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FEATURE ARTICLES

SUMMARIES OF STUDENT WORK

Washington University in St. Louis

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The primary requirement for inclusion in the Digest is that a paper represent research—contribution of new knowledge through data collection and original source analysis. Students need not be seniors, or receiving honors, or have been funded by our office. Work need not be performed here at Washington University. Work need not be prepared alone; in fact, because research involves working with others, we anticipate including much collaborative work in these pages.

The Office of Undergraduate Research is funded by the College of Arts & Sciences.

The logo for the Office of Undergraduate Research, on the front cover of this publication, consists of an "impossible triangle" within a starburst. To some, the triangle evokes the challenge of puzzles to be solved or the eternal research question "How does that work?" To others, the triangle represents the Greek letter Δ, the mathematical symbol for change.

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UNDERGRADUATE RESEARCH DIGEST
VOLUME 12 ~ 2016-2017

TABLE OF CONTENTS

Foreword

Undergraduate students at Washington University in St. Louis engage in research in a wide variety of disciplines and areas of study. Mentored by faculty who are dedicated to the training of future scholars, students conduct research that may lead to solutions to many of today's pressing social problems, to new interpretations of the past, as well as creation of new knowledge. In many cases, their research may even lead to new questions to be studied by future investigators.

Of the students whose work is contained in this volume of the *Washington University Undergraduate Research Digest*, some conducted research in St. Louis while others traveled abroad. They worked over the summer and into the school year. They spent hours in the field, in laboratories, in libraries, collecting, analyzing and interpreting data. They have written theses, published papers, and presented findings. Consider the work of the authors of our feature articles:

Luke Churchill explores the role of conscious and unconscious semantic activation, helping gain new insights that provide great relevance in academic contexts including memorization-based learning. His research and others like it that explore the processes that drive retrieval will help policy-makers and educators alike to better design classes and pedagogical techniques for a new generation of students.

Michael Seitanakis and Ryan Wahidi both conducted research in the area of physics. Seitanakis investigates a novel way to couple a ruby spin ensemble to a double post reentrant three-dimensional copper cavity. His findings open new avenues using nano-fabrication techniques to construct superconducting quantum circuits and aid future research focused on understanding and controlling open quantum systems. Wahidi's investigation of a sample-thickness dependence, comparing his simulation to experimental results previously reported, will permit researchers to understand the underlying physics of the observed anomaly in bone sonometry studies.

These feature articles and the many students whose abstracts follow could not have conducted their research without dedicated faculty mentors, whom we owe a debt of gratitude. We also gratefully acknowledge the work of the Peer Review Board in carefully editing our feature articles. Finally, we invite you to enter the world of research at Washington University and become inspired by the works herein.

Respectfully,

LINDSEY PAUNOVICH
Editor

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UNDERGRADUATE RESEARCH DIGEST

VOLUME 12 — 2016-2017

FEATURE ARTICLES

Conscious and Unconscious Semantic Activation in Episodic Memory Retrieval

Author:

Luke Churchill

Luke majors in Psychology, Neuroscience, and Philosophy with a minor in French. He has worked as a research assistant in Dr. Julian Ramirez's behavioral neuroscience laboratory and in Dr. David Balota's cognitive psychology laboratory here at Washington University in St. Louis. He is currently starting a new project focusing on collective memory as a part of his senior honors thesis.

KEY TERMS

- Semantic Memory
- Retrieval Processes
- Unconscious Priming
- Conscious Priming
- Spreading Activation

ABSTRACT

This research examines the role of conscious and unconscious semantic activation in the episodic retrieval of paired associates. It finds that semantically activating the target of a given cue-target paired associate increases the likelihood that the associate will be successfully retrieved. This increased retrieval accuracy was found in both suprathreshold and subthreshold priming conditions. The study found that subjects responded faster to a given target when said target was semantically activated in both suprathreshold and subthreshold conditions. These findings together support the idea that semantic activation plays a role in the retrieval of episodic memories.

FACULTY MENTOR: DAVID BALOTA, PH.D. PROFESSOR OF PSYCHOLOGICAL & BRAIN SCIENCES, PROFESSOR OF NEUROLOGY

Professor Balota works on issues related to visual word recognition, semantic memory, priming on implicit memory tests, and attention systems that modulate performance within each of these domains. He investigates these phenomena within young adults, older adults, and individuals who have dementing illnesses such as senile dementia of the Alzheimer's type.

ACKNOWLEDGEMENTS

I would like to thank Peter Millar, Dr. David Balota, and Dr. Jan Duchek for their invaluable assistance at all stages of this project. I would also like to thank the Washington University in St. Louis Office of Undergraduate Research for their funding via the Summer Undergraduate Research Award.

Peer Editors:

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INTRODUCTION

Humans are constantly retrieving information from their vast storehouse of knowledge. They appear to do this quickly and efficiently. Current models of memory (Tulving, 1972) suggest that there is an important distinction between semantic memory (our storehouse of knowledge) and episodic memory (our autobiographical memory for previous events, e.g., what I had for breakfast). One way to conceptualize semantic knowledge is as a storage of nodes and that these nodes are connected to other nodes via associative pathways. For the specific piece of knowledge stored in a given node to be retrieved (pulled into conscious awareness), that node must be activated above a certain threshold. The theory of spreading activation (Collins & Loftus, 1975) suggests that when a given node is activated, activation spreads to other nodes related to the original node through both conscious and unconscious paths. If a node is strongly related, it will be pushed into conscious awareness and thus recalled. This semantic spreading activation has been a thoroughly-explored concept of psychological research for decades. While this idea has been tested in areas ranging from illusions of memory to recognition paradigms, little research has focused on the role semantic activation might play in episodic memory retrieval.

In semantic priming paradigms, semantically related or identical primes have been shown to increase processing fluency of their targets through semantic activation (Maddox and Balota, 2014). This increased processing fluency, or ease in facility and speed of processing, is reflected by a decrease in response latency and an increase in accuracy. Researchers such as Collins and Loftus (1975) have suggested that upon the presentation of a prime, the semantic representation of that prime is activated, and that activation in turn spreads to representations of semantically related words or concepts. Researchers such as Balota (1983) and Jacoby and Whitehouse (1989) have shown that this activation persists even if the primes are presented below the threshold of conscious processing. Jacoby and Whitehouse studied masked priming in the context of recognition, whereas Balota studied masked priming in a lexical decision paradigm.

The present study addressed the role of spreading activation in a more effortful episodic memory paradigm, i.e., memory retrieval of paired associates. In the present study, participants studied paired-associates, or word-pairs (e.g., DOG-CHAIR) during an initial learning phase. After studying the word-pairs, they were tested during retrieval in which they were given the cue (DOG) and were required to retrieve the word that was paired with this stimulus. It is important to note that, during this testing phase, participants were presented with both masked (in a backwards lexical masked priming paradigm) and unmasked primes. These primes could either increase activation of the target via the identity prime (e.g., CHAIR) or related prime (e.g., TABLE), compared to a baseline unrelated condition (e.g., FROG). It was predicted that increasing the activation of the target in semantic memory would in turn make it easier for participants to successfully recall the target. It was also predicted that subjects would show greater effects in the conscious prime duration, as both conscious and unconscious processes would be engaged by the prime.

METHODS

Subjects

The subjects were 26 undergraduate students living in St. Louis for the summer who participated in the experiment for payment. All subjects were between the ages of 18 and 23. Twenty-five subjects were right handed and one was left handed. Nineteen of the subjects were female, and the remaining seven were male. Fourteen subjects underwent a control procedure as well as the experimental procedure. Subjects were randomly assigned to one of eight counterbalances based on the order in which they signed up.

Materials, Procedures, and Design

A pool of 76 cue-target pairs was selected from Maddox and Balota (2014). In order to reach an even 80, four new word pairs were created using data from the Nelson Free Association Norms (NFAN). Each new word pair was assigned a prime related to the target (second word) of that word pair, taken from the NFAN. The word pairs and their respective primes were then divided into four groups of 20 word pairs each, which would be used to make the word lists for each counterbalance. Across the lists, the word pairs were controlled for word frequency, word length, and strength of both forward and backward relationships.

Subjects were tested for their ability to recall word pairs in various prime conditions. There were three prime conditions: identity (identical to the target), related (related to the target), or unrelated (unrelated to the target). Given the word pair "DOG-chair," an identity prime would be "chair," a related prime would be "table," and an unrelated prime would be "salt." There were also two presentation duration conditions. Primes were either presented for 33 milliseconds (in the masked, unaware condition) or 150 milliseconds (in the aware condition). Each of these manipulations were within subjects; each subject saw all prime types and both prime durations.

Three 20-word pair groups were shown to each subject, with the fourth withheld. The primes for the word pair group in the unrelated condition were taken from the related primes of the withheld word pair group. Therefore, eight lists of 80 words each were created, with the 20-word groups rotating between being used in the identity condition, the related condition, the unrelated condition, or the withheld condition. The 20-word groups also rotated between timing conditions. This counterbalancing insured that every word pair was seen in each condition the same number of times.

Subjects went through three phases of the experiment. The first phase involved a study/encoding phase in which subjects were presented with all word pairs (except those from the withheld list). This phase took approximately eight minutes. Subjects were instructed to learn and memorize the word pairs. They were also informed that immediately after this learning phase they would be tested for their memory of the presented word pairs. Word pairs were presented one at a time for a duration of 4.5 seconds, and were presented CUE-target (e.g., DOG-chair). All word pairs were presented in the same location, the center of the screen. No priming or masking procedures occurred during this encoding phase. The screen advanced from word pair to word pair automatically, to ensure that subjects had equal exposure to all word pairs. Each participant was presented with 60 word pairs.

The second phase involved the primed testing phase, which took between 12 and 15 minutes. On each trial of the second phase, subjects were instructed to provide the target of one of the word pairs they had just studied when given the cue. They were told that throughout the testing phase other words may be flashed on the screen, but when given the first word of the pair, they were to respond with the second. Subjects were first presented with a row of hashtags as an initial mask for 250 milliseconds. They were then presented with a prime in any of the three conditions (word pairs were presented in random order) for either 33 milliseconds or 150 milliseconds. This prime was immediately followed by the cue, which both served as a backwards lexical mask and cued the participant to begin retrieval. The cue was presented in the format "CUE - ?????", to remind the participant of the word pair structure of the task. Participants had ten seconds to recall the target and press enter. If they did not press enter, the program automatically advanced to the response-entering screen. They then typed in their response and pressed enter again to move on to the next trial. Participants were quizzed on all 60 of the word pairs they studied in the previous phase.

The following graphic shows the time course of each trial.

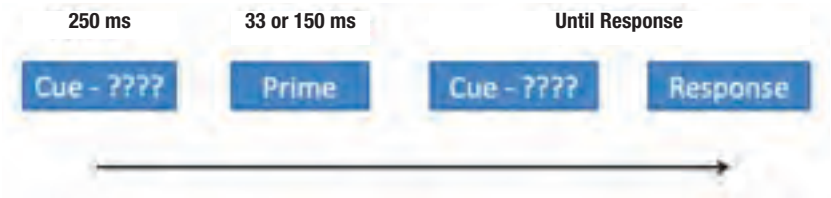

Figure 1

In the third and final phase, subjects were explicitly told that a prime would be flashed between the presentation of the initial stimulus (the hashtags) and the presentation of the cue. This phase was intended to determine if participants could see and produce the unaware, 33 millisecond (ms) primes. The phase followed an identical format to the second (hashtags, followed by prime, followed by cue), but in this case, participants were instructed to identify the briefly presented prime item rather than the target. The primes were presented in both duration conditions, 33 ms and 150 ms. If subjects could not read or see the flashed prime, they were instructed to enter "x" in its place. The word pairs in the withheld list were paired with the related primes from the word pair list in the identity condition, to ensure that participants had never seen either the presented cues or the presented primes previously in the experiment. Participants ran through a total of 20 trials.

The entire procedure was run using E-prime software. Stimuli were presented on a Samsung LCD monitor paired with a Dell PC. The stimuli were presented in the center of the screen and were formatted as white text on a black background. Subjects responded by typing their responses on a keyboard. Subjects were tested individually and sat approximately two feet away from the screen.

RESULTS

Analysis was run on SPSS software using a repeated-measures within-subjects ANOVA. All statistical tests used an alpha level of .05. It is important to note that because we have not yet run our target number of subjects, the experiment is not yet fully counterbalanced. Therefore, it is possible that list effects or stimuli effects are present. It was also found that four words were repeated in the word lists. Trials which contained those repeated words were removed from the analysis.

Accuracy

In the identity condition, participants were correct on 78% of trials in the 150 ms duration, and 52% of trials in the 33 ms duration. In the related condition, participants were correct on 56% of trials in the 150 ms duration, and 54% of trials in the 33 ms duration. Finally, in the unrelated condition, participants were correct on 46% and 44% of trials for the respective durations. These results are displayed in the below graph.

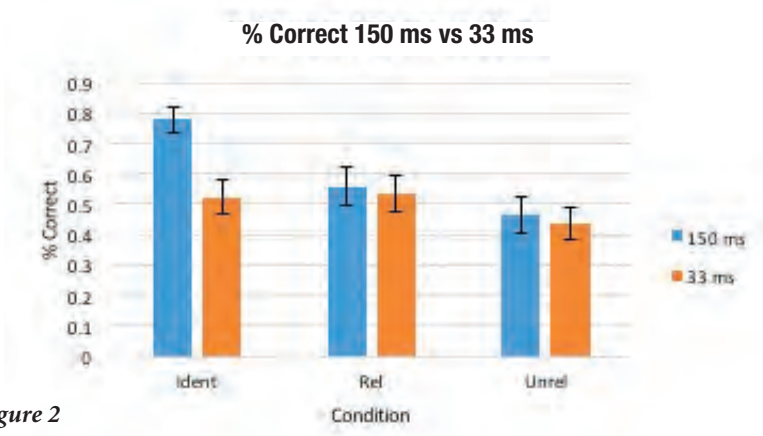

Figure 2

Mean accuracy as a function of condition is displayed in *Figure 2*. Subject means for percentage retrieval accuracy were compiled for each condition and analyzed in a 2x3 repeated-measures ANOVA. The analysis showed a significant effect of the manipulation of prime condition, $F(2,50) = 25.2$, $p < .001$, $n_p^2 = .50$, a significant effect of the manipulation of prime duration, $F(1,25) = 29.6$, $p < .001$, $n_p^2 = .54$, and a significant interaction of time and condition $F(2,50) = 6.9$, $p<.01$, $n_p^2 = .22$.

Pairwise comparisons were then conducted for both duration and prime condition. Participants were significantly more accurate in the 150 ms condition than in the 33 ms condition ($p < .001$). Also, subjects were significantly more accurate in the identity condition than the related condition ($p < .01$), significantly more accurate in the related condition than in the unrelated condition ($p < .001$), and significantly more accurate in the identity condition than in the unrelated condition ($p < .001$).

As there was a significant interaction between prime duration and condition, post hoc repeated measures ANOVAs were run on both the 33 ms and 150 ms conditions separately (1 factor ANOVA, 3 levels (identity, related, unrelated)). There was a marginally

significant effect of condition for the 33 ms prime duration, $F(2,50) = 3.0$, $p < .06$, $n_p^2 = .10$ and a significant effect of condition for the 150 ms prime duration, $F(2,50) = 22.6$, $p < .001$, $n_p^2 = .48$.

Pairwise comparisons were again run for both durations. In the 33 ms prime duration, there was no significant difference in retrieval accuracy between the identity and related conditions ($p > .05$), but both the identity and related prime conditions showed significantly increased retrieval accuracy relative to the unrelated prime condition ($p < .03$ and $p < .05$, respectively). In the 150 ms condition, participants were significantly more accurate in the identity condition than in the related or unrelated conditions ($p < .01$ and $p < .001$, respectively). Subjects were also significantly more accurate in the related condition than in the unrelated condition ($p < .03$). Therefore, the significant interaction between duration and prime condition is likely due to the increased retrieval accuracy in the identity condition at the 50 ms condition. This pattern is expected because at 150 ms, participants are able to see the correct answer in the prime.

Response Time

It is important to note that the response time result reported below is taken from an incomplete segment of participants (N = 18), because some subjects did not perform well enough to have means in certain conditions. More subjects will be run in the future to account for this fault.

Response times were taken from trials in which participants correctly recalled the target. Response times below 250 ms or above 9000 ms were trimmed out. Next, response times greater than 4 standard deviations from the mean or less than -4 standard deviations from the mean were trimmed as well. Response times were then standardized and run through a 2x3 repeated measures ANOVA (see *Figure 2* for mean standardized response latencies).

The analysis showed a significant main effect of prime condition, $F(2,34) = 5.42$, $p < .01$, $n_p^2 = .242$. There was no interaction present across prime durations. This is likely due to the fact that, across prime durations, participants were slower in responding when

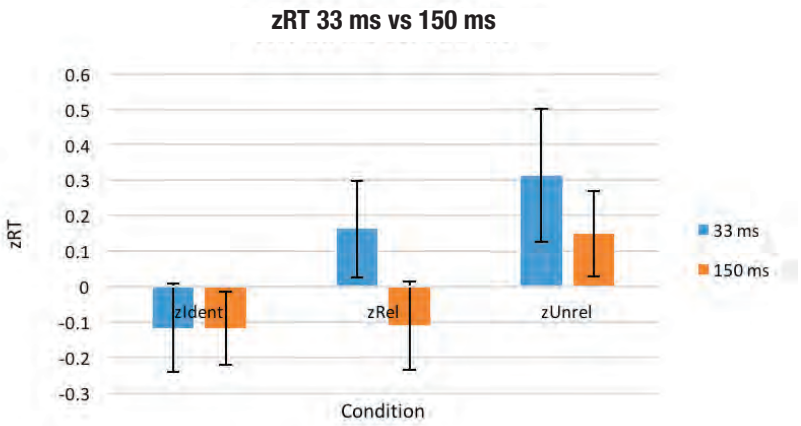

Figure 3

given an unrelated prime than a related or identity prime. *Figure 3* displays the mean z-scored response times.

Control

On average, subjects correctly identified 33 ms primes in the control phase only 5% of the time. In the 150 ms duration, they correctly identified the prime with 91% accuracy. Nine out of the 14 subjects run in the control phase identified 0 primes in the short duration. The analysis showed a significant main effect of prime duration, $F(1,13) = 789.7$, $p < .001$, $n_p^2 = .984$.

DISCUSSION

These results indicate that, as predicted, semantic activation does play a role in controlled episodic memory retrieval. There was a significant effect of prime condition in both prime durations. Importantly, retrieval accuracy increased when the prime was semantically related to the target. Subjects were faster to respond when the prime had some semantic relationship to the target in both durations, indicating that semantic activation facilitates both accuracy of retrieval and ease of retrieval, which together make up retrieval fluency. This result is consistent with the findings of facilitation in both the Balota lexical decision/recognition study and the Jacoby and Whitehouse study of false recognition. This work extends to a controlled episodic retrieval situation.

The analysis of the control items indicates that the 33 ms masked primes were nearly impossible for participants to correctly identify. Therefore, the significant facilitation of the identity and related conditions are associated with unconscious processes rather than conscious direction of attention, as the primes were not available to the conscious mind.

It is noteworthy that both the identity and related conditions showed approximately equivalent facilitation. Hence, the facilitation is likely due to the semantic relationship of the primes and not to the lexical characteristics (letter shape, length, etc.). If subjects were picking up on the lexical characteristics of the primes, the identity condition would produce a larger benefit, because the related primes do not share lexical characteristics with their semantically associated targets. It is the spread of semantic activation that facilitates retrieval in the 33 ms duration.

The fact that participants responded significantly faster to word pairs in the related and identity prime conditions than to word pairs in the unrelated condition lends further support to the idea that semantic activation facilitates retrieval. This finding is in line with the results of Balota's 1983 paper, which saw faster response times to words followed by a related prime than words following an unrelated prime. Interestingly, however, Balota (1983) did not observe an effect of semantic activation from threshold primes in a recognition task: he saw a deleterious effect of prime in the suprathreshold condition, but not in the threshold condition. This apparent conflict, however, appears because Balota et al. used a context recognition test, whereas this study uses a direct retrieval task.

The key difference between the 150 ms prime duration and the 33 ms duration lies in the mean accuracy within the identity condition. Participants reached a mean accuracy of 78% in the 150 ms duration and 52% in the 33 ms condition. This large difference is responsible for the significant time by condition interaction found in the above analyses.

It is likely that at the 150 ms identity condition participants have conscious access to the lexical characteristics provided by the identity prime, which exactly match the lexical characteristics of the target. This would lead to both lexical and semantic priming, greater activation, and easier recall. Additionally, presenting the target to the participant as the prime directly rather than indirectly semantically activates the target in memory, which leads to greater activation of the target in memory. On a threshold-based model of retrieval processes, greater activation should lead to easier recall, as is displayed in the 150 ms results of this paper. While there should be greater semantic activation in the unconscious prime duration as well, there is not significantly greater facilitation, which may detract from this interpretation.

It is also possible that in the 150 ms conscious identity condition, participants are using a different process than in the related and unrelated prime conditions. In the latter two conditions, participants are forced to retrieve the target from memory, while in the identity condition, participants must simply recognize the presented prime as the correct target. This condition requires recognition rather than retrieval. More research is needed to investigate this possibility.

It is important to note that a replication of this study was conducted during the fall of 2016 at Washington University in St. Louis with 19 subjects. The study failed to replicate the effects reported above. Therefore, the results above must be taken with caution. These results are not easily replicable, and are a great example of the importance of the replication in science.

The results of this paper imply that semantic activation affects ease of retrieval both in unconscious and conscious prime durations. This semantic activation can come from either suprathreshold or subthreshold primes. Future research should experiment with Stimulus Onset Asynchrony (SOA) by varying the duration between the presentation of the prime and cue, and with varied retrieval paradigms. It would also be interesting to examine the time course of the activation by testing the participants later in the day or in a second session.

The results of this paper have great relevance in academic contexts, specifically in the memorization-based learning. For instance, it is possible, given these results, that the order of word presentation or choice of words in test questions could have a measurable effect on student performance on said tests. Teachers, when made aware of the importance of enforcing semantic relationships between concepts, could improve their student's ability to retrieve the required information when tested. This study, and others like it exploring the processes that drive retrieval, will help policy-makers and educators alike better design classes and pedagogical techniques for a new generation of students.

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Strong Coupling of a Spin Ensemble in Ruby Crystal to a Three-Dimensional Copper Cavity

Author:

Michael Seitanakis

Michael majored in Physics, graduating with College Honors from the College of Arts & Sciences at Washington University in St. Louis in May 2017. Next year he will work for Epic Systems Corporation in medical software with the eventual plan of pursuing a graduate degree in physics.

KEY TERMS

- Electron-spin ensemble
- Three-dimensional double post reentrant copper cavity
- Qubit
- Quantum computer

ABSTRACT

In the pursuit of developing quantum technology, researchers study novel ways to measure and control quantum phenomena. For example, if strong enough coupling is attained with the spin ensemble in a ruby crystal that has a small enough linewidth, this system could serve in a quantum computer as a quantum memory. Previous research has shown strong coupling to spin ensembles, but achieving a smaller spin linewidth is required to create quantum memory devices. This study examines the coupling between a spin ensemble and a double post reentrant three-dimensional copper cavity, which could take advantage of its higher mode volume and a more constant magnetic field through the ruby volume to achieve higher coupling and a smaller spin linewidth. Measuring the transmittance through the cavity, the change in quality factor, Q, and resonant frequency of the cavity indicate coupling strength, g, and the spin linewidth. As the advent of the quantum computer nears, this research adds to the body of work that attempts to access the vast expanse of Hilbert space.

FACULTY MENTOR: KATER MURCH, PH.D.
ASSISTANT PROFESSOR OF PHYSICS

Dr. Kater Murch's research group conducts experimental research at the interface of atomic, molecular, optical, and condensed matter physics. They use nano-fabrication techniques to construct superconducting quantum circuits that allow them to probe fundamental questions in quantum mechanics.

ACKNOWLEDGEMENTS

I thank my research mentor Dr. Kater Murch for his guidance on this project and in my development as a scientist. I would also like to thank Patrick Harrington, Mehti Naghiloo, and Dian Tan for their insightful discussions. Finally, I thank my cohort in the lab, the Under(grad) Achievers for such a fun summer.

