE TRANSPORTERS BY WF-23: EFFECTS ON G-PROTEIN ACTIVATION AND BEHAVIOR

K.A. O'Connor¹; S.R. Childers¹; L.J. Porrino¹; H.M.L. Davies²

1. Physiol/Pharmacol, Wake Forest University School of Medicine, Winston-Salem, NC, USA; 2. Chemistry, SUNY-Buffalo, Buffalo, NY, USA

WF-23 is a highly potent tropane which binds to the dopamine transporter (DAT) with 1400x greater affinity than cocaine. Previous studies showed that a single i.p. injection of WF-23 (1 mg/kg) in rats decreased DAT binding in striatum by at least 50% for two days and produced stereotypy and increased locomotor activity similar to cocaine. Since blockade of DAT increases extrasynaptic dopamine levels(DA), we hypothesized that chronic treatment with WF-23 may desensitize DA receptors in striatum by decreasing coupling of receptors to G-proteins. To explore this question, receptor/G-protein coupling was assayed in rat brain sections using [³⁵S]GTPγS autoradiography for several G-protein coupled receptors. Rats were injected with WF-23 (1 mg/kg, i.p.) or saline every 48 hr. Following injections of WF-23 for 14 days, D2-stimulated G-protein activity was reduced by 59% in nucleus accumbens of WF-23-treated animals with no significant effects in caudate/putamen. The reduction in D2-activated G-proteins was not accompanied by any change in D2 receptor binding. 5-HT_{1A}-stimulated G-protein activity was significantly reduced in the hippocampus, but not in septum or dorsal raphe. Mu opioid-stimulated G-protein activity was not decreased in WF-23-treated animals. To explore behavioral effects of WF-23, locomotor activity was analyzed in rats treated with WF-23 or saline for 1-14 days. Animals were placed in locomotor chambers for up to 3 hr following injection. Significant increases in horizontal activity were found at all time points, but the increased locomotor activity was significantly attenuated at day 14. These changes in locomotor activity parallel changes in D2 receptor activation of G-proteins following chronic blockade of DAT in brain.

Supported by: PHS grants DA-06634 and DA-07246 from NIDA

Sherry D. Oden

**Physiology & Pharmacology
Advisor: Dr. Debra I. Diz**

Rats with Low Brain Angiotensinogen Maintain Normal Levels of Insulin and Components of the Circulating and Intra-Renal Renin-Angiotensin Systems During Aging

Sherry D. Oden, Detlev Ganten, Carlos M. Ferrario, Mark C. Chappell, and Debra I. Diz

Development of elevated systolic blood pressure (SBP) in aging Hannover Sprague-Dawley (SD) rats by 68 weeks (wk) of age is absent in transgenic [ASrAogen(680) rats (AS)] with low brain angiotensinogen. We assessed the effects of aging on both circulating and intra-renal tissue renin-angiotensin system (RAS) and serum insulin levels. Plasma Ang levels were similar in SD and AS at 16 wk with a decline in SD at 68 wk. There was no change in plasma Ang-(1-7) in AS over time such that AS have 40% higher levels at 68 wk than SD. Urinary excretion of Ang I, Ang II, and Ang (1-7) increased with age in SD with little change in AS over this time frame, revealing differential activation of the intra-renal vs circulating RAS in aging SD. There was 43% lower urinary and 44% higher serum creatinine in SD, suggesting impairment in GFR. At 68 wk, SD have 25% higher insulin levels than young SD and 75% than young or old AS. The data implicate a key role for brain RAS in the development of age-related hypertension and insulin resistance. Since there are few differences between SD and AS at the earliest time point, the maintenance of circulating and intra-renal RAS components leading to preservation of renal function and a shift in balance to Ang-(1-7) in plasma during aging in AS may result indirectly from maintenance of lower SBP rather than a direct effect. HL51952; AHA-MA0215151U; AHA-MA151521; HL56963

Megan E. Overcast

Molecular Genetics

**Advisors: Dr. Thomas C. Register
Dr. Michael R. Adams**

Estrogen Receptor Dependent Processes Mediate the Atheroprotective Effects of Soy Isoflavones in Apolipoprotein E^{-/-} Mice