Peer Editors:

Chase Antonacci, a sophomore majoring in Philosophy-Neuroscience-Psychology

Kelsey Pitts, a senior majoring in Biochemistry

INTRODUCTION

The successful development of a quantum computer would be "more revolutionary than anything before, including the classical computer and the internet"[1]. Research in quantum computing consists of creating and developing technology that measure and control quantum phenomena in diverse physical systems. Each device has its advantages and disadvantages, suggesting the need for a quantum computer made of different integrated components with different specializations. For example, much research has been conducted on the precise measurement, fast control, and efficient coupling of the transmon qubit[2]; however researchers cannot overcome the shortcoming that quantum information disappears quickly when stored in a transmon relative to computation time. To circumvent the issue of information loss in transmons, recent research has gone into developing quantum memory devices, which store quantum information for long amounts of time (relative to the computation time). Spin ensembles in ruby hold information much longer than fast-processing transmon qubits[4] and they also have a resonance in the energy range of transmons, which suggests direct coupling is feasible. Current research attempts to develop different devices that access the ruby spin ensemble through electromagnetic coupling[6]. Previous works have achieved strong coupling, but the spin linewidth was too wide for the quantum information storage application[6]. We hypothesized that a three-dimensional double post reentrant cavity would achieve strong coupling to the ruby spin ensemble since it can focus the magnetic field within the ruby, and would have better spin linewidth. To test the coupling, we designed a cavity and ruby shape to maximize magnetic coupling, measuring the change in cavity resonance and quality factor as an external magnetic field changed the ruby spin ensemble resonance. Achieving strong coupling between the cavity and this spin ensemble along with finding a larger spin ensemble quality factor would lead to further research in coupling ruby spins to other quantum systems like transmon qubits. A benefit of the 3D cavity is the potential to couple the ruby spins with part of the cavity mode to transmon qubits with another part of the cavity mode. The strong coupling found in this experiment shows promise in this cavity's ability to control ruby spins and eventually couple them to transmon qubits or other components like them.

II COUPLED OSCILLATORS

This summer I studied coupled oscillators, systems that store energy in each of their oscillators as well as in the interactions between the two. This interaction, or coupling, allows experimentalists to follow a simple line of logic that leads to amazing discoveries: if I can measure oscillator *A* and oscillator *A* is coupled to oscillator *B*, then I can indirectly learn information about oscillator *B*. Later Section III describes the physics of the two oscillators that I studied, a spin ensemble in ruby and a resonant cavity. However, first I will start by describing coupled harmonic oscillators, a simplified case. A more detailed description of coupled oscillators can be found in most classical dynamics texts[5].

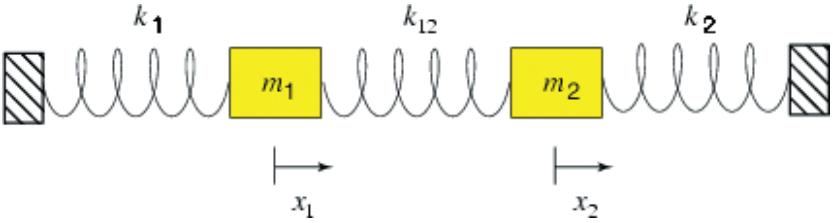

Figure 1: Schematic of Two Masses Attached to Simple Springs Oscillating without Friction.

Spring with constant k_1 (k_2) attaches mass m_1 (m_2) to a fixed wall on the left (right). A third spring of constant k_{12} couples the two masses in the middle. Define the position of m_1 and m_2 as x_1 and x_2 respectively where $x_1 = x_2 = 0$ at equilibrium.

Consider a system of two masses, m_1 and m_2, connected to fixed walls with simple springs of Hooke's constant k_1 and k_2 respectively and connected to each other with a simple spring of constant k_{12} as shown in *Figure 1*. In order to explore the motion of the masses in this system, one can write down Newton's law for m_1 and m_2:

$$\begin{aligned} m_1\ddot{x}_1 &= -(k_1 + k_{12})x_1 + k_{12}x_2 \\ m_2\ddot{x}_2 &= -(k_2 + k_{12})x_2 + k_{12}x_1 \end{aligned} \tag{1}$$

To solve the equations of motion, one can use the ansatz

$$\begin{aligned} x_1 &= B_1 e^{i\omega t} \\ x_2 &= B_2 e^{i\omega t} \end{aligned} \tag{2}$$

where ω describes a radial frequency at which both masses could sinusoidally oscillate in the steady state, ignoring friction, and B_1 and B_2 are complex numbers that contain the amplitude and phase of each mass' oscillation. Plugging in the guessed forms of x_1 and x_2, the equations of motion become

$$\begin{aligned} B_1(k_1 + k_{12} - m_1\omega^2) - B_2k_{12} &= 0 \\ -B_1k_{12} + B_2(k_2 + k_{12} - m_2\omega^2) &= 0 \end{aligned} \tag{3}$$

Observing that these coupled linear equations can be written in matrix form, the possible values for ω that would satisfy both equations would also cause the determinant of the coefficients of B_1 and B_2 to vanish:

$$det \begin{vmatrix} (k_1 + k_{12} - m_1\omega^2) & -k_{12} \\ -k_{12} & (k_2 + k_{12} - m_2\omega^2) \end{vmatrix} = 0 \tag{4}$$

Since the determinant yields a quadratic equation in ω^2, this system has two possible steady state frequencies.

This mathematical framework predicts the results of experiments. For example, let's say we want to know the effect of changing k_1 (i.e., making the first spring tighter) on the possible steady state frequencies of the system, $\omega(k_1)$ while holding all other parameters constant. After some careful algebra, one can isolate ω^2 and put it in terms of k_1. The resulting equation takes the form of a hyperbola with one asymptote parallel to the *x*-axis:

$$y = a(x - c) + d \pm \sqrt{a^2(x - c)^2 + g^2} \tag{5}$$

where each constant has graphical meaning as shown in *Figure 2*.

To understand *Figure 2*, first notice that the limit where *y* becomes its asymptotes, $g \rightarrow 0$, represents the situation of two decoupled oscillators. In this limit, the line of zero slope would represent the frequency of oscillating mass m_2, unaffected by the changing spring constant k_1, and the sloped line would represent the frequency of mass m_1, linearly dependent on k_1. As coupling increases, the spacing between the frequencies increases at the crossing. This avoided crossing spacing, *g*, allows for a good measurement of coupling strength between two oscillators; larger spacing implies stronger coupling.

Thinking about the physics of the system as you sweep through k_1 values leads to interesting places. When k_1 is far from the crossing region, the values for ω closely match the asymptotes, the frequencies when the oscillators are decoupled. In this range of k_1, one can think of the oscillators as roughly separate, they do not have a great affect on each other, as seen by the small change in ω. However when k_1 is in the crossing region, the coupled resonances differ much more from the decoupled resonances. For this range of k_1, one can no longer think of the oscillators as separate. They now behave as a hybrid oscillator that has distinct modes compared to its separate parts.

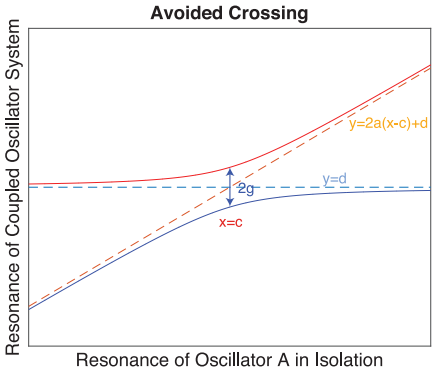

Figure 2: Avoided Crossing Graph of Equation 5

The asymptotes of the hyperbola $y = d$ and $y = 2a(x - c)+d$ represent the modes of the two oscillators if the spring with constant k_{12}did not exist. The gap between *y* values where the two asymptotes cross indicates coupling strength. Notice the *y* values nearly match the asymptotes far away from the intersection, but greatly differ near the intersection. Physically this relationship means that the oscillators act like decoupled oscillators far from where their modes cross, and the coupling shows most strongly near the cross.

The following sections focus on an experiment that uses the coupled oscillator model. You might find it useful to refer back to this section and draw analogies to the mass and spring model.

III COUPLING SPIN MODES IN A RUBY CRYSTAL TO A COPPER CAVITY

This section describes an actual experiment that follows the theoretical framework laid out in Section II. An ensemble of spins in a ruby crystal plays the role of one oscillator, the other, a three dimensional copper cavity resonator. The electromagnetic field mediates an interaction between the spin ensemble and cavity. First I will describe the physics of the two oscillators separately, then I will describe their coupling and the experiment that follows.

A. Spin Ensemble In Ruby

Ruby is composed of a lattice of Al_2O_3 with chromium ions infrequently replacing the Aluminum in the lattice (*Figure 3*). Chromium electrons exist in orbital states with angular momentum and a dipole moment that follow the dynamics of a spin-$\frac{3}{2}$ quantum system. Since the chromium ions are spin-$\frac{3}{2}$ fermions, there are two dominant interactions between Cr^{+3} ions: magnetic dipole-dipole coupling and the exchange interaction. The derivation by Stancil in *Quantum Theory of Spin Waves*[7] predicts that the wavelength of the resonance determines which of these two interactions dominates: wavelengths much longer than spin spacing follow dipole dynamics and wavelengths on the order of spin spacing follow the exclusion interaction. The wavelength of our ruby's resonance suggests that the exclusion interaction dominates.

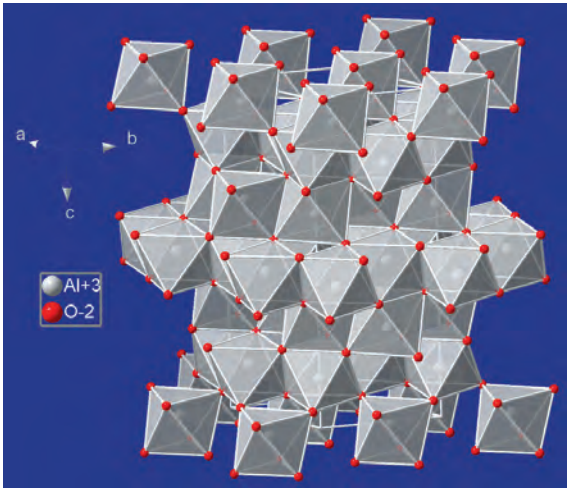

Figure. 3: Ideal Lattice of a Ruby Crystal
Some Al^{+3} sites are replaced by Cr^{+3}, differentiating the ruby crystal from sapphire, which consists of pure Al_2O_3.

In a thorough description of the exclusion interaction and spin dynamics, Stancil's *Quantum Theory of Spin Waves*[7] derives many fundamental spin dynamics from the hydrogen atom to a three dimensional magnon system. To model a lattice of exclusion-interaction-coupled spins, Stancil combines the Heisenberg Hamiltonian with the Zeeman Hamiltonian:

$$\mathcal{H} = -2\frac{\mathcal{J}}{\hbar^2}\sum_{j,\boldsymbol{\delta}} \mathbf{S}_j \cdot \mathbf{S}_{j+\boldsymbol{\delta}} - \frac{g\mu_B B_0}{\hbar}\sum_j S_{jz} \tag{6}$$

The Heisenberg Hamiltonian encapsulates the exclusion energies between each pair of nearest-neighbor spins (the first term), and the Zeeman Hamiltonian represents the energy of dipole orientations in an external field B_0 (the second term). The index j represents a specific spin site in the crystal, and the vector $\boldsymbol{\delta}$ represents a vector to one of the nearest neighbors of spin j. The Heisenberg Hamiltonian comes from the exclusion interaction between spins which depends on only the relative orientation of the spins, as shown by the prefactor

$$\mathcal{J} = \tfrac{1}{2}(\varepsilon_S - \varepsilon_T) \tag{7}$$

where $\varepsilon_{S(T)}$ is the energy of the symmetric (antisymmetric) spin orientation. The Zeeman Hamiltonian, on the other hand, depends on the strength of the external magnetic field, B_0. Stancil goes on to derive a mathmatical analogy of this 3D system to a harmonic oscillator with quantized energy levels. Solving the eigen problem for this Hamiltonian leads to discrete energy levels of the oscillator for a given wavevector $\boldsymbol{\kappa}$:

$$\hbar\omega_\kappa = 4\mathcal{J}sZ(1-\gamma_\kappa) + g\mu_B B_0 \tag{8}$$

where s is an integer and Z and γ_κ depend on the relative orientation of the spins. Most importantly for this experiment, the Zeeman term causes *the energy levels to depend linearly on external magnetic field* B_0. This means that the resonant frequency of the spin ensemble (a harmonic oscillator) can be changed by a changing magnetic field enabling us to conduct the experiment described in Section II.

B. Resonant Copper Cavity

Although the spin ensemble described in Section III A exhibits amazing solid state physics, measuring the resonator requires clever experimental design. Because spin is a magnetic phenomenon, external electromagnetic excitations would affect the spin ensemble. A resonant conducting cavity provides a well understood, measurable oscillating field that can affect the spin dynamics and therefore couple to the ruby resonator.

Before diving into how a cavity interacts with the ruby spin ensemble, first let's consider a cavity in isolation. Solving Maxwell's equations for a given geometry of a conducting cavity allows one to explore the resonance and shape of its electromagnetic modes. Griffiths[3] describes the boundary conditions and solutions to such problems in much more detail. Briefly, since the exterior of the cavity is assumed to be perfectly conducting, $\mathbf{E} = \mathbf{0}$ around the boundaries. The following boundary condition applies just inside the walls of the cavity:

$$\mathbf{E}^{\parallel} = \mathbf{0} \tag{9}$$

Assuming sinusoidally time varying solutions of **E** and **B**, one can solve the relevant Maxwell's equations by applying the boundary conditions. To solve complicated cavities, one can use software like HFSS to approximate the time-varying fields for different modes. Notice a few features of the simulations shown in *Figures 4*, *5* and *6* that guide the design of a useful cavity shape: 1) E-field is perpendicular to B-field at any point 2) E-field maxima and B-field maxima occur at different coordinates. 3) One can identify patterns like the E-field of a parallel plate capacitor where there are two close flat metal surfaces and the B-field of a current carrying wire around the side of an extrusion.

In order to strongly couple the magnetic field of the cavity to the magnetic spins of the ruby, the maximum magnetic field in the cavity should occur inside the volume of the ruby. In fact, ideally all of the magnetic mode volume occurs in the ruby while all of the electric mode volume avoids it. The electric field should avoid the volume of the ruby because the crystal is a dielectric which causes damping in oscillations of the electric field. Our experiment used the double post cavity in *Figure 6*. Most of the magnetic field occurs between the two posts, where the rectangular shaped ruby is inserted. The electric field mostly occurs outside of the ruby, minimizing loss. The HFSS simulation also suggests where to put the probes that couple the cavity to our measurement ports. These probes couple to the electric field of the cavity, so they are placed where the electric field resides: between the roof and the top of the posts.

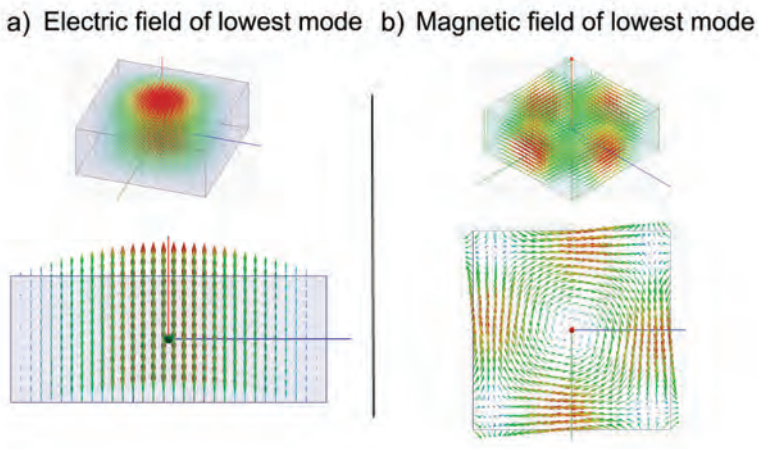

Figure 4

The simulated representation of the electric and magnetic field inside a box whose walls are conductors and inside is vacuum shows the maxima and minima of the fields in the cavity. a) The three dimensional view of the electric field demonstrates that the boundary condition $\mathbf{E}^{\parallel} = \mathbf{0}$ is satisfied. From the side view of the electric field, one can see that for the lowest mode, the electric field is maximum through the center of the cavity along the red-axis and minimized farthest away from the axis. b) Looking down the red-axis at the magnetic field, one can see that the boundary condition $B^{\perp} = 0$ is satisfied and the maximum of the magnetic fields occurs on the periphery of the cavity. Notice that the maxima for the electric and magnetic field occur in different locations.

C. Coupling between the Spin Ensemble and the Cavity

Section III A and Section III B describe the physics of two separate oscillators: a spin ensemble in a ruby crystal and a conducting cavity. Since spin is a magnetic phenomenon, the magnetic field in the cavity affects the spin ensemble. To achieve the strongest effect, the most coupling, one should maximize the amount of magnetic field in the ruby volume. (I would like to find a derivation of the coupling).[8]

D. Solenoid

As described in Section III A, the experiment needs a constant external magnetic field to tune to frequency of the spin waves. In order to do this, we use a solenoid made of Niobium wire, a superconductor. Previous research[6] suggests that the ruby will be degenerate with the cavity when the external magnetic field reaches about 30mT. The magnetic field produced by a solenoid at its center follows the equation

$$B = \frac{\mu NI}{L} \tag{10}$$

where N is the number of turns of wire, I is the current, μ is the magnetic permeability, and L is the length of the solenoid. The length of the solenoid must be large enough to create a constant magnetic field through the ruby, a requirement of the spin ensemble phenomenon. Calculating the magnetic field of a finite solenoid, I approximated 6 cm to provide a sufficiently constant magnetic field. Given that the maximum current that the wire can handle is 1 A (I would stay below this value), $N \geq 3000$ turns to achieve a good sweep through 30 mT. In fabrication, I found all of these parameters to be reasonable.

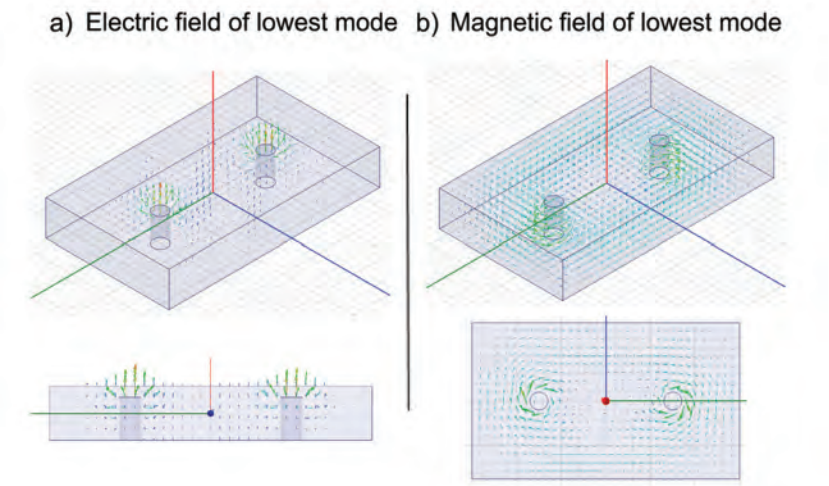

Figure 5

The modes for this cavity take a different shape due to the cylindrical, conductive extrusions in the interior. a) From the side, one can see that the electric field is maximized where the conductive walls become most close, at the top of the cylinders. The vectors pointing from the top of the cylinder to the roof mimic the pattern of the electric field for a parallel plate capacitor. b) The magnetic field maximum occurs closer to the bottom of the cavity. The concentric circles around the posts mimic the magnetic field vectors around a current carrying wire.

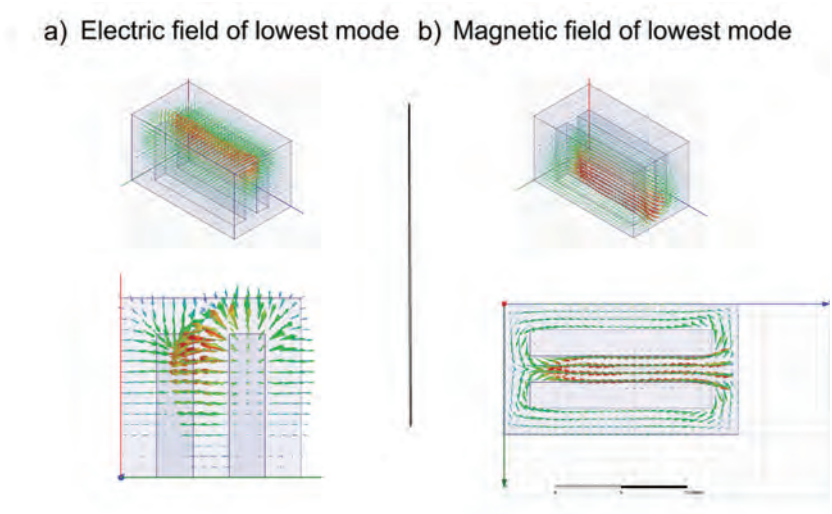

Figure 6

Similar to the cavity in *Figure 5*, the conducting rectangular posts shape the electric and magnetic fields. a) The electric field occurs near the top of the cavity with the vectors mimicking a parallel plate capacitor between the posts and the roof. b) The magnetic field maximum occurs near the bottom between the posts. The longer rectangle extrusions cause the magnetic field maximum to be evenly distributed in the middle of the two posts.

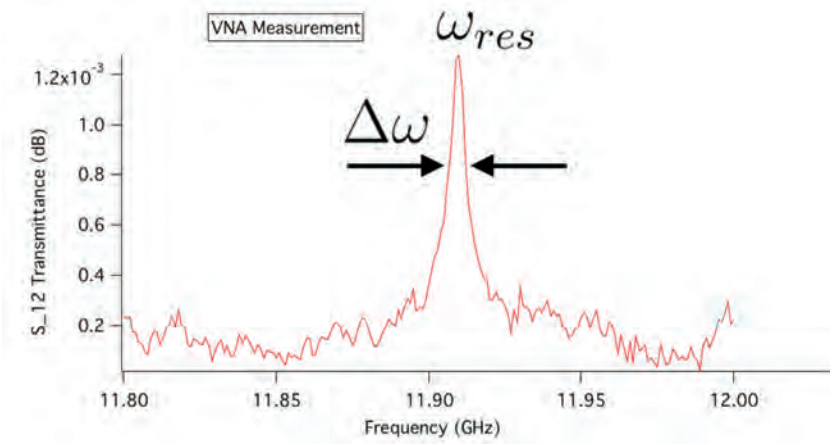

Figure 7

Output of Vector Network Analyzer (VNA) measurement of S_{12} for the double post cavity at roughly 0 K. Labels indicate the values that determine quality factor Q.

E. Data and Analysis

Understanding the underlying physics, one can now perform a simple experiment. Just like the experiment outlined in Section II, one can tune resonance of the spin ensemble with an external magnetic field created by a solenoid and observe the effect in the resonance of the cavity, which is electromagnetically coupled to the spin ensemble. To measure the resonance of the cavity, a Vector Network Analyzer (VNA) probes the cavity with a radio frequency signal through one antenna and observes the transmitted power in another. The power of transmittance between probe antennae in the cavity peaks at the resonance of the cavity (just like when you sing in the shower: a certain note resonates in the bathroom and sounds the loudest).

The graph of frequency versus transmitted power shown in *Figure 7* ideally follows a Lorentzian function. The maximum value and the full width at half of the maximum value parametrize the curve. These two values combine to give an important metric of a resonant cavity, the quality factor Q:

$$Q = \frac{\omega_{res}}{\Delta\omega} \tag{11}$$

where ω_{res} is the resonant frequency and $\Delta\omega$ is the full width half max as shown in *Figure 7*. A higher Q indicates a sharper resonant peak, which provides clearer data. Another definition of Q reveals another advantage of a higher quality factor:

$$Q = 2\pi \frac{\text{Energy Stored}}{\text{Energy Dissipated per Cycle}} \tag{12}$$

A resonator with higher Q has less energy loss. In fabrication, discussed later in Section IV, one should maximize the Q of both the cavity and spin ensemble.

Once we can tune the frequency of the spin ensemble and measure the resonance of the cavity, we can measure the effect of one on the other. I used the LabView programming language to orchestrate the experiment.

The experiment produces a 2D intensity plot of the transmitted power at a given external magnetic field and frequency (*Figure 8*). A vertical slice of the graph is an averaged VNA measurement like that in *Figure 7* at a given magnetic field. One should note that the experiment should be done slowly (about 1 second for a change in one mA) because rapid change though the current in the solenoid will heat up the fridge. This measurement that took a half hour heated the fridge from 9mK to 115mK.