In a previous study we found that atheroprotective effects of dietary soy isoflavones in mice depended on the presence of estrogen receptor- α . We sought to determine if this atheroprotective effect was associated with the suppressed expression of pro-inflammatory molecules implicated in the pathogenesis of atherosclerosis. We studied atherosclerosis-susceptible (apolipoprotein E-deficient (*ee*)) mice that had been crossed with estrogen receptor- α and - β deficient mice to produce double-knockout *aee* and *bbee* mice and (estrogen receptor) wild-type controls (*AAee* and *BBee*). Ovariectomized female mice (n = 10 to 15 per treatment group) (total n = 100) were fed soy protein-rich diets that were either isoflavone-depleted [Soy (-IF)](0.04 mg/g protein isolate) or isoflavone-replete [Soy (+IF)](1.72 mg/g protein isolate). After 16 weeks, mice were necropsied for assessment of hepatic cholesterol content and hepatic inflammatory gene expression. Consistent with the observed effects on atherosclerosis, hepatic free cholesterol was reduced 17-44% (p<0.05) by Soy(+IF) in *AAee*, *BBee* and *bbee* but was unaffected in *aee* mice. Relative expression of mRNA for vascular cellular adhesion molecule-1(VCAM-1), monocyte chemoattractant protein-1(MCP-1), and tumor necrosis factor- α (TNF- α) was determined using quantitative real-time PCR. MCP-1 and TNF- α transcripts were reduced by Soy(+IF) in *AAee*, *aee*, and *BBee* but not *bbee*. VCAM-1 expression was reduced by Soy(+IF) in *AAee* and *BBee* but neither *aee* nor *bbee* were affected. The atheroinhibitory effects of Soy(+IF) did not appear to reflect effects on total hepatic cholesterol, hepatic cholesteryl ester, and triglycerides.

The results support previous findings that indicate a role for estrogen receptor- α -dependent processes in mediating the atheroprotective effects of dietary soy isoflavones and suggest that both ER- α and ER- β may play roles in anti-inflammatory effects of IF .

Carleitta Paige
(see Daniel Cole)

Biochemistry & Molecular Biology

PKCYON: A Tool for Classifying Proteins

Nichole Palmer

Biochemistry & Molecular Biology
Advisor: Dr. Donald Bowden

Genetic Evaluation of Protein Tyrosine Phosphatase-1B (PTP-1B) Gene Polymorphisms and Measures of Glucose Homeostasis: The IRAS Family Study.

N.D. Palmer¹, C.D. Langefeld², W.M. Brown², F. Hsu², D.W. Bowden¹. 1) The Center for Human Genomics; 2) Department of Public Health Science, Wake Forest University School of Medicine, Winston-Salem, NC.

PTP-1B is a ubiquitously expressed protein that dephosphorylates proteins at tyrosyl residues and in particular, has been shown to modulate the activity of the insulin receptor and substrates. For this reason, PTP-1B is a candidate gene for involvement in components of glucose homeostasis.

We have evaluated 24 SNPs in a 161kb region encompassing the ten exons spanning 74kb of PTP-1B. SNPs were genotyped on 1152 Hispanic (San Antonio, TX and San Luis Valley, CO) and African American (Los Angeles, CA) participants in the Insulin Resistance Atherosclerosis Family Study. To test for association among each PTP-1B SNP and trait, a series of generalized estimating equations was computed. A sandwich estimator of the variance and exchangeable correlation was used to account for familial correlation. SNPs within a region of 86kb, encompassing a large portion of the PTP-1B gene, were found to be in high linkage disequilibrium ($D' > 0.70$). Within this LD block, multiple SNPs show statistically significant associations with measures of glucose homeostasis. In combined population analysis there were significant associations with fasting glucose, insulin sensitivity (S_i), and acute insulin response (AIR) ($P < 0.001-0.045$). In population specific analyses, the San Antonio population showed associations to S_i , disposition index, and fasting glucose ($P < 0.0001-0.050$), the San Luis Valley population to fasting glucose and S_i ($P < 0.001-0.043$), and the Los Angeles population to AIR ($P = 0.003-0.035$). Measures of adiposity were also evaluated for association with PTP-1B SNPs. In combined populations analyses, visceral and subcutaneous adipose tissue, measured by computed tomography, were significantly associated ($P = 0.002-0.012$). In center specific analyses, the San Luis Valley and Los Angeles populations showed associations to waist and waist to hip ratio ($P < 0.001-0.050$). In conclusion, PTP-1B polymorphisms are associated with measures of glucose homeostasis and have moderate, but significant associations with adiposity measures in Hispanic and African American populations.