To understand *Figure 8* better, consider how the resonant frequency changes with magnetic field. For low magnetic field the resonance (lightest spot) and Q (approximated by the width of the light patch) do not change, which is expected because the two oscillators' resonances begin far apart. As the magnetic field increases, which increases the ruby resonance, the Q decreases and the resonance changes. The Q gets so small at around 18 mT that the resonance of the cavity becomes difficult to measure. In this area, the two oscillators become intertwined such that one cannot measure them as separate oscillators; however, the VNA measures the cavity as if it were a separate oscillator. This discrepancy explains the change in Q. At around 25 mT the ruby resonance surpasses the cavity resonance enough so that the Q and resonance begin to return to normal. At larger magnetic field, which is unattainable with this experimental set up, the cavity resonance

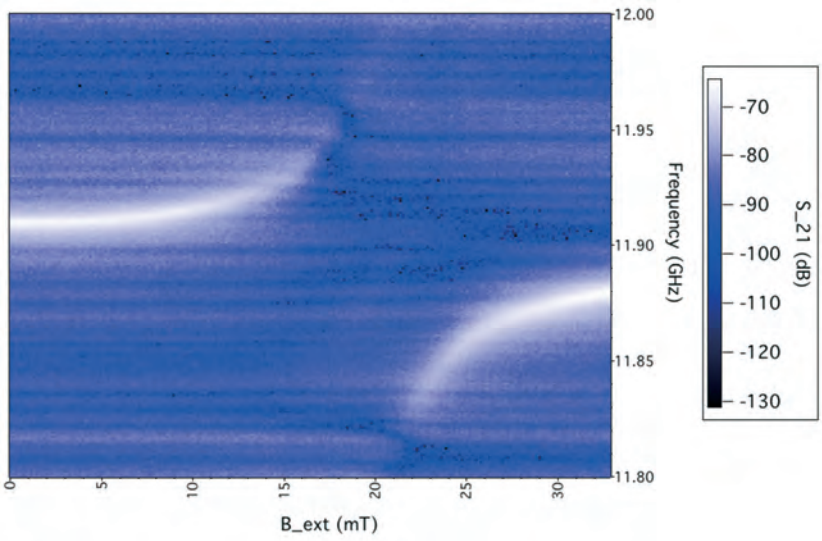

Figure 8
2D intensity plot of averaged VNA measurements at different magnetic fields.

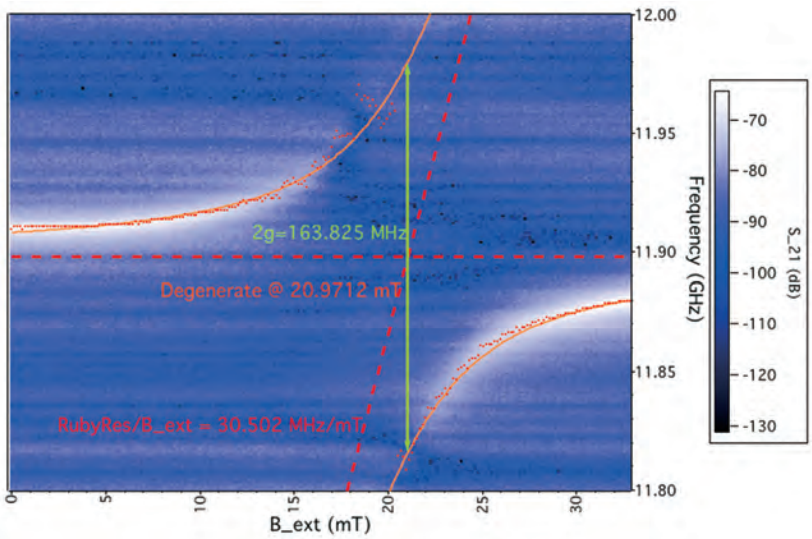

Figure 9
The data fits the avoided crossing curve, enabling a calculation of coupling strength *g*.

and Q would tend towards the values for an isolated cavity since the two oscillators grow very detuned in this limit.

The analysis of this data attempts to find the coupling strength, *g*, (see Section II) between the spin ensemble and cavity. Two curve fits provide independent approximations for *g*. One method uses the avoided crossing equation derived in Section II. The other method fits the data to an equation relating the Q of the cavity to external magnetic field, an equation used in similar crystal coupling experiments[6]. The results described below find similar values for *g* for the independent methods. Igor Pro facilitated the data analysis, graphing and curve fitting.

The first method fits the maxima of the VNA measurement at each magnetic field settingto the hyperbolic avoided crossing equation

$$f(x) = b(x-f) \pm \sqrt{(b(x-f))^2 + c} + d \tag{13}$$

where *b*, *f*, *c*, and *d* were fitting parameters. In reference to the avoided crossing graph in *Figure 9*, $2b$=30.502 MHz/mT is the slope of one asymptote, f=20.951 mT is the magnetic field strength at which the isolated resonances cross, $-d$= 11.898 is the resonance of the isolated cavity, and $\sqrt{c}/2 = g$ = 81:9125 MHz. Igor Pro allows one to simultaneously fit multiple sets of data to different equations using the same fitting parameters. Using this feature, the entire data set was fit to the avoided crossing curve, giving values for the these parameters as shown in *Figure 9*.

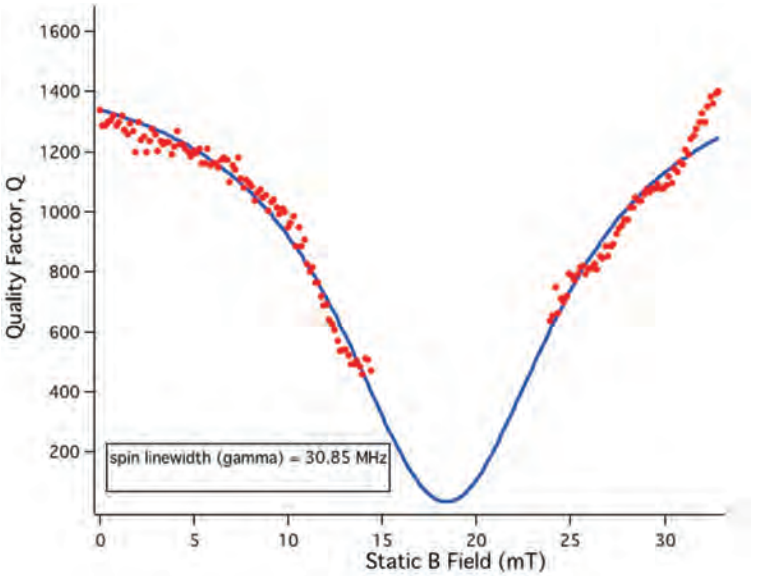

Figure 10: Quality Factor Dependence on Magnetic Field

The data in the small detuning range is discarded because Equation 15 only applies for large detuning. In other words, the peak in the VNA measurement becomes so indistinct that one cannot perform an accurate Lorentzian fit and therefore no Q.

The second method of finding g utilizes an equation that predicts the cavity Q as the resonance of the spin ensemble is changed:

$$Q = \frac{\Delta^2 + \gamma_2^{*2}}{2g_{s,eff}^2 \gamma_2^* + \kappa(\Delta^2 + \gamma_2^{*2})}\omega_r \tag{14}$$

In Equation 14, Δ, the detuning between the cavity and ruby resonances, is the independent variable. The cavity frequency $\omega_r/2\pi$ =11.89 GHz and the cavity linewidth $\kappa/2\pi$ =7.79 MHz are found far away from degeneracy and are constants in the curve fit. The collective coupling strength $g_{s,eff}/2\pi$ =74.84 MHz and the spin linewidth γ_2^* = 30.85 MHz, are extracted from the curve fit in *Figure 10*.

As you can see, the two values calculated for *g* are similar for this experiment. Comparing to a similar study[6], Schuster et al. found their cavity had $g_{s,eff}/2\pi$ =38 MHz, which implies less coupling in their 2D cavity. Also, their ruby had a spin linewidth γ_2^* = 96 MHz, which is wider than the result here.

The decrease in spin linewidth is promising, since that is the limitation on further applications of storing quantum information in spin ensembles.

IV BUILDING THE EXPERIMENT

A. Ruby Specifications

The ruby crystal was fabricated by Laser Materials Corporation. The shape is about 15mmx26mmx1mm with the axis of the ruby pointed along the longest length. The crystal is doped with 0.03 percent Cr_2O_3 by weight.

B. Milling a Cavity

This experiment requires a high Q cavity to attain strong coupling with the ruby spins. The Q of the cavity can be affected by the conductivity of the metal walls, smoothness of the metal walls, the shape of the cavity, the length of the probes, and impurities on the cavity walls. This cavity has a resonance of 11.9 GHz, a room temp Q of around 800 and a low temp Q of 1527. Copper was used for a few reasons. Mainly, copper does not superconduct and has a magnetic susceptibility close to vacuum, which allows an external magnetic field to easily pass through to interact with the spins to control Zeeman splitting. Superconductors have higher Qs since they have infinite conductivity, but the superconductors would either block the external magnetic field or fail to superconduct because of the external field. Copper also has a strong thermal conductivity, which cools the cavity and inner ruby to the base temperature of the dilution refrigerator. Copper is also easily machinable.

This cavity was sent to a company to machine it, but another option for making cavities that could be investigated is 3D printing metal cavities.

V CONCLUSION

Investigating a novel way to couple a ruby spin ensemble to a cavity, I found that the double post reentrant copper cavity improved coupling rate g and spin linewidth from

previous studies. These findings open new avenues to experiments with spin ensembles in crystals using similar cavity geometries.

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Sonometry for Osteoporosis: Assessing the Impact of Phase Sensitive and Phase Insensitive Detection

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KEY TERMS

- Osteoporosis
- Piezoelectric
- Attenuation
- Phase
- Bone Sonometry

ABSTRACT

Osteoporosis is a well-characterized disease that leads to structurally deficient bone. Currently, Dual Energy X-ray Absorptiometry (DEXA) is the primary diagnostic tool used to monitor osteoporotic bone tissue. However, quantitative ultrasonic methods should produce more diagnostic information than DEXA, and would reduce patient exposure to radiation. One obstruction to the improvement of bone sonometry is an unexplained sample-thickness dependence of the attenuation coefficient (α). This paper presents physical evidence and simulations of a Lexan™ model system in order to investigate this sample-thickness dependence.

Data was collected by employing a through-transmission substitution technique in a water tank. Experimental results provided phase sensitive data, while simulations for phase sensitive and phase insensitive trials were conducted. Further simulations in which the radius of the receiving aperture was varied were investigated as well. In every scenario, the sample-thickness dependence of α was reproduced. The persistence of the sample-thickness dependence in the simulations suggests that the current methods employed for data acquisition and reduction are not an underlying cause.

FACULTY MENTOR: JAMES G. MILLER, PH.D. ALBERT GORDON HILL PROFESSOR OF PHYSICS

Professor Miller's research focuses on the physics of anisotropic, inherently inhomogeneous media. These systematic studies of the anisotropic properties of the heart have led to fundamentally new insights, has provided the basis for significantly improved diagnostic images of the hearts of patients, and has been incorporated into commercially available echocardiographic imagers in use throughout the world. Miller's publication list includes more than 165 refereed manuscripts, more than 110 conference proceedings and book chapters, and more than 265 abstracts of presentations at national and international meetings. Current investigations include studies of the physics of ultrasound propagation resulting from causality-imposed generalized dispersion relations.

ACKNOWLEDGEMENTS

I would like to thank Dr. James G. Miller for his guidance, support, and inspiration throughout this project. His mentorship and dedication to teaching have been invaluable throughout this work and beyond. We are very grateful to a number of previous members of the Laboratory for Ultrasonics, especially Amber Nelson Groopman and Kirk D. Wallace. The present study made extensive use of experimental data reported by Amber Nelson Groopman and her collaborators and the software package Virtual Tank developed by Kirk Wallace. I would also like to thank the Department of Physics and the Office of Undergraduate Research for financially supporting this research.

Peer Editors:

Syrus Jin, a sophomore majoring in History and Political Science

Madison McManus, a sophomore majoring in Ancient Studies

INTRODUCTION

Fracture resulting from structurally deficient bone often leads to life-altering or life-ending sequelae. The long-term goal of this research is to contribute to the improvement of ultrasonic methods designed to reliably monitor bone composition and strength. Evaluating a course of treatment with pharmacological agents designed to arrest or reverse bone deterioration is one application for such an enhanced bone sonometry system.

Ultrasound is useful in characterizing tissue because wave propagation permits the determination of the physical properties of the tissue of interest. These ultrasonic tissue characterization techniques should offer improved methods for analyzing the physical properties of cancellous bone, permitting the detection of osteopenia and osteoporosis. Osteopenia and osteoporosis are characterized by a decrease in bone mass often associated with high osteoclast activity and low osteoblast activity, causing an individual to become more prone to fractures and other bone-related injuries. The potential for quantitative ultrasound to be used as a diagnostic agent for osteoporosis was demonstrated at least as early as 1984 in a study where the value of attenuation for normal and osteoporotic calcaneus bones were shown to differ (Langton C. et al., 1984). Previous work from our laboratory identified the potential existence of a small but significant "fast wave mode" during ultrasonic propagation through bone, resulting in qualitative and quantitative errors in bone sonometry measurements. Quantitative ultrasonic measurements of potentially osteoporotic bone should in principle yield more diagnostic information than the more widely employed X-ray method, which is known as Dual Energy X-ray Absorptiometry (DEXA). However, current bone sonometry methods at most equal, but do not surpass, the quality of X-ray-based tools.

Although recent methodological improvements introduced by our laboratory seem to offer the potential for significantly enhancing the field of bone sonometry, implementation of these enhanced methods is being impeded by an unexplained sample-thickness dependence for regional values of the attenuation coefficient (α). The goal of our present research is to investigate the scope of this apparent sample-thickness dependence, and develop methods of reducing its impact on bone sonometry.

The phenomenon of phase cancellation at the face of the receiving aperture is a well-known physical effect. One hypothesis is that this phenomenon coupled with the impact of diffraction might be playing a role in the observed apparent sample-thickness dependence of α. The transducers used for sending and receiving signals are piezoelectric devices. The electrical signals sent out by piezoelectric devices are proportional to the instantaneous complex magnitude of the incident ultrasonic field. The pressure field of the ultrasonic wave incident upon a spatially extended piezoelectric receiver can be written:

$$\tilde{P}(x, y, z, \omega) = P_R(x, y, z, \omega) + iP_I(x, y, z, \omega)$$

The magnitude of the piezoelectric response at the frequency ω of a plate located at some point z is:

$$|V_{PE}(z,\omega)| = \left\{ \left(\int_{\sigma_R} P_R(x,y,z,\omega)dxdy \right)^2 + \left(\int_{\sigma_R} P_I(x,y,z,\omega)dxdy \right)^2 \right\}^{1/2}$$

where σ_R is the face of the receiver. Potential signal loss arising from the integration of the real and imaginary parts of the incident pressure field over the receiver surface can be thought of as an instrumental effect. This effect is instrumental because it depends significantly on the size, placement, and geometry of the receiver. This effect represents signal loss because of the partial cancellation of electrical signals from regions of compressions and rarefactions in the ultrasonic field from different locations on the face of the receiving aperture. Thus, this interference effect is called phase cancellation at the face of the receiving transducer, and is the reason why piezoelectric receivers are phase sensitive.

METHODS

Computer simulations and physical measurements were performed to observe the relationship of the sample-thickness dependence with ultrasonic field diffraction and phase cancellation at the face of the receiving transducer. The computer simulations were carried out through Virtual Tank, a software package created by a former member of our laboratory, Kirk Wallace (Wallace, K. D., 2001).

Data was collected using a through-transmission substitution technique in a water tank. Two 0.5" diameter transducers were aligned on either side of a Lexan™ sample. Lexan™ was chosen for this experiment because it is a tissue-mimicking medium that has well-known ultrasonic indices. Data acquired as part of the present study was supplemented by similar data previously acquired by Amber Nelson Groopman, a former member of our laboratory. One piezoelectric transducer emitted a 2.25MHz signal with a focal length of 55mm, while the other piezoelectric transducer acted as the receiver.

The receiving transducer was attached to the receiver port of a Panametrics 5800 pulser/receiver, whose output was sent to a model 5052B Tektronix digitizing oscilloscope, permitting storage for subsequent off-line analysis. For each measurement, data was acquired from a flat and parallel slab of Lexan™. The Lexan™ slab was initially 30mm in length and was systematically shortened in 2mm steps down to a thickness of 10mm. Signals from a water-only reference path were compared to signals from sample paths for each Lexan™ thickness.

METHODS OF DATA ANALYSIS

To determine the speed of sound of the Lexan™ samples, the Sollish method was employed in which a single transducer is used to both transmit the signal and collect the echoes received. The transducer was aligned perpendicular to the face of a Lexan™ sample with a steel reflector plate placed on the opposite side the sample. Reflections of the signal from the front wall and back wall of the sample, as well as signals reflected by the steel reflector after passing through the Lexan™ sample were collected. By finding the time corresponding to the maximum value of the Hilbert transform for each of these time-domain signals, one can calculate the sample thickness and speed of sound of a sample:

$$d = \frac{c_w}{2(t_{ref} - t_{samp} + t_{BW} - t_{FW})}$$

$$c_{sample} = \frac{c_w\left(1 + t_{ref} - t_{samp}\right)}{t_{BW} - t_{FW}}$$

The apparent attenuation coefficient was determined through a technique known as log-spectral subtraction. Reference path and sample path time domain signals that were captured by the oscilloscope and stored for off-line procession were Fourier transformed to yield their frequency domain equivalents. We model the signal propagation through the sample as a one-dimensional wave

$$A = A_0 e^{-\alpha x} e^{i(\omega t - kx)}$$

where A is the amplitude, and k is the wave number. The transfer function, H(ω), relates the input signal expressed in the frequency domain to the output signal that has traveled through the sample expressed in the frequency domain. The transfer function can be expressed in terms of the attenuation coefficient, α, phase velocity, c_{phase}, sample thickness, d, and the angular frequency, ω, which is defined as $2\pi f$, where f is the frequency,

$$H(\omega, d) = e^{-a(\omega)d} e^{-id\omega/c_{phase}}$$

With the log spectral subtraction method, the signal loss due to the propagation of the signal through a sample is

$$Signal\ Loss = Power_{ref}(\omega) - Power_{samp}(\omega)$$

The power spectra for the signal path, $Power_{samp}(\omega)$, and the reference path, $Power_{ref}(\omega)$, are proportional to the square of the corresponding frequency domain signals. The signal loss is defined by the difference on a logarithmic scale (that is, the ratio) of the sample and the reference power spectra.

At the front and rear boundaries of the sample, some power is transmitted and some is reflected. The total power loss at the boundaries, T(ω), is determined by expression

$$T(\omega) = 10\log(T^I{}_{h\to s} + T^I{}_{s\to h})$$

where $T^I{}_{h\to s}$ and $T^I{}_{s\to h}$ are the intensity transmission coefficients from host medium to sample and sample to host medium, respectively. The intensity transmission coefficients are related to a complex impedance of the material, $\tilde{Z} = \frac{\rho\omega}{k - i\alpha}$. The complex value $\tilde{Z}$ can often be adequately approximated by $\tilde{Z} = \frac{\rho\omega}{k - i\alpha} \approx \rho c_{sample}$ provided that α/κ is sufficiently small.

The relationship between the transmission coefficient and the impedances of the sample and reference media is

$$T^I{}_{1\to 2} = \frac{4\left|\tilde{Z}_1 \cdot \tilde{Z}_2\right|}{\left|\tilde{Z}_1 + \tilde{Z}_2\right|^2}$$

where $\tilde{Z}_1$ and $\tilde{Z}_2$ represent the impedances of the sample and host mediums.

The attenuation coefficient in units of dB/unit length can be determined as

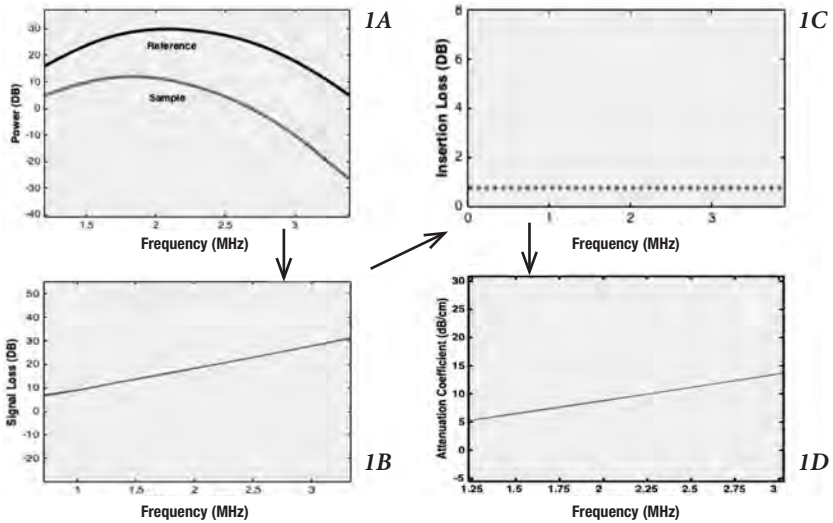
$$\alpha(\omega) = \frac{Power_{ref}(\omega) - Power_{samp}(\omega) - T(\omega)}{d}$$

Experimental studies on Lexan™ and a wide range of other plastics indicated that the attenuation rises approximately linearly with frequency in the range of frequencies employed in this study. Consequently, it is common to characterize the attenuation

properties by reporting the slope of a least squared fit line to the attenuation coefficient as a function of frequency. That "slope of attenuation" value is often expressed in the form

$$\alpha = \beta f$$

In the field of bone sonometry, the "slope of attenuation" β is termed "normalized Broadband Attenuation" and abbreviated nBUA.



Figures 1A, B, C and D
Summary of obtaining Attenuation coefficient from Reference and Sample Power Spectra.

SIMULATION

Previous work conducted by Dr. Mami Matsukawa's group at Doshisha University in Kyoto, Japan introduced a fruitful approach for evaluating the strengths and limitations of methods to deal with the complexities that result from the presence of overlapping fast and slow ultrasonic waves in cancellous bone (Nagatani et al., 2008). In that work, a sample of cancellous bone was systematically shortened, with through-transmission ultrasonic measurements made at each sample thickness. For the longer lengths, the fast and slow wave modes were sufficiently separated in time such that time-gating could be reliably employed to separate the fast and slow waves, with each mode subsequently analyzed using log spectral subtraction as described above. For intermediate and short thicknesses, conventional time-gating was not feasible. However, a technique introduced earlier by our laboratory making use of Bayesian probability theory had been shown to be capable of separately processing the fast and slow waves in other bone samples. Professor Matsukawa shared the time domain signals captured earlier at her laboratory for those systematically shortened specimens with our laboratory. Amber Nelson Groopman and others from our laboratory applied those Bayesian methods to the Matsukawa lab data.

The results of that analysis were highly encouraging because it was shown that fast and slow waves could be well separated by the Bayesian approach, yielding values for the attenuation properties, phase velocity, and surface losses for each thickness. However, the results showed a small systematic variation of the attenuation properties as a function of sample thickness. After the slow and fast waves were separated using Bayesian analysis techniques, the apparent attenuation coefficient still decreased as a function of sample thickness. Amber Nelson Groopman of our lab demonstrated that this dependence could be replicated using tissue mimicking Lexan™ samples, as shown in *Figure 2* (Groopman, Amber Nelson, 2004).

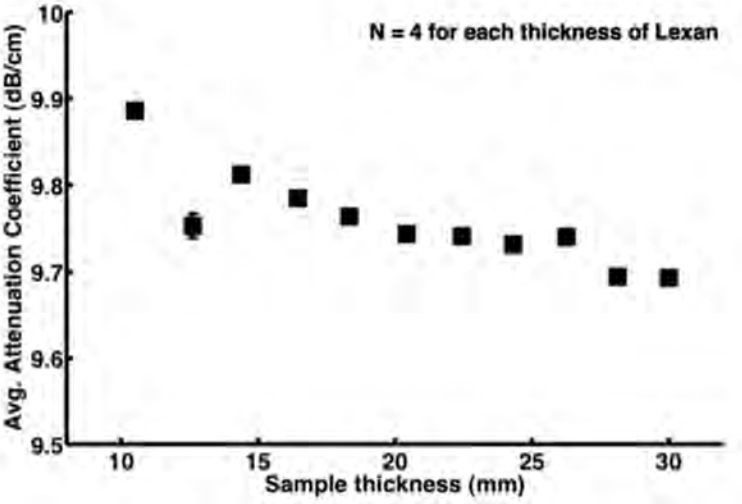


Figure 2
Experimental data demonstrating the unexpected sample thickness dependence of the attenuation coefficient from Amber Groopman.

To determine the scope of this sample thickness dependence on the apparent attenuation, Amber Groopman's experimental work on Lexan™ was simulated using the Virtual Tank software package in the present study. Among other features, Virtual Tank permits visualization of the signal in an azimuthal plane. In *Figure 3*, the three panels on the right show the real part, imaginary part, and magnitude of the signal, respectively.

By placing the transverse plane at twice the focal distance of the transmitting transducer, the right three panels illustrate the amplitude of the signal as it appears on the face of the receiving transducer.