Lu Peng

Physics

Advisor: Dr. Martin Guthold

Novel, single-molecule methodology to identify new aptamers

Lu Peng¹, Roger Cubicciotti², MartinGuthold¹¹Department of Physics, Wake Forest University, Winston-Salem, NC 27109, ²Nanomedita Inc. Newark, NJ 07102

We are developing a novel, single-molecule methodology to identify aptamer molecules in a pool of about 10^{12} oligonucleotides. Unlike SELEX, our approach does not require iterative cycles of selection and partitioning and it is readily amenable to automation. At the core of our methodology is unique instrumentation that combines a nanoManipulator Atomic Force Microscope (nM-AFM) and an inverted optical microscope with single-molecule fluorescence capabilities.

This instrument, in combination with single molecule PCR, is used to identify new aptamers as follows. Target molecules are labeled with a donor fluorophore and linked to a cover slip. Random-sequence oligo libraries are labeled with an acceptor fluorophore and a 10 nm bead (for AFM detection and pick-up). The oligos are then flowed over the target area. High-affinity, target-specific aptamers will bind tightly to the target for relatively prolonged periods resulting in a strong fluorescence signal. After a fluorescence signal has been observed with the optical microscope, the nM-AFM is used to obtain a high-resolution image of the fluorescence signal-generating region of the surface. The 10 nm bead attached to the aptamer is used as a landmark for the aptamer-target binding pair. Next, the conditions in the imaging chamber are changed so that the nM-AFM tip can be used as a “gripper” to retrieve the bead plus the attached aptamer. Single molecule PCR is used to amplify the extracted aptamer.

We have designed a new stage to combine the AFM and optical microscope. The instrument has been successfully used to detect and extract thrombin-aptamers labeled with both fluorophore and 30nm gold bead. PCR was used to amplify the extracted aptamer molecules.

Ramakrishna Pidaparathi

Chemistry

Advisor: Dr. Mark E. Welker

Cobalt mediated [6+4] and [4+2] cycloaddition reactions using tropones

Cobalt mediated cycloaddition reactions with tropones are described. R-pyridine cobalt bis(dimethylglyoxime) 1,3-pentadiene complexes (1) (R=H and *N,N*-dimethylamino) with tropones that are unsubstituted at the 2nd positions undergo thermally initiated higher-order $[6\pi+4\pi]$ cycloaddition reactions resulting in bicyclo[4.4.1]undecanone adducts (2). These reactions are complementary to those reported by the Rigby group. The cycloadducts are formed through *exo*-transition states with 93% yield, having high regio- and stereoselectivity compared to the organic reactions reported earlier. Unsymmetrically substituted tropones including substitution at the 2nd and/or 6th position having an electron withdrawing group participate purely in Diels-Alder [4+2] reactions, yielding *cis*-undecanone adducts (3) with 100% regio- and stereoselectivity. Tropones that are unsubstituted at the 2nd position, having an electron withdrawing group react in both [6+4] and [4+2] reaction pathways leading to the respective cycloadducts (4,5).

Karissa Piper

Education

Advisor: Dr. Raymond C. Jones

Teacher's Choice: Factors that Influence the Decisions about Teaching Christianity in World History

As a moral code, as an individual or community ritual, and as law, religion has influenced societies and their cultures throughout history. The growth of religious diversity in America, the personal nature of religion, and the separation of church and state all appear to the researcher to be factors that teachers consider when determining how to teach Christianity to students. It is the purpose of this study to determine what teachers themselves believe influence their decisions concerning teaching Christianity in their classrooms. Seven local World History teachers were interviewed and the data analyzed to determine consistent or common trends

Carrie Anne Platt

Communication

Advisor: Dr. Michael J. Hyde

"A Life Ever-Fasting": Religious Rhetoric and Acknowledgment in the Pro Eating Disorder Website