The values for all points on the transverse planes can then be exported as a table of values that represent the amplitude of the signal at each point on the receiving transducer. The local phase of the signal at each point on the receiving aperture is determined by the inverse tangent of the ratio of the imaginary to the real components. For this simulation, the resolution of the receiving transducer was set such that the face could be visualized as a 256x256 table of values.

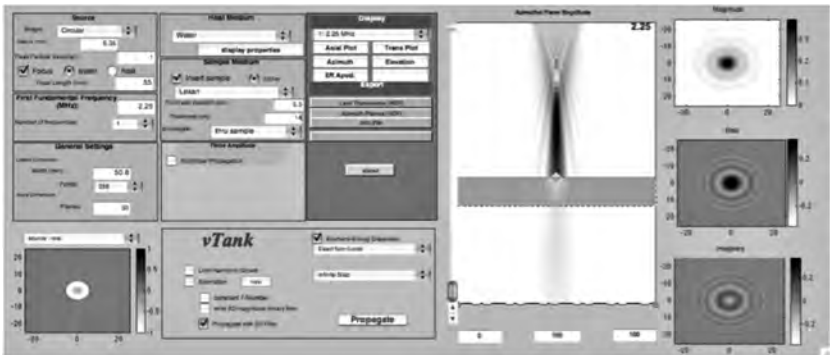


Figure 3
The interface of Virtual Tank

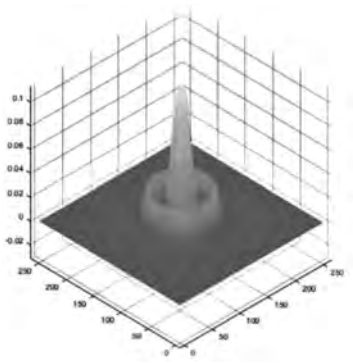


Figure 4A
Real part of the signal at the face of a 1" receiving transducer

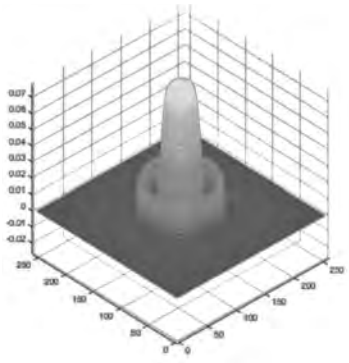


Figure 4B
Imaginary part of the signal at the face of a 1" receiving transducer

The receiving aperture was set to be a square region with 2" on a side. From the stored numerical values, the results that would be obtained with a receiving transducer of any radius up to 2" can be obtained by appropriate masking. From these real and imaginary stored values, the attenuation coefficient can be determined in a phase sensitive manner, yielding results that should be identical to those obtained with the piezoelectric receiving transducers used in the experiment.

The results of the simulation are summarized in *Figures 5* and *6* on the next page. These results correspond to the use of a 12.7mm diameter, 55mm focal length, 2.25MHz center frequency receiving transducer, identical to the transducer used by Groopman.

As shown in *Figure 5*, the agreement between the simulated results and the experimental results is good. The numerical values obtained with simulation are slightly larger (on average approximately 3.5%) than those observed experimentally, perhaps because the value for the slope of attenuation (β) employed in the simulation might be slightly larger than that in the samples studied by Amber Groopman. In *Figure 6*, we show the results

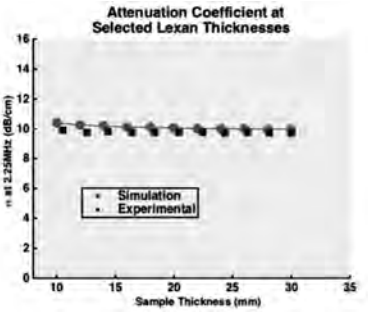


Figure 5
Comparison of experimental data to simulation.

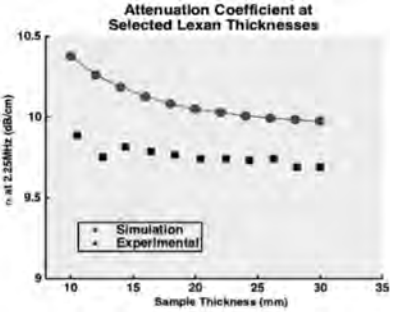


Figure 6
Comparison of experimental data to simulation on an expanded vertical scale.

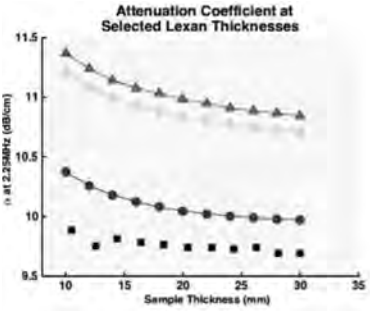


Figure 7
Comparison of attenuation coefficient values obtained from ½" (●), ¼" (◆) and ⅛" (▲) phase sensitive receiving transducers.

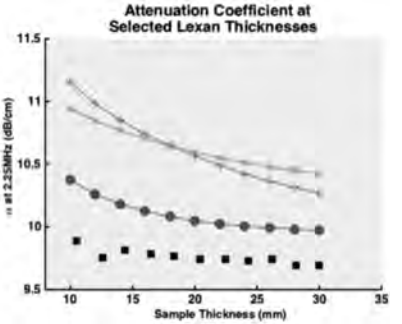


Figure 8
Comparison of attenuation coefficient values obtained from ½" (●), 1" (+) and 2" (×) phase sensitive receiving transducers

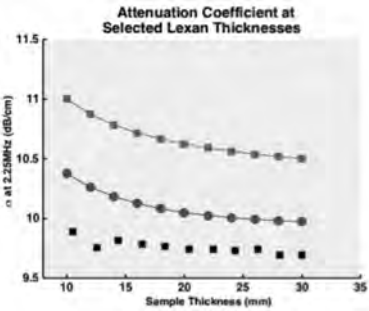


Figure 9
Comparison of experimental data with phase sensitive (●) and phase insensitive (top line ■) simulations

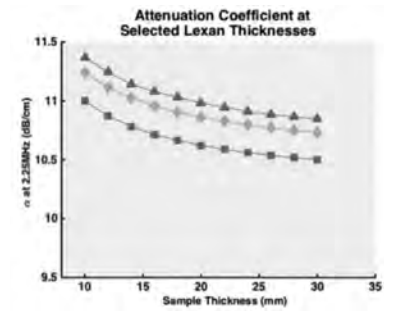


Figure 10
Comparison of attenuation coefficient values obtained from ½" (■), ¼" (◆) and ⅛" (▲) phase insensitive receiving transducers.

with an expanded vertical scale. The data from the simulation follow a trend similar to that observed in the experimental studies by Groopman in that both show an unexpected dependence on sample thickness for a property that should be inherent to the medium and thus independent of the thickness of the sample. In addition, the simulated data differs most from the experimental data at small sample thicknesses. This disagreement may arise in part because the error associated with experimental measurements at small sample thicknesses is significantly larger than that at large sample thicknesses.

Additional simulations were conducted by choosing a range of diameters for the aperture of the receiving transducer. *Figure 7* presents the results for ½", ¼", and ⅛" transducers are presented. The results suggest that smaller receiving apertures can result in errors arising because some of the received signal is missing the receiving aperture, thus producing an overestimate of the attenuation coefficient. Larger diameters of 1"and 2" are considered in *Figure 8*. The resulting overestimate of the attenuation coefficient might be associated with an increase in signal loss resulting from phase cancellation at the face of the receiving aperture. Such losses should increase with increasing aperture, as the simulations in *Figure 8* indicate. In spite of the changes resulting from the use of different receiving apertures, the unexpected trend of slightly decreasing values of the attenuation coefficient as a function of increased sample thickness remains.

In addition to considering phase sensitive piezoelectric receivers, phase insensitive receivers were also considered. This was done in part to determine if removing the effects of phase cancellation at the face of the receiving aperture could eliminate the unexpected sample-thickness dependence of α. Previous work from our laboratory demonstrated that phase insensitive receivers yield more reliable results than phase sensitive (piezoelectric) receivers because the effects of phase cancellation at the face of the receiving aperture are absent. In previous experimental studies conducted in our laboratory, phase insensitive detection was achieved with the use of acoustoelectric transducers made from single crystals of cadmium sulfide (Busse, L. and Miller, J. G., 1981a, 1981b). The results of this phase insensitive analysis are summarized in *Figures 9*, *10*, and *11*.

In *Figure 9*, experimental results obtained with a ½" diameter phase sensitive piezoelectric receiver are compared with simulations for a ½" diameter phase sensitive and ½" diameter phase insensitive receiver. The same unexpectedly small, but systematic decrease with sample thickness is seen for all three results. The fact that the phase insensitive values exceed those obtained with phase insensitive detection will require further investigation.

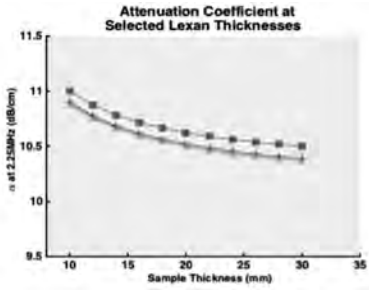


Figure 11
Comparison of attenuation coefficient values obtained from ½" (top line ■), 1" (+) and 2" (×) phase insensitive receiving transducers.

In *Figure 10*, simulations for phase insensitive receivers of ½", ¼", and ⅛" diameter are compared. As anticipated, results for the apparent attenuation coefficient obtained with smaller diameter receivers appear to be larger than those for the ½" receiver, again presumably because a portion of the signal is being missed. In *Figure 11*, results for the apparent attenuation coefficient obtained with larger diameter receivers appear to be slightly smaller than those for the ½" receiver, suggesting that even more of the signal is being captured by the use of large diameter receivers than by the ½" receiver.

The results of the phase sensitive and phase insensitive simulations for a ½" receiving aperture, as well as Groopman's results, are summarized in the following table:

Sample Thickness (mm)	Groopman's Measured Attenuation Coefficient (dB/cm)	Phase Sensitive Simulation Attenuation Coefficient (dB/cm)	Phase Insensitive Simulation Attenuation Coefficient (dB/cm)
10	9.89	10.38	11.00
12	9.75	10.26	10.87
14	9.81	10.18	10.78
16	9.78	10.13	10.72
18	9.76	10.08	10.67
20	9.74	10.05	10.62
22	9.74	10.03	10.59
24	9.73	10.01	10.56
26	9.74	9.99	10.54
28	9.69	9.98	10.52
30	9.69	9.97	10.50

Figure 12
Data table comparing experimental data to simulations obtained with phase sensitive and phase insensitive ½" diameter receiving apertures.

DISCUSSION AND CONCLUSIONS

These studies represent the first successful simulation of the experimental results obtained and reported previously by our laboratory. Good agreement between the simulations and the experimental results was obtained, with agreement to 3.5% for the attenuation coefficient. Furthermore, the unexpected small but systematic variation of the attenuation coefficient with sample thickness that had previously been reported in our experimental data was found in the corresponding simulations. Although only phase sensitive data was available from experimental work, simulations for both phase sensitive and phase insensitive receiving transducers were investigated. Results of simulations for a range of diameters of a phase insensitive receiving transducer were consistent with expectations in that the apparent attenuation coefficient was systematically smaller as a function of increasing diameter. We do not as yet have an explanation for why the apparent attenuation coefficient obtained with phase insensitive detection was not smaller than that obtained with phase sensitive detection.

The observation in simulations of the unexpected systematic dependence of the apparent attenuation coefficient provides strong evidence that that sample-thickness dependence is not an artifact of either the experimental data acquisition system or of the methods of data reduction that had been employed previously. Data reduction in the current investigation employed entirely different methods than those used in the experimental studies. Investigations of the physics underlying the observed sample-thickness dependence are underway.

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Summaries of Student Work

Toward a Better Understanding of...

Kidney Outcomes in the Very Low Birth Weight Population

Prachi Aggarwal

Mentor: T. Keefe Davis

In critically ill pediatric and adult patients, acute kidney injury (AKI) has been associated with increased morbidity and mortality. AKI is more prevalent in the critically ill population. Therefore, the very low birth weight (VLBW) neonate (<1500g) is at risk for AKI due to critical illness during infancy. In addition, the risk for AKI may be further potentiated by kidney under development due to incomplete nephrogenesis leading to low nephron endowment. In this study we sought to determine the incidence, clinical factors associated with, and outcomes of AKI in a large cohort of VLBW infants.

488 neonates weighing ≤ 1500g and cared for at St. Louis Children's Hospital's Neonatal Intensive Care Unit were enrolled in the study. Comprehensive clinical data was recorded on clinical research forms developed and stored in REDCap. AKI was defined as an increase in serum creatinine of > 0.3 mg/dL from a previous value.

In patients for whom AKI could be determined, AKI occurred in 18.3% of the cohort. Based upon gender, 13.5% of females had AKI and 22.3% of males had AKI (P=0.06). Lung disease was a risk factor for AKI, 30.7% of subjects who required high frequency ventilation had AKI as compared to only 5.2% not requiring high frequency ventilation (P<0.001). Additionally, 35.7% of patients with necrotizing enterocolitis (NEC) had AKI compared to only 15.1% of patients who did not. Overall, there was a significant difference in survival between the two groups, 36% of patients who developed AKI expired versus 8.5% of patients who did not (P<0.001).

We conclude that AKI in the VLBW population is prevalent, multifactorial, and associated with a high mortality rate. Future directions include analysis of antibiotic exposure, blood pressure control, and ultrasound imaging in relationship to AKI and chronic kidney disease in this cohort.

Exploring the Role of FGF20 in the Gustatory System of Mice

Sakirat O. Akadri

Mentor: David Ornitz

FGF20, a member of the Fibroblast Growth Factor (FGF) family of signaling proteins, has been shown to play important roles in the development of neurosensory systems, including the auditory and olfactory systems. *Fgf20* is also expressed in the embryonic tongue surface, suggesting a role in the gustatory system. We hypothesized that *Fgf20* may have a role in the development and organization of taste buds, the sensory cells of the gustatory system. In order to determine when and where *Fgf20* is expressed in the tongue, we used genetically modified allele of Fgf20 that replaces the FGF20 coding region with that of Green Fluorescent Protein (GFP). As a surrogate for FGF20, GFP expression was examined in the tongue at embryonic day (E) 11.5, E12.5, E13.5, E18.5 and postnatal day (P) 0, which encompasses the significant stages of taste bud development. Analysis showed that taste bud and taste-bud epithelial progenitors in the anterior-most portion of the tongue expressed *Fgf20* during embryonic stages, but not postnatally. To determine whether FGF20 is involved in taste bud development, we compared P0 tongues from mice heterozygous for an *Fgf20*-null allele ($Fgf20^{+/-}$) and from homozygous null mice ($Fgf20^{-/-}$). We found no significant difference between $Fgf20^{+/-}$ and $Fgf20^{-/-}$ tongues in terms of width of taste buds, the number of cells in taste buds, and the width of the fungiform papillae which surround taste buds. We believe that FGF20 may play a very subtle role in taste bud development, or that another FGF may act redundantly with FGF20 (another FGF performs the same function as FGF20). Future experiments will focus on determining whether FGF receptors are necessary for proper taste bud development.

Fabrication of an Electronic Immersive Coater for Layer-by-Layer Assembly of 3D Printing Nanocomposites

Hari Anandarajah

Mentor: Julio M. D'Arcy

An Electronic Immersive Coater (EIC) was fabricated for Layer-by-Layer (LbL) assembly of thin films of nanostructural materials on Polylactic Acid (PLA) pellets. Inspiration for the design of this instrument originated from existing 3D printers and a 4-point probe station designed by a lab member, Mr. Yang Lu. The instrument is significantly less expensive than commercial alternatives, while still maintaining a durable structure due to its metal frame, and is powered by an open-source Arduino board. The user interface, Repetier Host, is a program commonly used for 3D printing. Given that PLA is a ubiquitous material for 3D printing, this project has the potential for facile development of advanced PLA composites for 3D printing. Here we develop LbL thin film coatings of polyaniline (PANi) nanofibers, this nanostructured conjugated polymer is an ideal candidate for energy storage applications due to its and other capacitive and pseudo capacitive properties. Conjugated semiconducting polymers can be doped and dedoped thereby inducing positive and negative charges on the molecular structure of a polymer. The flow process for engineering LbL coatings is based on alternating positive and negative electrostatic charged polyaniline layers, and results in exquisite control at the molecular scale for deposition of films with controllable thickness. Our Electronic Immersive Coater will provide homogenously coated PANi-coated PLA pellets that can be crushed and extruded as a filament for subsequent 3D printing applications. Future research will optimize these positive and negative charged electrolyte solutions for LbL coatings, thickness of films, and nanoscale morphology in order to engineer emergent properties in nanocomposites for 3D printing applications.

Forelimb Strength Meter — A Device to Measure Individual Forelimb Strength in Rats

Peter C. Andres

Mentor: Spencer Lake

The elbow is highly susceptible to post traumatic joint contracture (PTJC) and treating elbow contracture is a challenging clinical problem. We previously established an animal model in the rat elbow that allows us to study the development of PTJC in the elbow and explore rehabilitation methods. The objective of this study was to create a device that would measure individual forelimb strength in rats. By comparing control limbs to injured limbs we will be able to evaluate the magnitude of functional recovery in the injured animals. These data will be valuable in understanding the effectiveness of various rehabilitation strategies. This project consisted of designing and constructing a forelimb strength device, developing an experimental protocol for device use, testing and evaluating the device design using control animals, animal handling and data analysis.

Doping BiI_3: A Computational Study of Electronic Properties

Yvette Anguiano

Mentor: Rohan Mishra

Bismuth tri-iodide (BiI_3) has recently been proposed as a photovoltaic material. However, in order to improve the efficiency of BiI_3 based photovoltaics, suitable dopants need to be identified. We have used density functional theory calculations to study the electronic properties of BiI_3 with substituent dopants at either the bismuth or the iodine site. Based on the density of states calculations, we predict, Ti and Zr are potential *n*-type dopants substituting Bi with contributions to the conduction band minimum and Ni is a potential *p*-type candidate with contributions to the valence band maximum. For substitution at the iodine site, we examined Sb and Te, and they were found to be suitable *p*-type dopants.

When the Purging Process Goes Wrong: Investigating the Weed-Out Paradigm in Twenty-First Century Higher Education

Chase Antonacci

Mentor: Eileen G'Sell

In an effort to understand the pervasive nature of 'weed-out' STEM courses in higher education, this research explores not only the historical context and impacts of such an approach to teaching but also the potential ways to mitigate harms from within the current pedagogical system. Until recently, little research exploring the conventional concept of weed-out education had been published; scholars now indicate that American colleges and universities operate under a veil of corporate influence that fosters an educational paradigm built on inequality where certain demographics—particularly women and underrepresented minorities—are fundamentally predisposed to undue failure in large, introductory courses. Due to the historical difference in socialization that persists in the traditional academic setting, these students often lack the support and resources needed to be successful. This continuing complication in academia that fuels wider socioeconomic disparity arguably stems from the first semester weed-out class where students from elite high schools often succeed and persist towards a STEM degree while others with less premium college preparation quickly change majors. Though abandoning the large, lecture-style classroom model has been successful in eradicating the weed-out effect, it remains impractical for many larger institutions. Now, new programs such as Peer Led Team Learning and Process Oriented Guided Inquiry Learning appear to be effective supplements to large introductory courses. Such programs divide students into small groups and assign each a role in the learning and communication process, thereby allowing him/her to foster confidence engaging with the material and ultimately overcome the pervasive weed-out effect.

The Effects of Germline Sequestration on Multicellularity

Odion Asikhia

Mentors: David Queller and Joan Strassman

There have been many transitions in the history of evolution. For example, the transition of prokaryotes to eukaryotes, asexual to sexual populations, primate to human societies and so forth. We are specifically interested in the transition from unicellular to multicellular organisms. This transition is particularly interesting because multicellularity requires an immense amount of cellular cooperation. Our previous research focused on how relatively simple mechanisms such as growth and dispersal affected the evolution of multicellularity. In this study, we want to investigate the importance of germline sequestration(differentiation). A germline is the cellular lineage of an organism. Germ cells, distinct from other cells, pass their genetic material to following generations. The segregation of germline cells occurs early in development. Previous research suggests the presence of germline cells play a role in the transition to multicellularity. The goal of our experiment is to manipulate the germline cells and observe how they influence the evolution of multicellularity. We will create multicellular pseudo-organisms using Dictyostelium *discoideum. D. discoideum* is a eukaryote that transitions from a unicellular amoeba to a multicellular slug in order to form a fruiting body when starved. A fruiting body consists of an upright stalk (composed of dead cells) with a mass of surviving cells at the apex. A key characteristic of multicellularity is cooperation. We will add a mixture of non-fruiting cheaters to a mixture of wild-types. These non-fruiting cheaters are unable to form a stalk, thus preferentially reach the apex. We will manipulate the timing and location of our collection of germline cells. These cells will be passed from generation to generation and we will observe the effect on multicellularity. We theorize that the presence of cheaters, which are non-cooperative, should break down the multicellular system, but some types of germline sequestration may prevent this from occurring.

Cerebrospinal Fluid Parameters Alone Do Not Inform Infection Management in Posthemorrhagic Hydrocephalus

Brandon Baksh

Mentor: David Limbrick

Preterm posthemorrhagic hydrocephalus (PHH) is often managed with ventricular reservoir or shunt placement, which carry infection rates as high as 10%, necessitating long-term antibiotics. In patients who undergo a septic workup, cerebrospinal fluid (CSF) samples may show pleocytosis, precipitating antibiotic treatment despite the lack of positive cultures. In this study, we analyze the CSF and complete blood count (CBC) profile from the same day in subjects with culture positive (CP) meningitis compared to culture-negative CSF across eight groups, including patients with PHH.

A retrospective analysis was performed on 200 subjects — 30 controls, 9 central line associated blood stream infection (CLABSI), 38 intraventricular hemorrhage (IVH) grade I or II, 9 IVH grade III or IV, 36 culture negative PHH, 43 CP viral meningitis (VM), 25 CP bacterial meningitis (BM), and 10 CP/BM with PHH. Subjects on antibiotics or ≤ 7 days post antibiotics were separated into another group. CSF samples were obtained by lumbar puncture, reservoir tap, or operating room procurement. Statistical significance was based on one-way analysis of variance (ANOVA) among all groups and Tukey's multiple comparison test between groups ($p < 0.05$).

Significant results include: CSF total protein was higher in PHH compared to other groups, including VM. Macrophages in IVH III/IV were higher compared to other groups. White blood cells (WBC) were higher in CLABSI than other groups. VM WBC was lower than PHH. Hemoglobin was lower in PHH than VM and IVH I/II. Hemoglobin in PHH with BM was lower than controls. Hematocrit in PHH was lower compared to other groups. Platelets in CLABSI were lower compared to VM.

We therefore conclude that CSF profile alone should not be used to dictate antibiotic initiation. CSF and blood culture results in combination with CSF and CBC profiles may be a better guide for infection management.

Studying Implicit Social Exclusion Using Pupillometric Analysis

Jared Balbona

Mentor: Lori Markson

The desire to avoid social exclusion is a fundamental human trait. Previous research suggests people show physiological reactions, such as an increase in pupil dilation, when they are explicitly rejected by others compared to when they are accepted. However, to our knowledge, no research has investigated pupil dilation in response to more subtle and implicit forms of social exclusion. To address this gap, we obtained pupil dilation values from 11 participants using a *Cyberball* paradigm, in which participants were either included or indirectly excluded in the course of playing online ball games. Participants were told before each game that they would be playing with either human players (i.e., other undergraduate participants in the study) or pre-programmed computer players; in reality, all players were computerized. We then calculated the difference in maximum pupil dilation on each trial by subtracting the maximum pupil size collected before the game from the maximum pupil size collected after the game, and found that the difference in pupil dilation with human players was significantly larger after exclusion trials (M = 63.96, SD = 107.01) than after inclusion trials (M = -35.08, SD = 123.73), $t(10) = 2.947$, $p = .015$. However, difference in pupil dilation with computer players did not differ between exclusion (M = -10.04, SD = 116.04) and inclusion trials (M = -6.93, SD = 114.77), $t(9) = -.087$, $p = .933$. Consistent with the extant literature, participants also reported lower self-ratings of mood, control, belonging, existence, and self-esteem following exclusive games compared to inclusive games. These findings suggest that pupillometry is a sensitive and useful measure for investigating responses to social exclusion. We plan to further analyze the data obtained from this pilot study, and to continue testing participants.

Toll-Like Receptor 4 Is Critical in the Development of Resection-Associated Steatosis

James Bao

Mentor: Brad Warner

Forty to sixty percent of children with short bowel syndrome (SBS) experience intestinal failure associated liver disease (IFALD), a major cause of mortality in patients who survive long term with SBS. Steatosis is a key component of the hepatic dysfunction and persists even after weaning from parenteral nutrition. We recently demonstrated accelerated steatosis after 50% small bowel resection (SBR) in mice when compared with unoperated mice under identical conditions. IFALD has been associated with the massive inflammatory cytokine responses seen during recurrent episodes of sepsis in SBS patients. Toll–like receptor 4 (TLR4) is a key regulator of the inflammatory cytokine response seen in these episodes. Further, TLR4 signaling outside of sepsis has been implicated in the development of steatosis in other disease processes such as non-alcoholic fatty liver disease. The purpose of this study was to determine whether TLR4 signaling is critical to the development of resection associated hepatic steatosis.

Male C57BL6 (control) and TLR4-knockout (KO) mice underwent 50% proximal SBR. Liver sections were analyzed to obtain the percent lipid content and Ileal sections were assessed for morphological adaptation. Intestinal TLR4 mRNA expression was measured at 7 days and 10 weeks. Compared to controls, TLR4 KO mice demonstrated similar weight gain and morphological adaptation after SBR. Hepatic steatosis was decreased 32-fold in the absence of TLR4. Intestinal TLR4 mRNA expression was significantly elevated 7 days after SBR. We also found that TLR4 expression in the intestine is 20-fold higher in whole bowel compared with isolated enterocytes.

TLR4 signaling is not required for functional or morphological intestinal adaptation after massive small bowel resection. Conversely, it is critical in the development of resection-associated steatosis. This combination of effects makes TLR4 signaling a potential target for preventing resection-associated hepatic dysfunction without adversely affecting adaptation and thus weaning from parenteral nutrition.

Exposure to Bacteria and Bacteria Carriage in the Social Amoeba

Anthony Bartley

Mentor: Debra Brock

Primitive forms of farming have been found in various organisms such as ants and termites (both of which participate in mutualism with their fungi). Recently, farming practices have also been discovered in some clones of the social amoeba *Dictyostelium* discoideum. These clones, dubbed "farmers", carry the inedible bacteria *Burkholderia* throughout the social stage. The presence of *Burkholderia* allows the farmers to carry edible bacteria that can be cultivated by *D. discoideum* in environments where food is scarce. Previous studies have shown that when food bacteria are in abundance non-farmers will produce more spores than farmers, indicating that bacterial density may play a role in *D. discoideum's* interactions with *Burkholderia.* To test whether bacterial density or *Burkholderia* are the sole determinant of *D. discoideum's* bacterial carriage, farmer clones with and without *Burkholderia* were grown at different bacterial densities. Results showed that the ability to carry bacteria was unaffected by the density of the environment, and that clones without *Burkholderia* were unable to carry bacteria at all.

A Micro and Macro Analysis of Israel's Organ Donation System

Ronny Bass, Grace Dearing, Sara Miller, and Nathan Ross

Mentor: Charlie Kurth

The objective of this study is to better understand Israel's organ donation system following the implementation of a prioritization law by the Organ Transplantation Act of 2008. The primary data collection method includes an anonymous survey, distributed in September 2016, of just over 425 Jewish-Israelis and 75 Arab-Israelis. On a micro level, this study investigates factors that impact willingness to donate organs, considering whether the individual is Arab or Israeli. On a macro level, this study investigates factors that impact support for Israel's organ donation system, considering Israel's population as a whole. This study found education, age, and religion to be significant variables in both the micro and macro analyses. The findings suggest interventions that organ donation advocates and policymakers might implement in Israel and abroad to help reduce the organ shortage.

The *in vitro* Biosynthesis of Obafluorin β-lactone Analogs for Use in a Biological System

Catherine Beamish

Mentor: Tim Wencewicz

Since the discovery of penicillin in the 1940s, microbial resistance to antibiotics has been a widespread issue in the medical community. This problem has been exacerbated by the overuse of antibiotics, exploitation of the same molecular targets, and the natural ability of microbes to defend themselves when put under evolutionary pressure. In order to combat the rise of microbial resistance, researchers are constantly searching for new molecular scaffolds to use against pathogens and new biological targets to pursue. The β-lactam containing antibiotics make up over 50% of the antibiotic prescriptions worldwide. Obafluorin (obi) is a molecule with a novel antibiotic scaffold containing a β-lactone ring that is similar to the β-lactam. This new molecule is hypothesized to disrupt quorum sensing between bacteria. The mechanism of action is bacteriostatic, not bactericidal like most other antibiotics. While seemingly counterintuitive, halting the growth of a pathogen and allowing the infected organism's innate immune response to clear the bacteria is gaining ground in the research community because bacteriostatic antibiotics have shown lower incidences of resistance. The lab has recently fully characterized the biosynthetic gene cluster of obi in the producer organism *Psuedomonas fluorescens* and has performed an *in vitro* reconstitution of the biosynthetic enzymes. This project explored the possible unnatural substrates that were commercially available and relatively inexpensive, by feeding them through enzymes in the gene cluster. The substrates that had high product concentration were fed through to make obi analogs, which were quantified by LCMS to determine product content. These obi analogs synthesized as part of this project will help to elucidate the natural mechanism of β-lactone formation and the viability of targeting the quorum sensing abilities of bacteria as an antibiotic target.

Trehalose as a mTOR Independent Inducer of Autophagy in a Mouse Model of Tuberous Sclerosis Complex

Brennan Beeler

Mentor: Michael Wong

Tuberous sclerosis complex (TSC) is a genetic condition resulting from mutation in the *TSC1* or *TSC2* genes. TSC1 and TSC2 normally form a complex which downregulates the mammalian target of rapamycin (mTOR) pathway, a regulator of cellular proliferation, but in their absence, mTOR hyperactivation occurs. This causes the development of benign tumors throughout multiple organ systems, leading to systemic problems, the most concerning of which are neurological symptoms like seizures and autism spectrum disorder.

A major downstream target of mTOR is autophagy, a catabolic process which breaks down cellular waste, and whose dysregulation may contribute to TSC pathology. As mTOR normally suppresses autophagy, in TSC autophagy may be excessively inhibited. Rapamycin (a direct mTOR inhibitor) can induce autophagy and has demonstrated beneficial effects in TSC mouse models, however, the mTOR pathway regulates many cellular processes, making side effects of rapamycin numerous. This study was designed to: 1) determine whether autophagy is dysregulated in a mouse model of TSC, and 2) test the disaccharide trehalose as a potential mTOR independent regulator of autophagy. Evidence has shown trehalose may have the capacity to increase autophagy levels, which could help reduce symptoms of TSC.

To investigate this hypothesis, *Tsc1*^{GFAP} KO mice were treated with 3% trehalose, and autophagy activity was assessed using western blotting of autophagy pathway markers. These markers were compared to rapamycin treated mice, vehicle-treated wild-type, and KO control mice. The results demonstrated that autophagy was inhibited in KO mice compared to control mice, and rapamycin was effective in increasing autophagy levels, however, trehalose did not show a significant shift in autophagy levels relative to controls. Future work will assess whether this negative result with trehalose was due to a mechanistic compensation in the *Tsc1*^{GFAP} KO mouse model, insufficient bioavailability, or some other factor.

Development of an Algorithm to Calculate Torsional Angles of Polypeptide Structures

Krish Tejas Bharat

Mentor: Rohit Pappu

Dihedral angles ϕ (phi) and ψ (psi) are important structural factors that determine local conformations of peptides. As a part of an effort to assess ϕ-ψ angle distributions within amino acid motifs known as short linear motifs (SLiMs) found in intrinsically disordered regions (IDRs) that are implicated in diseases such as Alzheimer's disease and Mad Cow disease, this study reports the development of a tool to calculate torsional angles of given polypeptide structures. From a trajectory file generated by a molecular simulation software, the algorithm generates ϕ-ψ angle distributions at different time points along the length of a simulation. To illustrate its application, we used OpenMM, a molecular simulation package, to run molecular dynamics simulations on various dipeptide chains, and parsed dihedral angles to obtain ϕ-ψ distributions for different systems.

The Role of Notch Signaling on Heart Rate and Atrial Conduction Velocity

Somya Bhatnagar

Mentor: Stacey Rentschler

Heart disease is the leading cause of death worldwide and can result in arrhythmias, or dysregulation in the electrical activation of the heart. Sick Sinus Syndrome (SSS) is characterized by sinus bradycardia (slowed heart rate, HR), slowed conduction through atrial myocardium, and can predispose to the development of atrial fibrillation. A developmental signaling pathway, Notch, regulates cellular identity through differentiation of cardiomyocytes (CMs) into cardiac conduction system-like cells. Previous data show that Notch electrically remodels the right atrium, causing slowed conduction velocity (CV) and hallmarks of SSS including sinus pauses, sinus bradycardia and a predisposition to atrial fibrillation. However, the molecular mechanisms behind these phenotypes are not known. We hypothesized that Notch activation produces slowed CV through downregulation of major cardiac voltage-gated sodium channel ($Na_V1.5$) and atrial gap junction (Connexin40, Cx40). A "Tet-On" doxycycline-activated system using transgenic adult mice was used to activate Notch specifically in CMs. We assayed various determinants of CV, including fibrosis, cellular hypertrophy, and Na^+ channel and gap junction expression. Trichrome stain and hydroxyproline assay indicated normal levels of non-conductive fibroblasts. To determine whether Notch activation is associated with pathophysiological hypertrophy, I quantified cell area using immunohistochemistry and found no difference in Notch activated hearts when compared with controls. Furthermore, immunohistochemistry indicated no gross changes in $Na_V1.5$ or Cx40 expression within the atrial myocardium. However, localization of $Na_V1.5$ and Cx40 within the plasma membranes of CMs, as well as post-translational modifications that may result in slowed conduction velocity are yet to be analyzed. Future studies will determine whether Notch-induced slowed HR is due to autonomous changes within the pace-making sinus node (SAN) region or non-autonomous changes within the atrial myocardium. Notch will be activated specifically in the SAN of the adult mouse heart using an HCN4-creER tamoxifen-inducible system and HR will be evaluated using electrocardiograms.

Toward a Better Understanding of...

Doppler Shift Human Detection Using a Microphone Array

Michael J. Billington

Mentor: Arye Nehorai

The purpose of this project was to see if Doppler Shifting could be used to measure the real-time velocity of a person walking through a room. Some basic speakers were used to generate a sound, and a 16 microphone array was used to take in the reflected, Doppler Shifted signals. Once determined that this was feasible, the final goal was to set up a demonstration that could show the real-time velocity of a person walking within the effective radius of the speaker and microphone array over 180 degrees.

Mapping Prejudice: A Perceptual Dialectology Approach to Evaluating Language Attitudes towards South-Perceived Speech in the United States

Marie Bissell

Mentor: John Baugh

How individuals conceptualize and determine language attitude judgments is a recurring question in the field of sociolinguistics. This study provides evidence that everyday speakers of English in the United States think about and assign characteristics to speakers perceived to be from the American South in a particular, negative way. 77 undergraduate students were asked to complete a survey consisting of 12 audio samples from different regions, each of which was paired with a Likert matrix of attitudinal labels (intelligent, educated, wealthy, likeable, formal, correct) and a heat map for indicating where the participant perceived the sample's origin to be located. Statistical analyses using single sample t-tests reveal that South-perceived speech samples were rated significantly lower than average ($p = .01$) on measures of intelligence, education, wealth, and formality. A vowel variant analysis of each speech sample demonstrates that the consistently common phonetic feature among these South-perceived items is multiple instances of the Southern Vowel Shift in words such as /fav/, which reflects monophthongization, and /kiɪdz/, which reflects what is often termed the "Southern twang." On the other hand, speech samples that are not South-perceived are often interpreted as regionally ambiguous, with responses ranging from California to Chicago to New England. Even though these samples contain internal vowel variance as well, participants are less accurate at differentiating among their potential geographic origins than they are at distinguishing the South. The persistent distinctiveness of the South as a region in the consciousness of everyday Americans, as proposed by Preston, is discussed.

Mu Opioid Receptor Desensitization in Inflammatory Pain

Matthew Bredder

Mentor: Jose Moron-Concepcion

Due to the epidemic level of opioid overdose deaths in the United States, improving the treatment of chronic pain has become a pressing concern. Opioid treatments such as fentanyl and morphine activate mu opioid receptors (MORs), causing an increase in dopamine release. Long-term use of opioids, even as prescribed by a physician, can desensitize the MORs and lead to the appearance of withdrawal symptoms when the receptors are no longer stimulated. Since pain increases endogenous opioid release, we hypothesized that this increase may cause MOR desensitization and the appearance of withdrawal syndrome upon blockade of MORs, as seen in long-term opioid use. To test this hypothesis, we bilaterally inserted cannulae into the ventral tegmental area (VTA), a region containing MORs and involved in reward processing, of Sprague-Dawley and Long-Evans rats of both sexes. Complete Freund's Adjuvant (CFA) was used to induce chronic inflammatory pain. CTAP, a highly selective MOR antagonist, was injected via cannulae to induce withdrawal symptoms. Each animal experienced one of three conditions: CFA + CTAP, Saline + CTAP, or CFA + Saline. Wet dog shakes (WDS), a common sign of opioid withdrawal in rats, were measured in five-minute periods one, two, three, five, and eight hours after CTAP injection. Significant increases in WDS were observed for male Sprague-Dawley rats in the CFA+CTAP group compared to the other conditions. This increase in WDS may be explained by chronic pain causing MOR desensitization in the same manner as long term exposure to opioids. More work investigating how pain impacts opioid dependent dopamine release is necessary and may ultimately lead to improved pain treatment and decreased opioid dependence.

Higher Income Predicts Poorer Long-Term Health Outcomes in China

Ethan Brodeur, Ben Rosenkranz, and Haoshu Xu

Mentor: Phil Dybvig

Since the implementation of Deng Xiaoping's "reform and opening-up" policy in 1978, "改革开放," internal restructuring and international trade have fueled rapid economic growth and societal change in China. *Throughout history, times of large economic change have been natural times to look for health problems in a population. This study looks at whether past income predicts future health outcomes during the remarkable socioeconomic shifts generated in China since 1978.* Are the poorer members of society at greater risk for developing health problems from malnutrition, such as low BMI? Are more affluent members of society at greater risk for developing health problems from stress, overeating, or sedentary lifestyle, such as diabetes, high BMI, or hypertension?

Data from the China Health and Nutrition Survey, collected from 1989 through 2011, is used to build longitudinal binomial logistic models that test the effect of past income on various lagged health outcomes. Explained variables include current BMI, blood pressure, and diabetes, controlling for age, gender, and corresponding past health measures, with "past" defined as 1989 and "current" defined as 2011, the most recent year of the survey. The main findings indicate that higher past income implies an increased likelihood of becoming overweight, while current income does not have similar predictive power. Additionally, past income significantly *predicts diabetes* diagnoses, but not hypertension or malnutrition (proxied by low BMI). The results remain mostly robust when tested with data from different years, though potential biases from changes to the cross-sectional sample over time are investigated. Overall, past income's relationship with current health in this dataset seems to better illustrate the negative impact of Western lifestyles on wealthy Chinese than the negative impact of malnutrition on poorer Chinese.

Toward a Better Understanding of...

Catalytic Hydrogenolysis of Aryl Ether Substrates

Alex Brown

Mentor: John Bleeke

The goal of our work is to replicate the procedure for the selective catalytic hydrogenolysis of aryl ethers as determined by preliminary research done at the University of Illinois by the Hartwig lab. Upon confirming the procedure, we hope to further test its efficacy on larger aryl ether substrates, and eventually Lignin. The importance of this project would be adding further knowledge to the existing literature on this topic. The belief in the scientific community is that selectively cleaving Lignin could lead to products that can be utilized as alternative fuel sources, which would have a significant impact on future options for combating the ongoing climatic change that our planet faces. We used commercial ether substrates, homogenous Ni-catalysts, N-heterocylic Carbene (NHC) ligands, and commercial bulky bases to further investigate the procedure implemented by the Hartwig lab. Our lab's investigation of small aryl ether substrates produced inconclusive results so far in that phenol products, our target product, were rarely produced by the reaction in combination with all the starting material being used up. In other words, the reaction rarely went to completion. What we know from the results of the reactions is that Benzyl Phenyl Ether (BPE) was a more effective substrate than Diphenyl Ether (DPE) in terms of being selectively cleaved to produce phenol products. More importantly, we have reason to believe that the reaction is capable of running to completion without the use of the NHC ligands. In fact, it is very possible that the NHC ligands blocked the reactions from working as well as we had hoped. Our investigation into this possibility is ongoing. Synthesis of bulkier Ni-catalysts will likely be done for the larger ether substrates like Lignin.

Identifying Protective Genes Against Cognitive Sequelae Following West Nile Mediated Encephalitis

Jasmine Brown

Mentor: Robyn Klein

West Nile Virus (WNV) is the most common cause of epidemic viral encephalitis in the United States. More than half of patients who survive West Nile neuroinvasive Disease (WNND) exhibit chronic cognitive impairments, such as spatial learning deficits, that resulted from the disease. Little is known about the cellular and molecular mechanisms that underlie the neurocognitive sequela that follows the infection. Previously, the lab discovered that some infected wild type mice exhibited spatial learning deficits while some did not, these mice were labeled "good learners" and "poor learners". Something is naturally protecting the good learners from the spatial learning defects. The lab identified more than thirty target genes that could play a role in this protective mechanism. Because interferon gamma receptor (IFNgR) knockout mice are also protected from spatial learning defects, we used IFNgR knockout mice as a model to study the natural mechanism present in the good learners. We hypothesized that alterations in gene expression that are conserved between "good learners" and IFNgR knockout animals following WNV infection would point to a common protective mechanism. qPCR was done to compare gene expression in good versus poor learners and infected IFNgR versus wild type mice. The qPCR reactions revealed a significant decrease in the expression of Crry, a complement regulatory gene, in the infected IFNgR knockout mice hippocampi compared to wild type mice. Decreased expression of Crry was also seen in the hippocampi of WNV good learners when compared to the poor learners. Our next step is to look at gene expression at earlier time points to see if the protective mechanism works acutely or if it is a continuous process, long after the virus has cleared. Determining the details of this protective mechanism could lead to therapies for people experiencing cognitive deficits following WNV infection.

The University Features Gothic Collegiate Architecture and a Glass Ceiling: Gender Inequality, Numbers Game Logic, and Top-to-Bottom Moral Licensing in American Academia

Alisa Caccamo

Mentor: Eileen G'Sell

This research examines the glass ceiling of academia, with particular emphasis on gender inequity at elite American universities as it pertains to tenure and promotion for female faculty and administrators, respectively. Drawing from sociological research on concepts such as tokenism and moral self-licensing, interviews with female faculty at Washington University in St. Louis, and data regarding female leadership at America's top 89 colleges and universities, this work asserts that a glass ceiling does exist for women in academia, and is exacerbated by *numbers game logic and top-to-bottom moral licensing.* Numbers game logic refers to the tendency of universities to specifically hiring women to achieve quantitative gender balance. Top-to-bottom moral licensing occurs when having a female in a top leadership position can breed complacency on gender inequality in other areas of the university. This research provides an alternative framework for understanding persistent gender inequity in higher education, as it challenges common misconceptions regarding the causes, consequences and best courses of action when it comes to understanding and combating discrimination in academia.

Ocean's Deadliest: Who Is Morally Responsible for Microfiber Pollution?

Luka Cai Minglu

Mentor: Jason Gardner

Microplastic fiber pollution (MFP) is the persistence of microfibers (fibrous plastic particles less than 5mm in diameter and length) in the environment in levels sufficient to harm aquatic/marine ecosystems, primarily caused by the laundering of polyester garments. MFP is a compelling issue because it causes harm to natural habitats, animals, and human beings, harm that moral agents need to be held accountable for. I define moral responsibility as an agent's accountability for an act which they voluntarily committed/contributed to. Causal responsibility is the relationship between an agent and an outcome of the agent's act. I theorize that an agent's moral responsibility for an outcome is proportional to their causal responsibility for that outcome. An agent's causal responsibility for an outcome depends on both the directness to which the agent's act contributes to the outcome, and the degree to which the agent's behavioral change would alter the outcome. Most people might think that apparel manufacturers are most morally responsible for MFP. However, I argue that the global collective of individual launderers (GCIL) is most morally responsible for MFP. The GCIL, through the sum of individuals' laundering practices, contributes most directly to and holds the greatest potential to reduce MFP. First, the individual launderer is the central agent necessary to make laundering happen by physically carrying out laundering. Even one launderer laundering one garment is sufficient to cause harm to the environment. Second, the GCIL represents the crucial step in the microfiber's lifetime where agent intervention can most effectively prevent/reduce MFP. Since it is relatively easy for individuals to reduce their microfiber output, and individual launderers within the collective are capable of contagious acts that influence each other, the GCIL holds great potential to mitigate MFP through collective behavioral change. Hence, the GCIL is most causally and thus morally responsible for MFP.

Driving Gene Expression in the Heterochromatic Environment of the Fourth Chromosome of *D. melanogaster*

Jacob Cantrell

Mentor: Sarah Elgin

Genomes of higher eukaryotes can be divided into two fundamental and dynamic subtypes: euchromatin and heterochromatin. The fourth chromosome of *Drosophila melanogaster* is of particular interest because, despite the fact that it appears to be entirely heterochromatic, the genes within this densely packaged chromosome are expressed. Genes that are active in a euchromatic environment are silenced when transposed to heterochromatin. Our aim is to identify heterochromatic gene regulatory elements that drive their active transcription.

Insertion of a euchromatic *hsp70-white* transgene, which exhibits a uniform red eye phenotype when present in euchromatin, into heterochromatic regions on the fourth chromosome results in sporadic silencing, or Position Effect Variegation (PEV). We replaced the *hsp70* promoter of *hsp70-white* with a genomic fragment of a highly expressed fourth chromosome gene, *Rad23*. The fragment includes the *Rad23* promoter region and ~1 kb of an upstream sequence. Insertion of the *Rad23-white* transgene into the same location on the fourth chromosome switched the *hsp70-white* PEV phenotype to a uniform red eye, suggesting that the *Rad23* fragment is sufficient to drive strong expression of the euchromatic *white* reporter.

A series of transgenic reporter constructs containing fragments of varying lengths of the *Rad23* promoter region were prepared by molecular cloning and injected into embryos of the *Drosophila melanogaster* test line. Results show that the promoter region of *Rad23* containing 100 base pairs upstream of the TSS is sufficient to achieve full expression of *white* in a heterochromatic environment. However, a smaller fragment (only 50 bp upstream of the TSS) resulted in a fly with a completely white eye, indicating the loss of a key promoter element. Additional experiments to narrow down what elements of the noncoding regulatory region drive the expression of the reporter gene, and what constructs produce a PEV phenotype, are underway.

Reconciliation of Protein Coding Genes on the *Drosophila elegans* Muller F and D Elements

Jacob Cantrell, Emily Chi, Guanlan Dong, Ben French, and Monica Perumattam

Mentors: Sarah C.R. Elgin and Christopher D. Shaffer

The Muller F element is an unusual domain within the *Drosophila melanogaster* genome because it is packaged mostly as heterochromatin, but also contains 78 protein-coding genes. To understand the factors that enable F element genes to be expressed within a heterochromatic environment, students participating in the Genomics Education Partnership (GEP) produced gene annotations for the F element and the base of the D element for multiple Drosophila species. Manual gene annotation is a meticulous process that requires students to construct gene models based on multiple potentially contradictory lines of evidence (e.g., sequence homology, gene predictions, and RNA-Seq data). For quality control purposes, each project was annotated by at least two independent groups. These annotations must be reconciled before they can be used in subsequent comparative analyses (e.g., gene and repeat characteristics, identification of conserved regulatory motifs). We used WebApollo to reconcile 856 gene models from the *Drosophila elegans* F element (~1.9Mb) and the base of the D element (~2.1Mb). We find that 58% of the gene models submitted by GEP students are in congruence with the reconciled gene models. The most common annotation errors made were the selection of incorrect splice sites (44%) and gene models with extra or missing exons (20%). As part of the reconciliation process, we also produced a report for each GEP faculty member that summarizes the mistakes and provides feedback so that faculty can improve their pedagogical approaches in subsequent years. We find that only 17% (21/127) of the reconciled genes in the *D. elegans* F element matched completely with a computer-based Genscan gene prediction. Hence the reconciled gene models will provide a more robust platform for the subsequent investigations into the unusual characteristics of the F element.