This rhetorical analysis argues that the purposeful deconstruction and (re)construction of religious rhetoric in pro eating disorder websites bolsters the rhetorical transformation of anorexia and/or bulimia from a deviant illness to an elite lifestyle, significantly altering how the eating disordered woman is acknowledged in this cyber community. It analyzes the religious rhetoric found on such websites, specifically looking at the appropriations of religious themes, sacred imagery, and religious text for persuasive purposes. Burke's categories of western religious communication serve to clarify the connections between religion, pro eating disorder websites, and the phenomenon of acknowledgement. I begin by briefly discussing the key elements of pro eating disorder websites. I then analyze the religious rhetoric found on three exemplar websites. I end my analysis by discussing the implications of subversive rhetorical appropriation by these websites and commenting on how they are rotten with the same "perfection" sought by both anorectics and Christians.

Deborah Ramsey

Microbiology & Immunology
Advisor: Dr. Daniel Wozniak

Residues in the Beta-sheet Motif of the *P. aeruginosa* Transcriptional Activator AlgZ are Required for Binding to AlgZ Cis Sequences at the *algD* and *algZ* Promoters.

Ramsey, D.M.; Baynham, P. J.; VonCannon, J. L.; and Wozniak, D. J.

The *Pseudomonas aeruginosa* transcriptional regulator AlgZ is a ribbon-helix-helix (R-H-H) DNA binding protein that utilizes protein-DNA contacts to activate expression of the *algD* gene and repress transcription of its own promoter. The goal of the current study was to determine how the structure and amino acid composition of AlgZ mediate its DNA binding activity at both the *algD* and *algZ* promoters. Glutaraldehyde cross-linking studies of purified, hexahistidine-tagged AlgZ showed the formation of several oligomeric species in solution. Comparison of the amino acid sequences of AlgZ with other members of the R-H-H family suggested that conserved residues in the AlgZ beta-sheet motif may play a role in DNA recognition. Alanine substitutions were made at residues 14, 18, 20 and 22 of AlgZ. Mutant proteins were tested for binding to *algZ* and *algD* cis sequences using electrophoretic mobility shift assay. Substitutions at residues 18 and 22 resulted in decreased DNA binding affinity for both cis sequences. These findings suggest that AlgZ forms oligomeric species in solution, and residues 18 and 22 within the beta-sheet motif of AlgZ are crucial for recognition and binding of multiple DNA ligands.

Melissa Rawley

Psychology
Advisor: Dr. Terry Blumenthal

The simultaneous investigation of prepulse inhibition and the psychological refractory period

Prepulse inhibition (PPI) and the psychological refractory period (PRP) measure the protection of information processing with cognitive overload and share an overlapping time course. PPI, or a reduction in the startle eyeblink response, occurs when a weak stimulus precedes a startle stimulus. PRP reflects the delay in responding that occurs to the second of two stimuli presented close together in time. PRP and PPI were assessed in 25 college students by simultaneously measuring startle eyeblink EMG and reaction time to respond to a visual prepulse and an acoustic startle stimulus. As expected, startle response inhibition occurred at 120 and 240 ms lead intervals. However, PRP was not found; instead, the reaction time to the startle stimulus was faster when the two stimuli were presented together compared to when the startle stimulus occurred alone. Due to the methodology used, the PRP effect may have been eliminated.

Adam Reilly
(see Daniel Cole)

Computer Science

PKCYON: A Tool for Classifying Proteins

Jennifer Rust

Chemistry

Advisor: Dr. Bradley Jones

Multi-Element Detection for Clinical Samples using High-Resolution Continuum-Source Atomic Absorption Spectrometry with a Tungsten-Coil Atomizer

The objective is to develop an instrument with a single radiation source to detect numerous elements in a short amount of time. A continuum-source high-resolution atomic absorption spectrometer with tungsten-coil atomization for use on clinical samples is illustrated. Two different setups were employed in detecting Cu, Cd and Zn. The first setup utilizes a high-intensity xenon arc lamp as the radiation source, a tungsten-coil as the atomizer, and a high-resolution Czerny-Turner monochromator. Detection is accomplished with a 1024 element diode array. The second setup utilizes a deuterium lamp as the source, a tungsten-coil as the atomizer, a Czerny-Turner monochromator, and a charged-coupled device as the detector. Both instruments allow for multi-element detection within the ultra-violet region with a spectral window of 4 nm. Testing clinical samples has a great significance in heading off metal deficiency and chronic diseases. Urine samples were analyzed for Cu, Cd and Zn. The limit of detection for each was found to be around 1.0, 7.5, and 50 ppb respectively. The ability to detect several different elements in a short amount of time is the main advantage of this instrument, as well as having simple background correction without the need for magnetic fields, pulsed high current sources, or extra radiation sources.