Co-application of the Steroid Alfaxalon Enhances the GABAergic Effects of Propofol and Diazepam

Lily Cao

Mentor: Gustav Akk

The $GABA_A$ receptor modulators propofol and diazepam are in clinical use as anesthetics, anxiolytics and anticonvulsants. However, both drugs, particularly at high doses, cause clinically undesired effects. Propofol can cause irregular heart rate and low blood pressure, while diazepam, like many other benzodiazepines, has long-lasting effects. Thus, it can be clinically advantageous to find ways to administer lower doses of these drugs while still maintaining overall efficacy. One approach is to combine either drug with another GABAergic agent, such as a potentiating neuroactive steroid that by itself has minimal effect. In this study, we looked at the ability of the steroid alfaxalone to amplify GABAergic responses to either propofol or diazepam using three experimental approaches. In the first experiment, we used whole-cell patch clamp to study the effect of combinations of alfaxalone with either propofol or diazepam on decay times of spontaneous inhibitory postsynaptic currents (sIPSCs) in rat hippocampal neurons. Co-application of 300 nM, but not 10 nM, alfaxalone with propofol or diazepam resulted in an enhancement of the decay time constant of sIPSCs. Next, we verified these results on recombinant human $\alpha1\beta2\gamma2L$ $GABA_A$ receptors expressed in *Xenopus* oocytes using two-electrode voltage clamp. We found that exposure to alfaxalone enhanced the ability of propofol or diazepam to potentiate responses to a low concentration of GABA. In the third experiment, we studied the effect of alfaxalone on loss-of-righting induced by propofol or diazepam in *Xenopus* tadpoles. Loss of righting is a proxy for loss of consciousness and mediated by actions on $GABA_A$ receptors. We observed left-shifted dose-response curves during coapplication of alfaxalone with propofol or diazepam. These results demonstrate that coapplication of alfaxalone can result in reduced dosage requirement for propofol and diazepam.

Using Cave Bacteria to Inhibit *Pseudogymnoascus destructans*, the White Nose Pathogen

Austin Chan

Mentor: Joshua Blodgett

Pseudogymnoascus destructans, the causative fungus of White Nose Syndrome (WNS), has rapidly spread across the world endangering many species of bats through accelerating their use of stored fuels during hibernation. Bats diagnosed with WNS have faced 100% mortality in caves, causing concern among scientists. In hopes of controlling this fungus, we are screening cave bacteria for antifungal compounds inhibitory to *P. destructans. Streptomyces*, a widely distributed genus of filamentous bacteria, have a long history of producing antibiotics. They have been known to synthesize a wide variety of our current day antibiotics (amphotericin, neomycin, etc.) and serve as a great discovery platform for new antibiotics. With this reasoning, we performed enrichments to isolate cave *Streptomyces*, amassing a library of over 500 individual strains. To screen for antibiotic activity, we tested our library against the yeast *Saccharomyces cerevisiae* and *P. destructans*. Strains giving the strongest inhibition were subjected to further analysis by mass spectrometry, chromatography and additional bioassays. Additionally, we are collaborating with the Doering Lab (Washington University) who has screened our antibiotic producing strains against *Cryptococcus neoformans*, a facultative intracellular pathogen that causes severe lung infections in humans. Within our library, we have found 58 *Streptomyces* strains that have produced antibiotic activity. Our strains have exhibited a wide range of activities from producing broad antibiotic activity to strains that have been more selective against *P. destructans*. Through our data, we are working to identify specific antibiotics compounds and find strain candidates that will control the spread of WNS.

Experimental Verificagtion of Bulk Metallic Glass Prediction from Machine Learning

Ryan Chang

Mentor: Ken Kelton

Unlike crystalline alloys that have a regular atomic arrangement, atoms are randomly arranged in the novel bulk metallic glasses (BMGs). From a practical standpoint, BMGs are much stronger than ordinary metal alloys, and are thus potentially important materials for commercial and military applications. Why some alloys form these glasses, however, is incompletely understood. Chris Wolverton uses machine learning to predict certain compositions of elements that will form BMGs. Among others, Wolverton's code predicts glass formation in (i)$Zr_{58}Ni_{26}Ir_{16}$, (ii)$Hf_{66}Fe_{32}Co_2$, (iii)$Hf_{58}Fe_{42}$, (iv)$Zr_{40}Cu_{44}Cr_{16}$, and (v)$Zr_{50}Fe_{46}Cr_4$ alloys. The subscripts indicate the atomic percentages of the elements in the alloy. Our goal is to determine experimentally whether the aforementioned alloys will form BMGs.

One gram alloys of each composition were first prepared. The masses of elemental materials needed (determined from equation 1) were measured using an analytic balance and mixed together.

Equation 1: $m^* \frac{Xs*\mu s}{\sum_i Xi*\mu i}$, where X is the atomic percentage of the element s, μ is the atomic mass of the element s, and m is the mass of the sample, which we take to be 1g.

This mixture was then melted using an electric arc-furnace to obtain spherical ingots. The ingot was arc-melted again and suction-cast into a copper mold to produce samples having a varying thickness along their length. X-ray diffraction and Differential Scanning Calorimetry (DSC) measurements were made to determine whether a BMG was formed as a function of the thickness.

The purpose of this experiment was to determine whether the aforementioned five alloys formed BMGs, which would show whether Wolverton's machine learning model is predictive. With the exception of $Zr_{40}Cu_{44}Cr_{16}$, the 4 other predictions did not form metallic glass. For $Zr_{40}Cu_{44}Cr_{16}$, our data indicate that it is only partially amorphous at a thickness of 20 microns.

Phenomenal Accent Patterns: A Computational Approach to Exploring the Application of Theoretical Frameworks from Music Theory to Linguistics

Alicia L. Chatten

Mentors: Brett Hyde and Kristin Van Engen

In theories of musical rhythm, there is a distinction between phenomenal accent and metrical accent. Phenomenal accents require overt acoustic cues, such as an increased duration, frequency, or amplitude compared to surrounding sounds. Metrical accents, however, are part of an abstract organizational structure and do not require the presence of an acoustic contrast. This project employs typological analysis within the framework of Optimality Theory to examine the feasibility of incorporating this distinction into theories of linguistic rhythm. In the analysis of both the patterns predicted by the optimality theoretical constructs and the patterns in attested, real-world data, the picture that emerges is one that identifies the mapping of a variety of phenomenal accent patterns to a smaller number of more general metrical accent patterns. These comparisons opened into two routes of investigation — the first in the building of two computer programs to predict language typologies, and the second in a thorough examination of documents of language description to establish a typology of attested patterns with which to compare the predictions. When these routes are taken in conjunction, generalizations can be made about the relationships between the two types of patterns that allow us to account for the wide variety of attested patterns in mapping the phenomenal accent patterns to their related metrical accent patterns. This broader typological picture can inform future work on both metrical theory as well as comparative linguistics.

A Role for Antennal Lobe Baseline Activity in Odor-Related Predictive Coding

Alex B. Chen

Mentor: Barani Raman

The brain is at every moment confronted with large amounts of sensory data; how it effectively processes this information and orchestrates appropriate responses is an important question in neuroscience. One proposed mechanism for this is predictive coding, whereby the brain uses information from memory and context to predict sensory input. What are the neural substrates underlying predictive coding? We examine the role of spontaneous activity in the locust antennal lobe in context of odor coding. We ask: how do the baseline activities in projection neurons of the antennal lobe change with repeated presentation of an odor? And how do these changes aid the function of the antennal lobe in odor detection? Based on extracellular PN recordings of responses to regular puffs of a single odor, interlaced with trials of a novel "surprise" odor, we report robust changes in antennal lobe baseline activity with repetitive odor stimulation that function to enhance the salience of odor-evoked activity. We propose that these changes in baseline activity in the antennal lobe carry odor-related information and thus may be a correlate of predictive coding.

Matrix Completion: Climate Field Reconstruction Using Tree Rings

Timothy Chen

Mentor: Arye Nehorai

The premise behind matrix completion is that given existing data entries in a matrix, we are able to interpolate missing data entries of the matrix, provided that the matrix is low rank. We use a particular method of matrix completion, called the Singular-Value-Thresholding (SVT) algorithm, to reconstruct a full climate field based on tree ring proxy data. As tree rings form year-to-year, they are a good indicator of the climate and temperature around its environment. However, existing tree ring data are sparse due to missing entries. Using existing tree ring data from North America, we build a complete tree ring matrix using the SVT algorithm. The complete tree matrix will subsequently be used to solve the temperature matrix using a singular value decomposition-based approach, and compared to previous reconstructions done using the incomplete data set.

A Man's Game: Analysis of the Gender Divide in Chess

Sarah Chiang

Mentor: Eileen G'Sell

Chess is a mental game, not a physical sport, yet men seem to dominate the chess arena just as they do in athletic competitions. Does this mean men are smarter than women? Or are there other social influences that might explain why female chess players generally are not as strong? To gather insight as to what might account for the gender rating divide in chess, I distributed a survey to 17 male and 14 female chess players (most of whom are in the top 99th percentile) asking various questions such as how many hours they studied, their comfort level while playing against the opposite sex, why they believed so few females play chess, and other similar questions. An anomaly surfaced when players ranked their comfort level competing against males and females of the same strength. Females reported feeling more comfortable (~13% increase) playing against either gender. A possible explanation for why men feel less comfortable is because they are more competitive and therefore experience more pressure to win which might be one explanation for why men have higher chess ratings. The survey also showed that both males and females were aware of gender stereotypes in chess which shows that stereotype threat is present during chess tournaments. Aside from examining the effects of stereotype threat on female chess performance, I also explored other potential causes for poorer results such as identity separation and the lack of female role models. The answer to why females generally have lower chess ratings is not simply because men are "hard-wired" for chess. It's far more complicated than that. Stereotype threat, identity separation, lack of female role models, competitiveness, and separate girl's sections all may explain the gender rating divide.

Synthesis of Bifunctional Molecules and their Aβ-Binding Ability

Justin Chu

Mentor: Liviu Mirica

In Alzheimer's disease (AD), abnormal interactions between the amyloid β (Aβ) peptides and Cu and Zn ions have been proposed to be a factor in the progression of the disease. In order to combat these interactions, a library of stilbene-derived molecules were synthesized which are known to have an affinity to Aβ peptides. Macrocyclic amine-containing molecules were also synthesized as they have metal chelating properties. These stilbene derivatives were then attached to the chelating macrocycle through the Mannich reaction. Current studies are probing the metal and Aβ-binding effectiveness of these synthesized bifunctional molecules, both *in vitro* and in living cells.

Optical Methods to Quantify Oxygen Tension in Microfluidic Devices

Yunli Emily Chu

Mentor: Steven George

Rapidly dividing tumor cells have high metabolic needs, which results in high oxygen consumption rates and an oxygen gradient in the tumor microenvironment. This change in oxygen tension also affects the neighboring vascular network which often results in tumor angiogenesis, the sprouting of vessels. To study the oxygen gradients present in the tumor microenvironment, a microfluidic device made of polydimethylsiloxane (PDMS) was used to recapitulate this phenomenon. Subsequently, to ensure physiological oxygen tensions, it was of interest to quantify this concentration in the devices in order to visualize the oxygen gradients.

Phosphorescent lifetime imaging microscopy (PLIM) utilizes a phosphorescent oxygen probe called Oxyphor G4 which was added directly to the media 24 hours before measurements were made. Oxyphor G4 does not permeate into cell membranes so the dye does not interfere with the cell behavior in the experiment. Measurements were made using a laser pulsed confocal microscope that measured the dye's lifetime decay. Oxyphor G4 relies on phosphorescent quenching such that high oxygen tensions result in lower lifetimes and low oxygen tensions yield higher lifetimes. At least 100 counts were taken at each pixel and the data was exported as an array of counts and an array of lifetimes.

To translate the array of lifetimes to an array of oxygen concentrations, a MATLAB script was first developed to filter out the PDMS in the oxygen map. The array of counts was used to threshold the image and the lifetimes of the remaining pixels were then mapped to the final image. By using PLIM to measure oxygen tension, heterogeneous distributions of oxygen were able to be quantified and visualized on an oxygen map.

Characterization of Four Novel Nonsense Mediated Decay Homologs in *Tetrahymena thermophila*

Joyce Chung, Jason Kunisaki, Kelsey Pitts, and Joshua Sands

Mentor: Douglas Chalker

The nonsense mediated mRNA decay (NMD) pathway is a ubiquitous post-transcriptional mRNA surveillance pathway in eukaryotes, including *Tetrahymena thermophila*. This pathway is implicated in the degradation of cytoplasmic mRNA containing a premature termination codon (PTC), which would otherwise lead to expression of aberrant proteins. While genes in this pathway are well characterized and studied in organisms such as Drosophila, mice, and even humans, such research has yet to be conducted in *T. thermophila*. To determine the temporal expression pattern of uncharacterized genes in *T. thermophila* NMD (*NMDP1*, *NMD2*, UPF1, and *UPFL1*), we generated cDNA for each gene throughout multiple time points in the *T. thermophila* life cycle. The gene was then attached to a YFP plasmid and transformed into *T. thermophila*, with subsequent visualization of the protein's localization. We identified 4 novel genes, *NMDP1*, *NMD2*, UPF1, and *UPFL1*, putatively involved in *T. thermophila* NMD. With an RNase and EST1 RNA binding domain, *NMDP1* appears to mediate the cleavage of target mRNA strands. The *NMD2* gene containing MIF4G domains is homologous to *UPF2* and may function to recruit proteins to the NMD complex during growth. Both *UPF1* and *UPFL1* possess ATP dependent RNA helicase function, and may be essential for the formation of the NMD complex to degrade PTC-mRNA at different points in the *T. thermophila* life cycle. All 4 genes in the present study appear to be involved in *T. thermophila* NMD. However, our data fails to identify the exact mechanism these genes interact with each other, if at all, to promote the degradation of PTC-containing mRNA. Future experimentation can identify the recruitment process of the NMD complex to facilitate nonsense mRNA decay in *T. thermophila*.

Characterization of Structural and Mechanical Properties of IPSC-derived Cardiomyocytes for Future Application to Familial Cardiomyopathies

Paige Cloonan

Mentor: Michael Greenberg

Familial cardiomyopathies are a leading cause of sudden death in young people, and as of now, there is no known cure. While mouse models and patient heart tissue have been extraordinarily useful in the study of the disease pathogenesis, the physiological differences between mouse and human cardiomyocytes can introduce many inconsistencies in disease presentation. Additionally, tissue from patients with the disease is difficult to obtain and it has undergone many compensations that make it difficult to understand the early stages of the disease pathogenesis. To develop a new model of the disease, we are using human stem cell derived cardiomyocytes bearing mutations that cause familial hypertrophic cardiomyopathies. We have introduced these mutations using CRISPR. Wild type stem cells were differentiated into cardiomyocytes. Immunostaining helped assess sarcomeric organization and traction force microscopy provided a tool to measure the force produced by single cardiomyocytes. We are now beginning to apply the same tools to study a hypertrophic cardiomyopathy disease causing mutation in troponin T, R92Q.

Automatic Sleep Stage Classification Using a Neural Network Algorithm

Zoe Cohen

Mentor: Arye Nehorai

For this project I developed and tested a neural network algorithm for the purpose of performing automatic sleep stage classification. Sleep is typically classified into five different stages: wake, N1, N2, N3/N4, and REM (rapid eye movement). The classification is based on various standards set by the American Academy of Sleep Medicine (AASM) and requires a trained sleep technician. I wrote a neural network algorithm to perform classification based on these standards, thus making the process automatic. The neural network algorithm was developed by improving and building on previous iterations, the final result being a classifier capable of discriminating between five different classes with 80.82% accuracy.

Pollinator Visitation and Plant Diversity in Tallgrass Prairie Communities

Cara Cook

Mentors: Claudia Stein and Scott Mangan

Successful pollination plays a key role in a species' survival, and while features of flowers have been well-studied in their effect on pollinator visitation, the effects of other variables, including the presence of soil microbes or the plant diversity of a community, are not well understood. We tested the hypotheses that 1) increased diversity of the surrounding plant community increases the rate of pollinator visitation as well as pollinator diversity; and 2) the presence of soil microbes mediates plant-pollinator interactions. During the summer of 2016, we observed the number and types of pollinator visitations on three tallgrass prairie species native to Missouri: *Monarda fistulosa*, *Echinacea purpurea*, and *Ratibida pinnata*. The plants have already been established at the Tyson Research Center in experimental plant communities differing in species richness (1, 3, or 6 species mix) as well as in the phylogenetic relatedness among community members. The monocultures were grown in the presence or in the absence of live soil microbes. The total number of pollinator visitations and pollinator diversity differed significantly among the three plant species. However, we found no evidence that plant diversity or soil microbes do influence total visitation and pollinator diversity for the three species. Species and species richness only interacted significantly on the total number of flies, but there was no interaction on the other pollinator groups or total pollinators. Our results highlight the importance of species specific interactions as we could show that specific pollinator groups are influenced by plant diversity as well as soil microbiota.

Correlates of Suicidal Ideation in Preschool-Onset Major Depressive Disorder

Sarah Curci

Mentor: Joan Luby

Prior research has documented the existence of suicidal cognitions and behaviors (SI) in children under the age of 10. Limited research, however, has focused on children under the age of 7. Now that a growing body of literature has found evidence validating the occurrence of major depressive disorder in preschool populations, further research is needed to investigate SI in this age-group. This paper investigates the prevalence and correlates of suicidal cognitions and behaviors (SI) in a sample of preschoolers, ages 3 to 7, with preschool-onset major depressive disorder (PO-MDD). This study supports previously documented correlates of preschool SI and extends areas necessitating further investigation. Specific demographic characteristics have emerged as potential risk-factors in the development of preschool SI and may serve to help clinicians identify those individuals most at-risk.

Inferring Natural Symbiotic Relationships Using Experimental Evolution

Ashley D'Costa

Mentor: Joan Strassmann

The symbiosis between *D. discoideum* and *Burkholderia* is fairly complex, where sometimes *Burkholderia* behaves antagonistically towards *D. discoideum* and other times mutualistically. It is still unclear though the extent to which these lab-observed interactions are present in nature, and how beneficial or harmful they actually are. Here, the goal is to try to infer mutualistic and antagonistic adaptations that would be found in wild strain pairs of the two species. This is done by isolating strains of the bacteria from their naturally occurring *D. discoideum* hosts, and experimentally evolving each on their own. Then using phenotypic assays where the newly evolved subjects are reunited and factors reflecting their symbiotic relationship are analyzed, the resulting level of toxicity of *Burkholderia* towards *D. discoideum* is measured. Early results so far show different strains of *Burkholderia* demonstrating opposite symbiotic effects, (where one seemed to evolve to become more toxic in isolation suggesting an initially more mutualistic relationship, and another evolving to become less toxic suggesting an initially more antagonistic one). Once more strains are analyzed, it will be interesting to conduct further studies with the experimentally evolved strains, and hopefully reveal more about this complex host-microbe interaction.

Parkinson's Disease Fibrils: Analyzing Aggregation Growth Properties in a Cell System

María I. Dabrowski

Mentors: Rebecca L. Miller and Paul T. Kotzbauer

Parkinson's disease (PD) is the second most common neurodegenerative disease in the world. It occurs when neurons in the substantia nigra degenerate, leading to tremors, rigidity, slow muscle movement and other physical and cognitive impairments. Presently there is no way to accurately diagnose PD prior to a post-mortem autopsy. In approximately less than 1% of PD patients, mutations in alpha-synuclein cause the protein to aggregate. There are five known mutations, and each cause slightly different aggregation outcomes depending on how the proteins misfold and clump together into fibrils. The purpose of our experiment is to generate these mutations in a cell system and test the cells to see how wild-type (WT) and mutated alpha-synuclein-expressing cells cause aggregation of the protein. Doing this in a cell system instead of *in vitro* will allow us to see how cellular lipids and proteins influence monomeric proteins to become integrated into fibrils, and how the aggregation properties differ across mutations. Additionally, completing experiments within a cell system will indicate what natural mechanisms cells have to remove or degrade monomers and fibrils, and how these removal pathways might be impacted by mutations. Studying the varying aggregation morphologies and growth patterns of these mutations will be a step in the right direction toward diagnosing PD and developing better treatments.

Role of Snail1 in Breast Cancer Progression and Metastasis

Caroline Davitt

Mentors: Audrey Brenot and Greg Longmore

The epithelial-mesenchymal transition (EMT) is a compulsory step in the progression from primary tumor to metastatic breast cancer. Because patients rarely die from primary tumors, we aim to better understand the biochemical mechanisms involved in EMT in breast cancer. One major regulator of EMT is the transcription factor Snail1 implicated in regulation of multiple cellular processes including cell proliferation and survival, cell invasion and migration, and tumor initiating potential. In order to understand Snail1 involvement in breast cancer growth and metastasis, we have generated transgenic knock out mice. Mice possess the allele MMTV-PyMT, leading to rapid development of highly metastatic breast tumors, using MMTV-LTR driven expression specifically in the mammary gland. The Snail1 gene is deleted in mammary epithelium using the Cre-lox recombination system, through crossing MMTV-PyMT to MMTV-Cre and Snail flox mice. Using this transgenic mouse model, we characterized primary tumor growth and lung metastasis through histological staining and microscopy. We find Snail1 to play an essential role in the growth of primary mammary tumors and progression to lung metastasis.

Identifying Novel Therapeutic Targets in Myeloproliferative Neoplasms

Elisa De Togni

Mentor: Stephen Oh

A Myeloproliferative Neoplasm (MPN) is a clonal hematologic disorder in which red blood cells, platelets, or certain types of white blood cells are produced in excess by the bone marrow. Some MPNs can progress towards Acute Myeloid Leukemia (AML) in which the patient's prognosis is extremely poor. Many MPNs have been linked with the presence of the JAK2V617F mutation or other lower frequency mutations in JAK2, CALR, and MPL which cause increased activity of JAK2, a non-receptor tyrosine kinase, leading to constitutive hyper-activation of the JAK-STAT signaling pathway. Recently, the emergence of JAK2 inhibitor therapy has benefited many patients with MPNs. However, not all of these patients respond to treatment with JAK2 inhibitors, indicating that other important signaling pathways may play a key role in the development of MPNs. In this ongoing study, Pevonedistat, a NEDD8-activating enzyme inhibitor is tested individually and in designed combinations with cytokines and other inhibitors to strategically target specific components of hyper-activated signal transduction pathways in order to promote apoptosis or suppress cellular proliferation. Cell viability assays are used to monitor the effects of Pevonedistat in cell lines that model growth and mutational characteristics of MPNs, such as Human Erythroleukemia (HEL) cells, a human mutant cell line of JAK2, and murine BaF3-MPL cells. Pevonedistat treatment of Myelofibrosis patient samples in colony forming unit (CFU) assays has shown promising results when compared to normal controls. Further testing will be performed on mice models with the ultimate goal of developing inhibitor therapies that may help to prevent the onset of AML and improve overall survival of patients.

A Novel Actinomycete Integration Plasmid Derived from WUSTL Soil-Isolated Phage

Ashby deButts

Mentor: Joshua Blodgett

Large serine integrases, a class of site-specific recombinases associated with some bacteriophage, are of great use in bacterial genetic engineering and synthetic biology; they stably and unidirectionally integrate genetic material into a bacterial genome without the requirement of accessory proteins. Of particular interest are serine integrases that allow for site-specific integration into Actinobacteria genomes. Tools like the cloning vector pSET152 (using the φC31 integrase) have revolutionized biotechnology in drug-producing actinomycetes and even found application in human cell lines. Additional phage recombinases are desirable, and to this end we bioinformatically mined the genomes of 17 newly sequenced *Streptomyces* bacteriophage from the Washington University Phage Hunters program, looking for the presence of novel large serine integrases. Three phage carrying large serine integrase genes of interest were identified, and two were selected for *int* and *attP* cloning from phage lysate. Recombinant plasmids carrying these genes were tested for integration ability on a range of *Streptomyces* hosts. Early results indicate that an *OzzyJ* phage integrase can integrate into a number of streptomycete genomes, allowing us to design a novel integration vector, pJMD9. Current experiments are determining the *attB* site in cognate hosts. We anticipate that pJMD9 will become another valuable tool for engineering *Streptomyces* genomes.

A Report on Motorcycle Taxi Policy Changes and Associated Effectiveness of Lay First Responder Training Programs in Uganda

Peter G. Delaney

Mentor: Shanti Parikh

Approximately 58,500 data points on traumatic injury were collected from the Iganga District Health Office in June 2016, demonstrating that over the five months for which data was available (Oct. '15 – Feb. '16), numbers of traffic accident injuries had risen to well over 300 cases consistently (as high as 499 injuries in Dec. '15), which had not happened once in the preceding 18 measured months. The other illuminating fact gleaned from the research was that motorcycle taxi (known as "boda-bodas")-related injuries averaged 52.05% of the total traffic accident injuries reported monthly. After researching boda-bodas more closely I proposed a boda-boda policy change to combat over-speeding and reckless driving. The proposal and data were presented to the chairmen of the respective boda-boda associations in Iganga District, which received their endorsement and backing, and was then successfully presented to representatives of all district government offices in Iganga, gaining their support in the process. The policy proposal is now passing through both the Municipal and District Government councils and awaiting approval. Following the World Health Organization's guidelines that lay first-responders should be the first step towards developing formal emergency medical services (EMS) in settings without a formal pre-hospital system (which Iganga District lacks), I locally sourced first aid kits for and trained 154 boda-bodas in basic first aid (by partnering with a local trainer from the Iganga Branch of the Uganda Red Cross Society), in ~25-person 4.5-hour sessions. Trainees were administered pre- and post-test surveys to measure skill improvement. Across all categories (Bleeding Control, Scene Management, Airway & Breathing, Recovery Position, and Victim Transport), trainees' scores improved, dramatically in most cases.

Enlightened Dissent: A Treatment of Eighteenth-Century Baptists and Moravians

Taylor F. DiRoberto

Mentor: Mark Valeri

During the eighteenth century, Protestant Christians adopted many diverse theological, sociological, and political forms in the British colonies of North America. The era between the famed religious revivalism of the First Great Awakening and the political upheaval of the American Revolution saw an unprecedented culture of religious pluralism rise and flourish along the Atlantic seaboard. Amidst this culture of increasing religious pluralism, certain ecclesiastic groups maintained exclusive political rights and privileges as the established religion of a geographic region, such as the Congregationalists in much of New England. Despite the reality of religious establishment, several dissenting religious factions gained widespread prominence throughout the colonies, including the Baptists and Moravians. Historians of this period have conventionally conceived of "dissent" as a political category. In this conventional view, disparate religious factions such as the Baptists and Moravians are grouped into one conceptual category based on the precarious political implications of their respective theologies regarding topics such as military service and ministerial taxes. However, the findings of this project point toward an understanding of religious dissent rooted in sociological, intellectual, and cultural factors, rather than the mere ecclesiological and political divisions which have traditionally classified the dissenters from the mainstream religious establishment. A thorough survey of printed theological tracts, personal conversion narratives, as well as private manuscript diaries demonstrates that certain religious groups, such as the Baptists, were participating along with the mainstream religious establishment in a theological discourse deeply influenced by British Enlightenment thinking. Conversely, the Moravians refused to participate in this same type of Enlightenment-influenced religious discourse, thereby marking themselves as true religious pariahs. This, then, proves to be an often overlooked and important dividing line amongst dissenting groups: how they responded to the ubiquitous, regnant Enlightenment moral discourse of the day.

Pathology of Right Ventricular Failure Following LVAD Implantation

Sarah Dyott

Mentor: Kory Lavine

The use of left ventricular assist devices (LVAD) in heart failure patients as bridge to transplant or as stand-alone therapy is becoming increasingly common. However, many LVAD recipients unpredictably develop *de novo* right ventricular (RV) failure, a leading cause of mortality in this population. Consequently, it is crucial to understand the pathology of RV failure in order to better understand this phenomenon and develop treatments for such patients. The goal of this project is to define the pathology of post-LVAD RV failure. To accomplish this we compared clinical data and tissue samples obtained from four groups of patient: normal RV function on medical or inotropic therapy (control); RV failure on medical or inotropic failure (chronic RV failure); post-LVAD with normal RV function; and post-LVAD with RV failure. Using these four groups, we analyzed interstitial and replacement fibrosis, cardiomyocyte hypertrophy, capillary density, and gene expression and ontology. Through this analysis, we demonstrated that the pathology of post-LVAD RV failure represents a distinct entity from chronic RV failure. Patients with post-LVAD RV failure displayed increased replacement fibrosis, decreased cardiomyocyte hypertrophy, and increased capillary density. Surprisingly, patients with apparent normal RV function post-LVAD displayed a similar pathology, suggesting that disease process may affect more patients than previously anticipated. Finally, RNA sequencing revealed alterations in pathways associated with RNA splicing, protein catabolism, and intracellular localization. Collectively, these observations provide pathological and molecular evidence that post-LVAD RV failure represents a distinct disease entity and highlights the importance of an improved understanding of LVAD associated complications.

The Costs of Altruism in the Social Amoeba *Dictyostelium discoideum*

Clarissa Dzikunu

Mentors: David Queller and Joan Strassman

Genotypic makeup of different *Dictyostelium discoideum* strains can contribute to its social behavior. For instance, some strains contribute disproportionally to the spore head rather than the stalk in mixes, thus, reaping the benefits of altruism without fully paying the associated costs. To gain further insight on social cheating, I will test the effects if genotype, cell frequency and the presence of symbionts on competition during the social cycle with fluorescent cell dyes. My hypothesis is that when a "cheater" genotype significantly outnumbers another genotype, the amount of cheating among the cheater will be reduced.

Trace Metal Fate during Reaction of Manganese Oxide Minerals with Small Organic Acids under Aerobic Conditions

Claire Elias

Mentor: Jeffrey Catalano

Manganese oxide minerals play an important role in biogeochemical cycles, as they are readily reactive and widespread throughout soils and aqueous environments. These minerals coexist with trace metals, in addition to organic acids produced by plants and microbes, often under aerobic conditions. The adsorption of trace metals to minerals affects their availability and speciation in the surrounding environment; this has significant implications for environmental remediation techniques and our understanding of biogeochemical systems. In this study, we examine the fate of trace metals when they adsorb to these minerals in the presence of organic acids and oxygen.

MnO_2 suspensions were reacted with Zn, oxalate, and citrate under aerobic conditions over a two week period, with samples taken approximately every 48 hours. The fluid chemistry of this system was tracked and the concentrations of Zn and aqueous Mn were recorded.

These experiments were conducted at pH 7 and pH 4, acidities typical of soil and groundwater environments. It was found that the mineral suspension containing citrate yielded the most Mn and Zn in solution, while the suspensions containing oxalate or no acid yielded significantly less reduction. Although this study should be considered a work in progress, the results of our experiment pose several research questions that may be examined to round out an understanding of the complications involved in the reactions between Mn oxides, trace metals, and organic acids.

Trumpeting American Exceptionalism: The Implications and Consequences of the 2015 Revision to the AP U.S. History Exam

Sophie Elliott

Mentor: Eileen G'Sell

In May 2016, approximately 500,000 high school students took the Advanced Placement U.S. History exam. The exam—and corresponding high school course—is created and administered by the College Board, a private nonprofit corporation that also owns the SAT and related programs. In 2014, the College Board revealed a complete revision of the course and exam for the 2014-2015 school year. Responding to teachers' complaints that the test covered too much material, the rewrite emphasized depth over breadth. The College Board touted an improved structure of the exam, highlighting historical inquiry and analysis over memorization of dates. However, the update to the *content* was met with a great deal of backlash primarily from conservative groups across the country, declaring it anti-American and inaccurate in its understatement of American accomplishments. These protests ranged from school-board level to a resolution published by the RNC denouncing the exam and recommending that the federal government withhold funding for the College Board. Consequently, the exam was once again rewritten for the 2015-2016 school year with more stress on the positive aspects of American history. The change itself is significant, because it means that an amended version of U.S. history is now the standard for curriculums across the country. Equally significant, however, is the fact political motivations undermined a decision that should have been purely educational. This change represents a lack of respect for students' ability to weigh material and come to an informed conclusion about the nature of our nation by withholding information. To decide what students learn is an extraordinary responsibility, and particularly given that the curriculum for this subject is effectively dictated by a private corporation, it is especially vital that we hold the College Board accountable for how that curriculum is shaped.

Self vs. Informant Reports on the Specific Levels of Functioning Scale Relationships to Depression and Cognition in Schizophrenia

Julia Ermel

Mentor: Deanna Barch

Schizophrenia is a debilitating disease, characterized by positive and negative symptoms, and its severity can vary across individuals. 50% to 81% of people with schizophrenia have poor insight into their illness. Thus, the reports that they fill out about their level of functioning and their quality of life (QOL) can be influenced by the amount of insight they have into their illness. People with schizophrenia with worse insight are more likely to have lower depressive symptoms and higher perceived QOL. The Specific Levels of Functioning (SLOF) scale for assessing both self and informant reports is used to obtain information about the interpersonal relationships, social acceptability, informant activities, and work capability of people with schizophrenia and other mental illnesses. The difference between these two reports (self and informant) may be able to help us understand the relationship between insight, life function, cognition, and symptoms in schizophrenia.

We hypothesize that individuals with schizophrenia who show more severe depression will underestimate their function and those with more psychotic symptoms will overestimate their function. In addition, individuals with schizophrenia who have worse cognitive function will overestimate their function.

Participant data for the current analysis were taken from two samples recruited by the Cognitive Neuroscience Test Reliability and Clinical Applications for Schizophrenia Consortium (CNTRACS). This resulted in a total of 186 individuals with schizophrenia or schizoaffective disorder in Sample 1 and 66 in Sample 2. We used the differences between self and informant reports in the SLOF scale to examine how these difference scores related to a number of cognitive factors and symptoms of mental illness.

It was discovered that under-estimators had significantly more depressive symptoms than either the correct or over-estimators. In addition, we found that over-estimators had significantly worse cognition than under or correct-estimators.

Effects of Grammatical Gender on Developing Lexical Representations in a Second Language

Rebecca Feltman-Frank

Mentor: Joe Barcroft

Grammatical gender is cited as support for the Sapir-Whorp Hypothesis (a 1929 hypothesis that postulates that languages affect the way the world is perceived) through demonstrations of how gendered objects and animals impact the lexical representations of such items for *both* first language speakers and second language learners. While multiple studies have supported the grammatical gender impacts on conceptual representations for second language learners, the time course of the development of cognitive changes is still not well understood. Although the 2002 study of Phillips and Boroditsky suggests a continuous development of lexical changes during second language acquisition, the 2009 study by Kuriniski and Sera suggests that conceptual changes occur during the first year of acquisition and remain constant with increasing proficiency. Our study used participants from an immediate and advanced level Spanish classroom in a task where participants were asked to rank the similarity between different object/animal—person pairs (some of consistent gender and some of inconsistent gender) on a scale from 1-9 (1=very dissimilar, 9=very similar) in order to evaluate whether grammatical gender differentially impacted conceptual representations for different levels of Spanish proficiency. Results indicated that the difference in grammatical gender impacts on conceptual representations were insignificant between the immediate and advanced levels; however, the discovery of methodological issues associated with the task served as a calling to evaluate previous research with caution and highlighted the need to clarify the variable findings in this field with future research that carefully addresses methodological issues highlighted in our study.

India's Influence on Soviet Culture

Ashley Ferguson

Mentor: Shefali Chandra

Throughout the twentieth century, the Soviet Union worked to establish a strong political friendship with India, recognizing the importance of having a powerful ally in Asia. While there has been a significant amount of research on the political relations between these two, I explore the way that this political relationship influenced culture within the Soviet Union.

I conducted the research using the archives at the Library of Congress in Washington, D.C. I worked with a number of primary sources by Soviet and Indian artists, writers, and diplomats, in which they discussed the various ways in which they had seen a blending of their two cultures. There were a number of accounts addressing the popularity of Indian music, poetry and literature, and its rapid spread throughout all regions of the Soviet Union. I also found that there was much cooperation between filmmakers and scientists, where representatives from both India and the Soviet Union worked side by side towards a common goal. Indian and Soviet citizens also published travel accounts in which they described their positive experiences traveling between the two countries.

This research exposes an often-overlooked aspect of Indo-Soviet relations. By looking at the music, literature, and films that citizens were exposed to, one is able to gain a greater understanding of their daily life and personal experiences. This research also shows how the Soviet government not only tried to pursue close political bonds, but also pushed the idea of close personal ties between their two countries.

X-Ray Flux/Spectral Variability of the Gravitationally Lensed Blazar PKS 1830-211

Christian Fogerty

Mentor: Henric Krawczynski

We present the X-ray light curves and spectra of PKS 1830-211 provided by the Swift X-ray telescope. Light curves and spectra were extracted. Further analysis of this data reveals intrinsic variability of the photon index φ and flux over time. At energies between ~1 keV to ~6 keV the spectra displayed a similar power law distribution consistent with most AGN at these energies. Observations were taken over a two-month period from April 19 to June 18 of 2016. Multiple operation modes were used during this time period, but only the longest exposure times for each observation ID in the "Photon Count" mode were used in data reduction. A time delay was unable to be determined owing to the discrete nature of the Swift data. From the spectra we assume it is a luminous, low accretion rate system.

Complicating 'Revitalization': Understanding How Urban LGBT Communities Impact Metropolitan Neighborhoods

Reuben Forman

Mentor: Margaret Garb

This research looks at how LGBTQ populations affect gentrification and urban development in city neighborhoods. In particular my project focuses on the greater Washington D.C. neighborhood of U Street Corridor and Shaw, which is situated between 16th Street and Georgia Avenue North West. This historic African-American neighborhood, which hosts many important cultural landmarks, is also the site of a growing visible gay white population. By analyzing the discourses surrounding gay men and their effect on the physical and social environments in the U Street Corridor/ Shaw, I explore the impact the introduction of a visible white gay male enclave has on a historically African-American neighborhood. How did the introduction of a visible white population in a historically African-American neighborhood impact the process of urban development and ever changing identity politics in the District of Columbia? I also plan to analyze economic and housing policies that have lead to such rapid redevelopment in the area.

Investigating the Mechanism of Microtubule Plus-End Tracking by the Arabidopsis Spiral1 Protein

Layla Foroughi

Mentor: Ram Dixit

Microtubules are tubulin-based polymers that are critical for numerous cellular activities such as division, morphogenesis, migration and intracellular transport. The ability of the microtubule cytoskeleton to perform different functions depends on its organization. While centrosome-mediated microtubule organization has been studied extensively, little is known about the mechanisms by which noncentrosomal microtubules become arranged into ordered arrays. This work focuses on the plus-ends of microtubules because they greatly influence the polymer dynamics and interactions of microtubules and thus array organization. I am particularly interested in plus-end tracking proteins (+TIPs), which preferentially associate with growing microtubule plus-ends and regulate microtubule behavior and function. Some +TIPs bind to microtubule plus-ends on their own, while others rely on the End Binding1 (EB1) protein to target them to the plus-ends. The *Arabidopsis thaliana* Spiral1 (SPR1) protein is a +TIP that is unique to plants and is implicated in cortical microtubule organization. Mutants lacking SPR1 contain skewed cortical microtubule arrays and show twisted growth, indicating that SPR1 is important for array organization and morphogenesis. I am using a biochemical approach combined with total internal reflection fluorescence (TIRF) microscopy to elucidate the mechanism for plus-end tracking by SPR1 and its impact on microtubule plus-end dynamics.

The Effects of Psychopathic Personality Factors and Gender on Substance Use, Depression, and Anxiety

Lauren Fournier

Mentor: Deanna M. Barch

Psychopathy is personality disorder often associated with antisocial behavior, criminality, and emotional and interpersonal deficits such as a lack of remorse. These characteristics can be divided into two factors: Factor 1 (callous-unemotional interpersonal-affective traits) and Factor 2 (impulsive-antisocial behavior). Though the relationship between psychopathic personality and substance use has previously been studied, the literature on this topic is somewhat lacking with regard to gender differences and differential relationships to factor scores. Previous studies have also found psychopathy to be inversely related to depression and anxiety, but a closer examination of gender and factor score differences is needed in this domain as well. The present study investigated the relationships between self-reported psychopathic personality factors, participant gender, substance use, and depression and anxiety using data collected as part of the Human Connectome Project (N = 1321). We hypothesized that Factor 2 traits would be positively related to measures of substance use, depression, and anxiety, while Factor 1 traits would not. The relationships between Factor 2 and substance abuse were expected to be stronger in men than in women, and relationships between Factor 2 and depression and anxiety were expected to be stronger in women than in men. Results from regression analyses supported these hypotheses, showing stronger relationships of Factor 2 to substance use, depression and anxiety. We also expected an interaction between the factors, such that higher Factor 1 traits would be protective against the relationship between Factor 2 traits and substance abuse, depression, and anxiety. This interaction between Factor 1 and Factor 2 was found for some measures of substance use, but was not present for depression and anxiety. These results contribute to an understanding of impulsive-antisocial traits as the more maladaptive factor of psychopathy when compared to interpersonal-affective traits, which are less associated with negative outcomes.

Investigating the Role of γ3, an Auxiliary Subunit of the BK Channel, in Myometrial Smooth Muscle Cells

Will Freeman

Mentor: Sarah K. England

The large-conductance Ca^{2+}-activated K^+ (BK) channel is known to be important in regulating contractility and relaxation in myometrial smooth muscle cells (MSMCs) by controlling the flux of K^+ ions across the cell membrane. The BK channel is activated by voltage and intracellular Ca^{2+} concentration ($[Ca^{2+}]_{in}$). In addition, the BK channel has been shown to be constitutively active in MSMCs isolated from pregnant women during labor as compared to MSMCs isolated from non-laboring tissue. This underlying mechanism for this constitutive activity in BK activity has not been fully investigated. The BK channel can be modulated by auxiliary proteins, of which one type, the γ subunits, have been shown to activate the BK channel at relatively hyperpolarized membrane potentials and at very low $[Ca^{2+}]_{in}$. Here we studied whether association with the γ subunits could underlie the BK channel phenotype seen at labor. We focused on the γ3 subunit since it was reported to have the highest abundance in uterine smooth muscle. We investigated the expression and role of the γ3 subunit in non-laboring (NL) MSMCs using both molecular biology and electrophysiological techniques. Our first experiments assessed whether γ3 protein was present in hMSMCs, however we were unsuccessful due to the non-specificity of the antibodies targeted against γ3. To identify the functional role of the γ3 subunit, BK channel currents were measured using patch-clamp in the inside-out excised-patch configuration. We recorded currents from HEK cells overexpressed with BK channel alone and the BK channel co-expressed with the γ3 subunit, but did not detect a change in BK activity in the presence of the γ3 subunit. We also investigated whether the channel activity changed with a 1:4 ratio and from NL MSMC. Future studies will determine whether the association of the γ3 is present in laboring tissue.

Comparative Annotations of Transcription Start Sites and Identification of Conserved Motifs on the *Drosophila* F Element

Ben French

Mentor: Sarah C. R. Elgin

The Muller F element is an unusual domain within the *Drosophila melanogaster* genome because it is packaged mostly as heterochromatin, but also contains approximately 80 protein-coding genes. Past studies have shown that Heterochromatin Protein 1 (HP1a) and the di- and tri-methylation of histone 3 at lysine 9 (both associated with heterochromatin) are depleted at the transcription start sites (TSS's) of active F element genes. This evidence suggests that the factors regulating the expression of F element genes are likely located near the TSS's. We are currently in the process of manually annotating the TSS's of *Drosophila biarmipes* F element TSS's. Manual annotation is a meticulous process that requires the interpretation of multiple lines of evidence (e.g. sequence homology, RNA-seq data, and RNA polymerase II ChIP-Seq data) to define TSS positions and search regions. The resulting high quality TSS annotations will be used in subsequent analyses. An initial investigation of a set of 11 *D. melanogaster* F element genes expressed in fly fat bodies has been conducted using the motif finding tool, MEME (http://meme-suite.org/). The three most significant motifs identified by MEME were similar to the known transcription factor binding motifs for *Trl*, nub, and *lrbp18*. Additionally, we performed comparative analyses of the known *Drosophila* core promoter motifs present in the F elements of *D. melanogaster* and *D. biarmipes*. The most common of these motifs are BRE^{d} (found in 6.6% of annotated TSS), Inr (9.8%), and DPE (4.9%). The presence of these known motifs was noted in the annotations of TSS's in *D. biarmipes* as part of the annotation protocol. With this analysis of the conservation of known motifs and the identification of possible novel motifs, we hope to uncover factors that enable F element genes to be expressed in a heterochromatic environment.

Effects of S1P Mutation on ER Stress and Cholesterol Synthesis Markers in Human Epithelial Cells

Connie Gan

Mentor: Brian N. Finck

Site-1 Protease (S1P) is a Golgi-resident enzyme required for activation and subsequent nuclear localization of several major transcription factors. A 24-year-old female patient with a *de novo* single point mutation in S1P presented with a complex phenotype of gut hypomotility, abnormal optic nerves, and polycystic ovarian syndrome. Furthermore, this patient suffers from phenotypes related to skeletal muscle dysfunction. This phenomenon has been described in the literature to manifest from myoedema and the breakdown of muscle that releases intracellular proteins into the blood, or rhabdomyolysis.

Exomic sequencing revealed a heterozygous amino acid substitution (P1003S) in the transmembrane domain of S1P. Previous research has shown that S1P plays an integral role in the activation of ATF6 and SREBP2, key transcription factors involved in the ER stress response and cholesterol biosynthetic pathway, respectively.

The goal of this study was to characterize the mutant S1P protein by assessing protein activity and localization. Over-expression of mutant S1P in a lipid and cholesterol auxotrophic S1P-null cell line rescued the dependence on exogenous lipids and sterols similar to null cells expressing wild-type S1P. Furthermore, induction of ER stress with tunicamycin showed a heightened expression of ATF6 target genes in mutant S1P patient fibroblasts relative to control patient cells. A similar elevated response in SREBP2 target genes was also observed when the SREBP2 pathway was stimulated in the mutant fibroblasts. In addition, EndoH sensitivity assays showed that localization of mutant S1P to the Golgi was not impaired. This initial characterization demonstrated that the *de novo* mutation produces a gain-of function phenotype and that the mutation does not disrupt proper localization of the protein. This is the first known case of S1P mutation in humans and it is unknown how many harbor similar mutations of the S1P protein, critical for sterol homeostasis.

Characterization of Biotinylated Molecules in Triple-Transgenic Alzheimer's Mouse Model

Evan Garden

Mentor: David Brody

Alzheimer's Disease (AD) is the most common neurodegenerative disease in humans, affecting approximately 11% of people aged 65 years and older. While AD pathology is characterized by amyloid-beta (Aβ) peptide aggregation into insoluble plaques, numerous studies have implicated water-soluble Aβ oligomers as the most toxic form of Aβ. To date, the structure and mechanism of toxicity of soluble Aβ oligomers remains unclear due to an inability to accurately purify and quantify soluble Aβ oligomers from human AD patient and animal model brains. In particular, several methods utilize the interaction between biotin and streptavidin to purify and quantify Aβoligomers. However, studies have shown endogenous biotin-containing molecules occur in many regions of the central nervous system. Thus, the reliability of these techniques may be compromised if any proteins—including Aβ oligomers—are endogenously biotinylated.

In this experiment, soluble lysates from the forebrains of triple transgenic AD (3xTg-AD) mouse models were prepared and treated with streptavidin-conjugated agarose beads and free avidin protein, followed by streptavidin-conjugated agarose beads. Samples were separated using size-exclusion chromatography (SEC), and the abundance of biotinylated molecules and Aβ species—both monomeric and oligomeric—were assessed through direct and indirect enzymelinked immunosorbent assays (ELISA) for all groups. We found that treatment with streptavidinconjugated agarose beads resulted in the complete loss of immunoreactivity previously attributed to Aβ oligomers. Therefore, it raises the intriguing possibility that Aβ oligomers derived from the 3xTg-AD mouse model are endogenously biotinylated. Additional analysis via mass spectrometry will be performed to confirm the biotinylation of Aβ oligomers in 3xTg-AD mouse model and human AD patient brains.

Noble Gas Mass Spectrometry

Nathan Gartlan

Mentor: Alex Meshik

This work was dedicated to studying the Helix MC mass spectrometer and to prepare it for experimental use. The Helix was purchased in order to measure the relative isotope abundances of noble gases contained within stardust and meteor samples. The lab is interested in noble gases because of their non-reactive nature; their inertness means that their current abundances in samples give insights billions of years into the past. For example, ^{40}K decays into ^{40}Ar, so measuring the ratio between ^{36}Ar, a trapped component, and ^{40}Ar, an *in situ* component allows researchers to determine a sample's age. The Helix specializes in precise measurements of the light noble gases Helium and Neon and was purchased primarily in order to establish a standard ^{20}Ne:^{22}Ne ratio for solar wind.

In order to prepare the Helix for experimental use, the electron impact ion source needed to be tuned to achieve ideal measurements. To accomplish this, samples of gas that contained known atmospheric noble gas abundances were admitted into the spectrometer, and these measurements were used to tune the ions source to achieve ideal peak shape. Once ideal peak shape was achieved, the multi-collectors were repositioned in order to measure up to five isotopes simultaneously. Unfortunately, the summer ended before the system was ready to measure actual samples, but the Helix is significantly closer to being experiment-ready due to these tuning efforts.

Can Cognitive and Negative Symptom Severity in Schizophrenia Predict Reward Learning Ability?