Samir Shah

Biomedical Engineering

Advisor: Bruce Rubin

An In Vitro Evaluation Of The Effectiveness Of Endotracheal Suction Catheters

Introduction: Tracheal suction catheters (TSC) are used to clear mucus from an endotracheal tube (ETT). Clearance rate is critical because airway mucus stasis leads to obstruction, but prolonged catheter suctioning can lead to hypoxemia. The rate of mucus clearance from an ETT is thought to be influenced by the properties of the mucus, the pressure used to suction the mucus, and the diameter of the catheter. In this study, different TSCs were evaluated for their ability to suction mucus simulants that had properties similar to airway mucus.

Methods: Six 14 French TSC designs were evaluated. All catheters had the same end hole size but had side hole sizes of 3, 4, or 5 mm. Mucus simulant was Polyox Water Soluble Resin Coagulant NF (Dow Chemicals) mixed with water at concentrations of 0.5%, 1.5%, and 3.0%. Effectiveness was evaluated by the mass percent of Polyox suctioned over 10 seconds at 100 psi

Results: Greater concentrations of mucus simulant increased viscoelasticity without changing surface properties and this decreased suction effectiveness. TSC with a side hole diameter of 5 mm were most effective suctioning the 1.5% and 3.0% simulant, and the TSC with the smallest hole diameter of 3 mm were most effective suctioning the 0.5% mucus simulant ($p < 0.05$).

Conclusions: Greater TSC side hole diameter was important for suctioning higher viscoelastic mucus. Because catheters had more difficulty suctioning higher viscoelastic mucus, increasing the side hole diameter would improve design effectiveness. End hole size, suction force, and duration of suctioning were not tested, but could also have an effect on TSC performance.

Erin Shannon

Physiology & Pharmacology
Advisor: Dr. Kathleen Grant

DISCRIMINATIVE STIMULUS EFFECTS OF PREGNANOLONE IN C57BL/6J AND DBA/2J INBRED MICE

The discriminative stimulus pattern of pregnanolone ($3\alpha,5\beta$ P) has been well characterized in rats but a pregnanolone discrimination has not been characterized in mice. Two of the most widely used inbred strains of mice in ethanol research are the C57BL/6J and DBA/2J strains. In this study, C57BL/6J(n=12) and DBA/2J(n=12) were initially trained to discriminate 10.0 mg/kg $3\alpha,5\beta$ P from saline. This dose produced adequate behavioral control without decreases in response rates in DBA/2J mice. However, in C57BL/6J mice, this dose produced severe decreases in rates of responding and therefore the training dose was reduced to 5.6 mg/kg. All twelve DBA/2J mice acquired the 10.0 mg/kg $3\alpha,5\beta$ P discrimination in 43 (\pm 21 days). In contrast, only 6 C57BL/6J have acquired the discrimination in 52 days (\pm 20 days). Of the mice that acquired the discrimination, $3\alpha,5\beta$ P dose-dependently substituted with an ED50 of 1.87 mg/kg for C57BL/6J and 4.02 mg/kg for DBA/2J. Ethanol did not substitute in DBA/2J mice at doses below those that suppressed response rates. Likewise, androsterone did not substitute for $3\alpha,5\beta$ P at any of the doses tested in DBA/2J mice. Overall, C57BL/6J mice appear more sensitive to the behavioral effects of $3\alpha,5\beta$ P. Also, the substitution patterns of ethanol and androsterone for $3\alpha,5\beta$ P differed between DBA/2J mice and previous findings with rats (Engel et. al, 2001). These results indicate that neurosteroids show large between strain and cross-species differences in discriminative stimulus effects.

Chanté Singleton

Physics
Advisors: Dr. J. Daniel Bourland
Dr. Keith Bonin

Radiation Surface Dose Using the DignicapTM Hypothermic Cap in Conjunction with Whole-Brain Radiation Treatment

A recent study (Shah et al., 2000) suggests the use of a hypothermic scalp cap, in conjunction with whole-brain radiation treatment (WBRT), with the expectation that vasoconstriction will reduce the radiation effect, in order to reduce the amount of alopecia, when treating brain metastases in cancer patients. Radiation surface dose effects from the hypothermic cap must be determined, since alopecia has a known dependence on radiation dose. This study determines and verifies the surface dose on the scalp (that is, hair follicle dose) using an anthropomorphic head phantom and three radiation dose measurement techniques: 1) LiF TLD-100 powder in capsules, 2) Gafchromic (Radiochromic-type) film and 3) a gas-filled ionization Markus chamber. A typical WBRT irradiation geometry was used: 300cGy to midplane, two parallel-opposed beams, and a 22cmx20cm field size. Beam energies of 6MV, 10MV and 18MV were studied. As expected, the TLD and film results show an increase in surface dose build-up by the hypothermic cap of -1%-87%. Markus chamber results show an increase in surface dose build-up greater than 100%.

Cody Smith
(see Kim Blish)

Biochemistry & Molecular Biology

Determining Significance in a Pair-wise Alignment

Ryan Smith
(see **Kim Blish**)

Biology

Determining Significance in a Pair-wise Alignment

Jessica Tipsord

Psychology
Advisor: Dr. Mark Leary

Including Others in the Self: Extensions to Generic People, Animals, Nature, and God

Aron and his colleagues have shown that the degree to which people incorporate significant others into their sense of self has implications for the nature of their interpersonal relationships. Extending this idea, it seems likely that people differ in the degree to which they generally incorporate others into the self and that people may incorporate not only other people but also animals and nature into their self. Furthermore, previous research suggests that a high sense of connection should be related to psychological well-being. One-hundred and forty-eight undergraduates rated how connected they felt to 25 entities that reflected close others, distant others, animals, nature, and God. Ratings were done using a modification of the Inclusion of Other in the Self (IOS) Scale on which participants indicated which of seven Venn diagrams, each portraying a different degree of overlap between "self" and "other," reflects their relationship with each entity. In addition, participants completed measures of personality, emotion, and well-being. Overall, feeling connected to people, animals, nature, and God was associated with greater psychosocial well-being. For example, rated overlap between self and close and distant others significantly correlated with life satisfaction, kindness, and low ego-grasping; kindness was also predicted by self/other overlap with animals and God. Linking oneself to close others predicted lower depression, and links with distant others predicted forgiveness. Growth-motivation was associated with closeness to distant others, animals, nature, and God.

JoLyn Turner

Biochemistry & Molecular Biology
Advisor: Dr. Suzi V. Torti

Tachypyridine, an iron chelator, triggers a DNA damage checkpoint by activating ATM and/or ATR.

JoLyn Turner, Timothy E. Kute, David Ornelles, Frank M. Torti, Roy P. Planalp, Martin W. Brechbiel, Suzy V. Torti. *Wake Forest Univ. School of Medicine, Winston-Salem, NC; Univ. New Hampshire, Durham, NH; Rad. Onc., NIH, Bethesda, MD.*

Iron is involved in essential biochemical reactions ranging from respiration to DNA synthesis. Consequently, iron deprivation has been proposed as a strategy for inhibition of tumor cell growth. We have described a novel iron chelator, tachypyridine that not only inhibits growth of cultured tumor cells, but actively induces apoptosis in a p53-independent manner. In order to study the mechanism of action of tachypyridine, we explored its effect on the cell cycle. We show that unlike other iron chelators, which induce G1/S arrest, tachypyridine induces G2 arrest. Activation of the checkpoint kinases ATM and ATR signal G2 arrest in response to DNA damage, with ATR also sensing replication inhibition. We show activation of these kinases as evidenced by phosphorylation of downstream targets, and through inhibition of their activity by caffeine. Further studies indicate that tachypyridine induces DNA damage, suggesting this is the proximal event that leads to the observed G2 arrest.

Jennifer L. Whelan

Education

Advisor: Dr. Robert Evans

The Effect of Problem-Based Versus Step-by-Step Laboratory Experiments on the Achievement and Attitudes of Honors and Standard High School Chemistry Students

This study attempted to further research that illuminates the positive benefits of inquiry-based science teaching by determining the effect of problem-based versus step-by-step laboratory experiments on the achievement of honors and regular high school chemistry students in two areas: understanding of chemistry content and ability to design experiments. Four intact chemistry classes from a North Carolina public school were selected to participate. One standard class and one honors class participated in a problem-based laboratory; the other standard class and the other honors class participated in a “cookbook” laboratory. All four classes took the same posttest. The difference in the means of the content scores was insignificant for both the honors groups ($t = 0.154$, $p = 0.878$) and the standard groups ($t = 0.398$, $p = 0.695$), but the honors PBL group scored significantly higher in experimental design than the honors cookbook group ($t = 3.558$, $p = 0.001$). There was not a significant difference in the experimental design score between the standard PBL and cookbook groups ($t = -0.928$, $p = 0.364$).

Alicia Wysong

Molecular Genetics

Advisor:

Identification and analysis of polymorphisms within STAT1 association with asthma and associated phenotypes

A.K.S. WYSONG 1,* T.D. HOWARD 1, G.A. HAWKINS 1, H. JONGEPIER 2, D.S. POSTMA 2, D.A. MEYERS 1, E.R. BLEECKER 1

1) Center for Human Genomics, Wake Forest University School of Medicine, Winston-Salem, NC; 2) Dept of Pulmonology, University Hospital, Groningen, the Netherlands.

Asthma is a chronic inflammatory disorder of the bronchial airways characterized by allergic responses and bronchial hyperresponsiveness. Asthmatic inflammation has been shown to be both directed and propagated by the secretion of a series of specific cytokines. Because cytokine effects often depend on signal transducers and activators of transcription (STATs), STAT1 is a functional candidate gene for influencing inflammatory disease. In addition, STAT1 is located on chromosome 2q33, where evidence of linkage has been observed in genome screens for asthma and associated phenotypes. To evaluate its role in asthma and associated phenotypes, we have sequenced all 25 STAT1 exons in 96 individuals for SNP identification. We performed association studies with over 10 SNPs in Dutch, Caucasian, Hispanic, and African-American asthma populations. We observed significant associations ($p < 0.05$) of several polymorphisms throughout STAT1 with allergy and asthma related phenotypes (e.g., bronchial hyperresponsiveness, FEV1, and log IgE). These data suggest that variations within STAT1 may contribute to the pathophysiology of allergy or asthma.

Xiuli Xu

Physics

**Advisors: Dr. Daniel Kim-Shapiro
Dr. Paul Pauca**

Simulation of the diffusion and reaction of nitric oxide using finite element method*‡

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Nitric oxide (NO) that is synthesized in endothelial cells must be able to reach its target in smooth muscle cells in order to function as the endothelium-derived relaxation factor, regulating vascular tone. This function of nitric oxide is made difficult by the known scavenging of NO by millimolar quantities of hemoglobin (Hb) in the blood. Contrary to the idea that Hb acts solely to destroy NO activity in the blood, Cosby et al.¹ recently presented data suggesting that deoxygenated Hb (deoxyHb) produces NO by reacting with nitrite, a proposed reservoir of NO activity. In order for the NO produced by this reaction to be active, it must be exported from the red blood cell (RBC) despite massive scavenging activity of Hb. In this work, we present a mathematical analysis of NO being produced inside RBCs through the nitrite reaction with deoxy Hb. We examine the ability of this NO to diffuse out of the RBC. Using FEMLAB (COSMOL, Inc.), a finite-element-method based program, we calculate the amount of NO exported under different conditions and discuss the results of our calculations on the hypothesis of NO activity being produced by the nitrite/Hb reaction within RBCs.

¹Cosby, Partovi, et al., Nitrite reduction to nitric oxide by deoxyhemoglobin vasodilates the human circulation. *Nat. Med.* (2003) 9,1498-1505.

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Physics

(see Daniel Cole)

PKCYON: A Tool for Classifying Proteins

Marc Yelle

Neurobiology and Anatomy
Advisor: Dr. Robert Coghill

Offset Analgesia and the Relationship Between Stimulus Fall Rates and Perceptual Fall Rates

Offset analgesia is a transient, yet disproportionately large, decrease in perceived pain intensity elicited by slight decreases in noxious thermal stimulus intensity. In order to better characterize offset analgesia, 13 healthy subjects (9 male, 4 female) were asked to give a real-time rating of perceived pain intensity on a continuous visual analog scale (VAS) (range = no pain to most intense pain imaginable) following decreases in noxious stimulus intensity. Noxious stimuli were delivered to the subjects' ventral forearms via a 1.6 cm² peltier device. Two stimulus paradigms were used in this experiment. The first paradigm used three temperatures presented in a continuous fashion. From a baseline of 35°C (approximately skin temperature), stimulus temperatures were first increased to 49°C (T1) for 5s, then to 50°C (T2) for 5s, and then decreased to either 35° or 49°C (T3) for 20s. A 30s constant 49°C stimulus was used as a control for this paradigm. Following the T2 to T3 transition, subjects rated the T3 in a presentation of 49-50-49°C stimulus train much lower than the T3 in a constant presentation of 49°C (ANOVA, $p=0.0046$). Furthermore, subjects could not distinguish between a T2-T3 decrease of 50° to 35°C and 50° to 49°C at the same time point ($p=0.1638$). The second paradigm used only one temperature pulse (48°C or 50°C) and varied the rate at which the stimulus intensity returned to baseline (0.5, 1.0, 2.0, 3.5, and 5.0°/s). VAS fall rates were largely independent of temperature fall rates. VAS fall rates evoked by temperature fall rates of 1, 2, and 3.5°/s were not significantly different from those evoked by temperature fall rates of 5°/s. Moreover, during temperature decreases, VAS ratings returned to zero at temperatures as high as 49°C (0.5°/s fall rate from 50°C). Data from both of these paradigms further confirm that a transient analgesic mechanism is activated at stimulus offset.

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Chemistry
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Nanosize Metal Clusters as Building Blocks of Hybrid Inorganic-Organic Materials

Hybrid inorganic-organic materials have received considerable interests recently due to their potential applications in catalysis, gas storage, chemical separation, and ion exchange to cite a few. Nanosize metal clusters can be used as building blocks to prepare hybrid organic-inorganic materials since metal clusters have several advantages over monoatomic metal species. We have chosen to use the edge-bridged octahedral cyanochloride niobium cluster $[\text{Nb}_6\text{Cl}_{12}(\text{CN})_6]^{4-}$ as one of the building blocks for its stability and solubility in common solvents. The cation metal complex $[\text{Mn}(\text{acacen})]^+$ was chosen as the second building block because of the availability of two free coordination sites and the possibility of bringing redox catalytic properties into the resulting cluster-based hybrid materials due to the d^4 electronic configuration of Mn(III). Three novel materials were prepared at room temperature using self-assembly processes. Depending on the nature of the solvent, reactions between solutions containing cluster units and metal complexes led to the preparation of three different materials characterized by different degrees of polymerization. The compounds were characterized by single crystal x-ray diffraction. The structures of these materials (Figure 1) changes from 1D hydrogen bonded species (1), to 1D tubular-like (2), and 1D coordination polymers (3).

Zhou Zou

Chemistry
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Carbohydrate-derived N-Hydroxyureas as New Nitric Oxide Donors

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Hydroxyureas is a new approved treatment for sickle cell disease. Oxidation of N-hydroxyurea produces nitric oxide (NO), an important biological messenger molecule. Recent experiments also indicate that hydroxyurea acts as an NO donor in vivo and suggest that the biological effects of N-hydroxyureas may be mediated by NO. Our previous results indicate that heme containing proteins and enzymes including hemoglobin and horseradish peroxidase oxidize N-hydroxyurea with NO release. Based upon these introductory results, we began to prepare carbohydrate-derived hydroxyureas as potential NO donors. The preparation of these N-hydroxyureas from various glucosamines using a newly developed coupling methodology will be described as well as the results regarding the ability of these compounds to release NO by oxidation and inhibit ribonucleotide reductase.