Maria Gehred

Mentor: Deanna Barch

Schizophrenia is a severe mental disorder consisting of positive, negative, and cognitive symptoms. The current project analyzes the link between cognitive and negative symptoms by examining how schizophrenia patients learn reward associations. It is increasingly indicated that people with schizophrenia experience reward-learning deficits. However, the literature investigating relationships between these deficits and the symptoms of schizophrenia is mixed. This study seeks to further examine the relationships surrounding reward-learning deficits in schizophrenia. Participants with schizophrenia (N = 49) completed clinical assessments measuring negative symptom severity and level of functioning, as well as running span and reinforcement learning tasks in the laboratory. Analyses revealed that working memory capacity, but not negative symptom severity, were related to reward-learning performance. However, there was some evidence that high and low negative symptom groups may learn reward and punishment associations in a different manner. In addition, reward processing was related to functional outcome among people with schizophrenia; better performance predicted higher levels of functioning. My findings suggest that further research is needed in order to reconcile conflicting evidence surrounding the relationship between negative symptoms and reward processing. With more information about both the intersection of negative symptoms and cognitive deficits as well as their underlying causes, treatments could be developed that would help improve both the quality of life and the practical functioning of people with schizophrenia.

MLL3-Mediated Changes in Chromatin Structure during Hematopoiesis

Natalie Gehred

Mentor: Todd Druley

The MLL3 gene encodes an epigenetic regulator thought to play a role in hematopoietic differentiation. Recent experiments in the Druley Lab suggest that MLL3-deficient iPSCs fail to form hemogenic endothelium, resulting in a lack of definitive hematopoiesis in these cell lines and potentially explaining why rare nonsynonymous germline mutations in MLL3 are implicated in the development of infant leukemia. The assay for transposase-accessible chromatin (ATAC-seq) can localize the structural changes in chromatin that accompany this change in hematopoietic potential by identifying peaks of open chromatin.

ATAC-seq peaks were compared between umbilical cord blood CD34+ stem cells (UCB), wild-type CD34+ iPSC cells (WT), and CD34+ MLL3$^{-/-}$ iPSC cells (KO). ATAC-seq libraries were produced from 50,000 UCB, WT, and KO cells according to a modified ATAC-seq protocol (Semenkovich et al. *PNAS*, 2016). After Illumina sequencing, the reads were analyzed with the Kundaje Lab ATAC-seq pipeline to generate peak files of each sample. DiffBind was used to compare samples and identify regions of significant change between the negative controls and KO.

Comparison of UCB, WT, and KO samples has yielded a list of 4923 differentially-called peaks, 248 of which were found within 3kb of a promoter, often of another known epigenetic regulator. 64% of these promoter peaks were increased in the KO sample.

We conclude that MLL3-mediated changes in chromatin structure are widespread, often affecting the accessibility other epigenetic regulators in a way that correlates with their under- or over-expression in cancer. The focus of additional research will be to repeat these experiments and supplement ATAC-seq data with other epigenetic assays to provide a more complete view of the mechanisms of epigenetic regulation involved in hematopoiesis.

Examining the Role of Asparagine 564 in *E. coli* MetH by Site-Directed Mutagenesis

Alyse Gellis and Charlotte Young

Mentor: April Bednarski

Cobalamin-dependent methionine synthase (MetH) is a large, modular protein that catalyzes the methyl transfer from methyl-tetrahydrofolate (Fol) to homocysteine (Hcy) to form methionine and tetrahydrofolate. MetH uses a cobalamin cofactor as an intermediate methyl carrier in the reaction. The primary focus of this project was the Fol domain. This domain activates methyltetrahydrafolate so that it can transfer a methyl group to cob(I)alamin (Cob) to form methylcobalamin (MeCob). The Asparagine 564 amino acid resides in the active site of the Fol domain and was previously hypothesized to stabilize the N5 atom of the pterin ring on methyltetrahydrofolate by forming a through-water hydrogen bond to the nitrogen atom. This interaction, observed in the crystal structure of MetH, is believed to be important for methyltetrahydrofolate activation. For this project, Asp564 was mutated to a glutamic acid residue (N564E). It was hypothesized this change would increase substrate activation due to the longer and more acidic nature of the side chain. Asp564 was also mutated to an aspartic acid residue (N564D). Primers were designed with these mutations, generating the mutant plasmids, then transformed into XL10 Gold Ultracompetent cells. The mutant MetH proteins were then purified and used in Fol kinetics assays using the wild type MetH as a control. The N564D mutant protein had a k_{cat} of 850 $M^{-1}s^{-1}$ for the Fol assay, compared to 550 $M^{-1}s^{-1}$ for wild type MetH. The N564E MetH, had a k_{cat} calculated lower than either the wild type or N564D MetH protein. These unexpected results may indicate that the acidic amino acid at this position is better at stabilizing the charge on the N5 during catalysis, but that the increase in length of the carbon chain from D to E leads either to crowding or non-ideal hydrogen bond geometries in the active site.

Genetic Interaction between *gpr125* and *knypek* in Convergence and Extension Movements

Songyuan Geng

Mentor: Lillianna Solnica-Krezel

Vertebrate gastrulation and formation of the embryonic body plan relies on polarized cell behaviors to drive convergence and extension movements (C&E). Wnt/Planar Cell Polarity (Wnt/PCP) pathway components, which function was initial described in Drosophila epithelial planar polarity have been identified as essential during gastrulation cell movements. Zebrafish embryos carrying mutations in core Wnt/PCP genes present characteristic phenotypes with shorter and wider body axes, a consequence of perturbed C&E movements. The Solnica-Krezel lab has identified Gpr125, an adhesion G protein-coupled receptor, as a modulator of the Wnt/PCP signaling. Zebrafish embryos carrying mutations in *gpr125* gene present characteristic phenotypes with shorter and wider body axes, a probable consequence of perturbed C&E movements. This is reminiscent of the Wnt/PCP pathway components mutant phenotype, for example: *knypek* (*kny*). In this experiment, we are trying to determine if there is a genetic interaction between the *gpr125* and *kny* gene to have a better understanding of the *gpr125* role during C&E. Based on previous data showing that gpr125 has a genetic interaction with *trilobite* and *scribble1* mutants, both components of the PCP pathway, our hypothesis is the *gpr125* mutant gene will affect *kny* mutant phenotype. The first stage of the experiment was carried out by incrossing the double heterozygous fish (gpr125$^{+/-}$ and *kny*$^{+/-}$). A stronger kny phenotype was observed in several clutches. Subsequently, the embryos were pooled according to their phenotype (length of the body axis). The different classes of the embryos were then subjected for genotyping to determine the presence of the mutant *gpr125* allele in the stronger *kny* mutant category.

Effects of Talker Intelligibility and Noise on Judgments of Accentedness

Sarah Gittleman

Mentor: Kristin Van Engen

The damaging effect of background noise on the intelligibility of foreign-accented speech has been well documented, but little is known about the effect of noise on listeners' subjective judgments of accents. Noise adds distortion to speech, which may cause it to sound more "foreign." On the other hand, noise may reduce perceived foreignness by masking cues to the accent. In this study, 40 native English speakers listened to 14 English-speaking native Mandarin speakers in four levels of noise: -4 dB, 0 dB, +4 dB, and quiet. Participants judged each speaker on a scale from 1 (native-like) to 9 (foreign). The results showed a significant decrease in perceived accentedness as noise level increased. They also showed a significant interaction between noise and talker intelligibility: intelligibility (which had been measured for the same talkers in a previous study) had the greatest effect on perceived accentedness in quiet, and a reduced effect with increasing noise levels. These findings indicate that listeners' decreased access to acoustic-phonetic cues in the presence of background noise also reduces their sensitivity to phonetic variation arising from foreign accents. Furthermore, the link between intelligibility and accentedness is weakened by the presence of noise.

Intracellular Localization of *Staphylococcus aureus* in Osteoclasts

Emily Goering

Mentor: Deborah Novack

Osteomyelitis (OM) is inflammatory infection of the bone caused by *Staphylococcus aureus* (*S. aureus*) which can lead to prolonged hospitalization, sepsis, and even death. Historically, *S. aureus* was thought to be an extracellular pathogen, yet new research has shown that *S. aureus* is internalized into osteoclasts, the cells that destroy bone, and avoid cell defense mechanisms to remain alive intracellularly. The purpose of this study was to investigate how *S. aureus* evades the cellular defense system by studying where *S. aureus* resides within osteoclasts. The location of the bacteria within the cell, particularly the acidification status of the vesicle in which the bacteria are confined, is thought to determine the ability of the cell to combat bacterial growth. To determine the location of *S. aureus* within osteoclasts, I used fluorescence-based confocal microscopic imaging of the fluorescent dye Lysotracker, which marks lysosomes, in osteoclasts. Specifically, I infected primary murine osteoclasts and their precursors with the GFP-expressing MRSA strain USA300 to assess the degree of co-location of bacteria with acidified vesicles. Osteoclasts were fixed at 1.5 hours, 3 hours, 6 hours, and 18 hours post-infection for image analysis of the localization of intracellular *S. aureus* in lysosomes over time. I found that *S. aureus* is localized to lysosomes in osteoclasts at 1.5 hours and 3 hours of infection, but at 18 hours of infection is not localized to lysosomes. This indicates that *S. aureus* may avoid the cellular defense system by avoiding progression of endocytic vesicles to lysosomes or escaping the endocytic vesicle system in osteoclasts. To further assess the endocytic vesicular location of *S. aureus* in osteoclasts late in infection, I will next use antibodies for markers of earlier endocytic vesicles.

Design and Activation of Frequency Tunable 200GHz Gyrotron

Natalie Golota

Mentor: Alexander Barnes

Dynamic Nuclear Polarization (DNP) when combined with Nuclear Magnetic Resonance (NMR) yields high sensitivity spectra while decreasing sample acquisition time. DNP transfers polarization from electron to nuclear spins, giving a strong enhancement of NMR signal. DNP is rapidly developing area of research due in part to application of cyclotron resonance masers (gyrotron) as high power microwave sources. Gyrotrons provide a high-power, high-frequency microwave source that can be used in close proximity to high field NMR magnets. Gyrotrons are operated under strong vacuum and within a cryogenic superconducting magnetic. Gyrotron microwave power is generated by a magnetron injection gun (MIG) composed of a molybdenum emitter coating a barium impregnated tungsten matrix cathode. In this 200 GHz gyrotron, a low capacitance between cathode and anode on the MIG and a variable potential field allow electrons to be accelerated into the magnetic field at variable frequencies. In previous DNP experiments, strong nuclear-electron spin couplings lead to short spin relaxation times and broad NMR line shapes. Voltage tunable gyrotrons are required for fast frequency sweeps of the irradiation bandwidth used for electron decoupling experiments. Using this tunable, fast frequency sweeping gyrotron, electron decoupling experiments will be possible, leading to higher resolution NMR spectra than previously possible. In this project, the assembly and use of a 200GHz gyrotron for DNP NMR is discussed.

Exercise, Social Support, and Structure: Involvement in Sports and Non-Sport Activities and Depression, Anxiety, and Intelligence in Children

Lisa Gorham

Mentor: Deanna M. Barch

Previous research suggests that engaging in an active lifestyle has health benefits, including reduced depressive and anxiety symptoms. Increased exercise is also positively correlated with cognition. However, these effects are often less pronounced in children, and children may experience similar health benefits by engaging in other types of organized activities that do not involve physical activity. Little research has been done to differentiate whether it is the exercise, the social support, or the structure of these activities that relates to depression and anxiety in children. To better understand the relationship of sports and non-sport activities to depression, anxiety, fluid intelligence, and crystallized intelligence in children, a nation-wide sample of 669 children ages 9-11 years completed surveys, interviews, and memory and cognition tasks. Parents of the children provided data about the child's depressive and anxiety symptoms, and the child's participation in sports and non-sport activities. Children completed the NIH Toolbox Neurocognitive Battery which measures both fluid and crystallized intelligence. Analysis of the data showed that depressive symptoms were related to involvement in sports ($p= 0.004$), but not involvement in non-sports ($p= 0.518$), even when adjusting for parental socioeconomic status and maternal education. Further, involvement in team sports, but not individual sports was related to less depression. Anxiety symptoms were not associated with involvement in any type of activity. Both crystallized intelligence and fluid intelligence are strongly related to involvement in any type of activity (sport or non-sport) ($p= <0.001$). These findings confirm a relationship between involvement in sports and lower depression. The fact that depression was related to team but not individual sports suggests that social support may be important. However, more research is needed to understand the causal relationships among these variables.

Robotic Arm Pile Sorting

Jonathan Gross

Mentor: Arye Nehorai

The purpose of this research project was to have a 6-axis FANUC robotic arm, in conjunction with a stationary 3D Kinect camera, pick up, then sort objects that were in a randomly oriented pile. In order to achieve this, we developed image processing algorithms in Matlab that analyzed images from the Kinect, searching for a location where the robotic arm would have a high chance of success to pick up a target object. These computer vision algorithms employed: Canny edge detection, Hough Transforms, image combination, and image filtering. After identifying this location in the Kinect image, we performed a coordinate transformation to translate these coordinates (XYZ and Roll-Pitch-Yaw) from the Kinect's coordinate system to the FANUC's coordinate system. This coordinate transformation matrix was determined using a calibration method that sampled 64 points. Once a target object was picked up, it could then be moved to a fixed position where it could be easily identified and sorted. Alternate methods such as 3D point cloud model detection, point feature matching, and object training were also tested, but proved to be infeasible.

Topological Transitions in a Superconducting Qubit

Arman Guerra

Mentor: Kater Murch

Topology, as it pertains to quantum objects, has become an important area of research because of recent discoveries pertaining to topological phases and insulators in condensed matter physics. It can be used as a tool to accurately describe phenomena in many different quantum systems. I present my study of topology as it pertains to two level systems, and experiments to probe the topology of transmon qubits. These simple quantum circuits allow for a high level of control which makes them good candidates to study topological properties and to model more complicated systems. Specifically, topological transitions of the first Chern number arise when manipulating the Hamiltonian of the system to form closed manifolds in Hilbert space, and watching the Berry phase of the transmon throughout the drive. There were problems having to do with the varying rotation of the qubit state based on the drive, which could be tackled by attempting to rotate the data, or by rotating the measurement procedure. This information has strong ties to quantum information processing, but will also eventually be used to more accurately simulate and study condensed matter.

The Potential Role of ER-Associated Degradation Protein DERL3 in Multiple Myeloma

Harshath Gupta

Mentor: Michael Tomasson

Multiple myeloma (MM) accounts for 13% of hematologic cancers and is characterized by a diversity of genetic lesions—translocations, copy number alterations, and single nucleotide variants. We designed a single-platform targeted sequencing approach capable of detecting all three variant types. Here, we focused on the translocations. We performed targeted sequencing of myeloma cells from MM patients (n=96) and detected novel IgH translocations with partners near *DERL3* (n=2) and observed outlying expression of *DERL3* from RNA-seq data. Since DERL3 regulates protein misfolding, we hypothesized that knockdown of DERL3 in MM would lead to increased apoptosis. After validating the translocation via PCR, we knocked down DERL3 with shRNA constructs in MM cell lines and observed increased cell death in one of two MM cell lines. This study provided some evidence suggesting DERL3 may play a role in regulating MM progression and may be a target of IgH-induced overexpression. Identifying *DERL3* as a tumor suppressor gene for MM could lead to increased understanding of MM development and potential use for therapy.

Third Party Punishment Preferences Toward White and Black Perpetrators: A Comparison in US Dollars

Gabriel Habtemariam

Mentor: Bryan Koenig

Abundant research suggests that the races of both the perpetrator and the victim play an important role in determining preferred punishments, but little research has related victim loss and perpetrator gain in directly comparable units to the penalty the perpetrator would receive. Following Koenig & Riley (in press), the current research employs a method that relates victim loss and perpetrator gain to the third party's fine within the context of theft. In this preregistered and high-powered study, 1079 participants read a scenario intended to activate punitive sentiment toward wrongdoers. Victim's loss and perpetrator's gain were manipulated in comparable units (US dollars). Punishment preferences of the participants (the third party) were measured in those same units. Afterward, we collected demographic data, including participant race. To reduce the risk of demand characteristics, we used a between-subjects experimental design. There are four experimentally manipulated variables, each with two levels: perpetrator gain ($50 and $1,000), victim loss ($50 and $1,000), perpetrator race (African American and Caucasian), and victim race (African American and Caucasian). Currently, data collection is complete and the data is being analyzed.

Best Practices in Peer Learning Sessions: Advice from Peer Leaders

Claudia A. Hendrick

Mentors: Regina Frey, Michelle Repice, and Gabriela Szteinberg

Peer learning/mentoring programs allow students to engage in deeper and more effective learning. At Washington University in St. Louis, students in our General Chemistry sequence are offered the opportunity to enhance their studies through our Peer-Led Team Learning (PLTL) program. New Peer Leaders are trained through a seminar course on academic mentoring. Available to them is a book with essays providing advice from the previous generation of leaders, a project which the new leaders themselves will undertake at the end of the semester to pass on their own tips, experience, and support to the next class. We developed a coding guide using thirteen years of Peer Leader advice books, and fully coded three of the latest books using qualitative discourse analysis and a community of practice theoretical lens to identify which challenges Peer Leaders encountered during their first semester of leading and the strategies they suggest to deal with each challenge. The program itself has grown and been reshaped with each new year of feedback, and here we present what our three most recent years of Peer Leaders believe to be the main challenges of PLTL programs, as well as their advice or best practices to handle them. This advice may be useful for instructors in their own courses or for training in their Peer learning/mentoring programs.

Human Definitive Hematopoietic Specification from Pluripotent Stem Cells Is Regulated by Mesodermal Expression of CDX4

Jolie T. K. Ho

Mentor: Christopher Sturgeon

All adult blood cells arise from hematopoietic stem cells (HSCs), which are multipotent stem cells found within the bone marrow. The generation of HSCs from human pluripotent stem cells (hPSCs) is a major goal for regenerative medicine, and can lead to transplantation of HSCs for the treatment of patients with immunodeficiency or cancers such as leukemia or lymphoma. Successful HSC transplantations would address issues with donors, and also allow for the correction of genetic illnesses that are untreatable with current stem cell technology. The Sturgeon lab aims to produce HSCs from hPSCs by replicating *in vitro* the signals that control embryonic HSC development.

Two programs have been identified as being involved in the development of blood cell progenitors: the primitive and the definitive program. The earlier primitive program does not yield HSCs, but transiently gives rise to a restricted subset of blood cell lineages. Shortly after, the definitive program produces bona fide HSCs, as well as all lineages found in the adult. Within our hPSC differentiation system, we have identified WNT signaling as a critical determinant of the definitive program, and have further found strong CDX gene expression within definitive hematopoietic mesoderm. Specifically, exogenous CDX4 expression resulted in repression of primitive hematopoietic potential, but increased definitive potential. Meanwhile, knockout CDX4 hPSCs had intact primitive potential but a significant decrease in multi-lineage definitive hematopoietic potential. Taken together, these findings indicate that CDX4 is a critical transcription factor in the regulation of human definitive hematopoietic specification, and provides a mechanistic basis for WNT-mediated definitive hematopoietic progenitor specification from hPSCs.

Induction of IDH2 R140Q Mutation in Stem Cells with Doxycycline Increases Rate of Cell Death

Reuben Aaron Hogan

Mentor: David Spencer

Mutations in isocitrate dehydrogenase 1 or 2 (*IDH1* or *IDH2*) occur in a variety of human cancers. IDH enzymes normally convert isocitrate to alpha-ketoglutarate (αKG) in the citric acid cycle. However, the cancer-associated mutations occur at specific positions in each gene, including position 140 of *IDH2*, and lead to the production of a novel molecule, R-2-hydroxyglutarate (2HG). 2HG has been shown to result in DNA and histone hypermethylation of leukemia samples in comparison to normal cells. To understand how this specifically blocks cellular differentiation and allows increased proliferation, we set up an experimental model within stem cells.

H9 cells were infected using a lentivirus which delivered DNA containing the IDH2 R140Q mutation, the GFP gene, and a promoter region that binds a receptor for doxycycline (DOX). When cells are treated with DOX, the receptors diffuse from the promoter, allowing transcriptional machinery to take over. The cell then produces mutant IDH2; however, induction of IDH2 R140Q kills stem cells instead of causing increased proliferation. Our hypothesis is that there is a differential gene expression in stem cells from leukemic cells that must be controlled for to use the model.

To test this hypothesis, we generated both an H9 IDH2 R140Q line and a H9 Vector line. Both were treated with DOX for at least 2 days and were brought up with untreated samples as controls. GFP expression was measured by flow cytometry as an indicator of IDH2 R140Q positivity. Cell counts were taken for all conditions (H9 IDH2 and H9 Vector ± DOX) at different time points to determine the rate of cell death. RNA sequencing was done for all conditions to determine what genes were differentially expressed, and analysis was done to compare the expression between samples and with leukemia tumor samples as well.

Assessing Astrocyte Neuropathology in Chronic Traumatic Encephalopathy

Eric Hsu

Mentor: David Brody

Chronic Traumatic Encephalopathy is a neurodegenerative disease associated with repeated brain trauma and has recently gained national prominence in sports leagues such as the National Football League. CTE is characterized by a distinct distribution of p-Tau pathology within the brain as well as other neuropathological changes. During the course of investigating the radiological pathological correlation in CTE using immunohistochemistry stains and diffusion tensor imaging, we serendipitously discovered an unexpected astrocytic pathology in our tissue. This astrocytic pathology has not been reported in previous literature. This pathology seems to be representative of astrocyte degeneration in regions of white matter. Astrocytes are one of the most abundant cells found in the brain, and play a variety of roles, including maintaining the blood-brain barrier, controlling cerebral blood flow, and maintaining pH. They are generally some of the more robust cells, not particularly prone to degeneration. We are now in the process of testing the novel hypothesis that this degeneration is a result of an autoimmune attack on the astrocytes. Previous studies have shown that human anti-GFAP antibodies are elevated in the blood after repeated traumas, and a possible mechanism involves these antibodies making it past the blood-brain barrier and attacking the astrocytes, leading to the degeneration that we see. Our methods include utilizing immunoelectron microscopy techniques to scan on a structural level. Additionally, IHC stains for typical autoimmune antibodies will also be performed. Learning more of the mechanism behind astrocyte degeneration could have implications for our understanding of CTE overall.

Activation of Dendritic Cell Subsets Following alum- or MPL-adjuvanted Vaccination

Kelly Hu

Mentor: Deepta Bhattacharya

An understanding of the mechanism of vaccine response is essential to elicit long-term durable antibody protection through vaccination. Why is it that some vaccines achieve lifelong antibody titers, while others begin to lose antibody protection soon after vaccination? In our research, we wished to identify the dendritic cell (DC) subsets involved in the initiation of differential immune responses following alum- or MPL-adjuvanted vaccination. We hypothesized different DC subsets would respond to the different adjuvants, such that each subset is specialized to prime a specific set of T-cells. MPL-adjuvants would be more likely to activate CD24+ DCs to mediate Th1 cell-mediated immune responses, while alum-adjuvants would be more likely to activate DN-DCs to mediate Th2 antibody-mediated immune responses. In order to determine the efficiency of DC antigen presentation, in addition to DC activation, a special peptide antigen was injected into mice along with a particular adjuvant. Mice were subcutaneously injected into the flank with a solution of adjuvant and peptide, and DCs were isolated from the draining lymph nodes 24 hours post-immunization. Another set of mice was intraperitoneally injected with the same solution, and DCs were isolated from the spleen 24 hours post-immunization. Activated DCs were quantified by flow cytometry using DC subset-specific markers compared to unvaccinated controls. Preliminary data has so far suggested there are no differences in DC activation and/or antigen presentation among the different DC subsets in response to injection with different adjuvants.

A for Average? Going Down the Rabbit Hole of Grade Inflation

Margaret Hua

Mentor: Eileen G'Sell

Since the 1960s, the most commonly rewarded college grade in America has shockingly veered from a C to an A. To understand such a dramatic swing, this research uses historical context from 1980-2016 to explain shifting economic attitudes of Millennials towards college and the impact of Student Evaluation of Teaching (SET) scores. Scholarly publications on the effect of SETs on grade inflation are polarizing: while some scholars believe SETs are reliable at assessing teaching quality, others claim SETs are deeply flawed devices. I composed a 14-statement survey to Washington University freshmen, in which the 96 participants responded to each claim on a 7-point scale where 1 = strongly disagree, 4 = neutral, and 7 = strongly agree. In response to the statement "If I have attended most classes and completed most of the reading for a course, I deserve at least a B," an overwhelming 54.2% of participants responded with a 5, 6, or 7. Only 27% of participants responded with a 1, 2, or 3. A disturbing 45.8% of participants answered the statement "I primarily see myself as a paying customer of a college" with a 5, 6, or 7. College students and their parents are plunged into the consumer mindset—as tuition increases, they are locked into the hopes of getting their money's worth. Colleges may function as businesses to cater to students to increase customer satisfaction—even at prestigious universities like Washington University. SETs may directly contribute to lenient grading, especially for untenured professors who may feel pressured to obtain favorable student reviews. To counteract grade inflation, ambiguous SET questions like "Is this class enjoyable?" or "Would you recommend this instructor to a friend?" must be amended to accurately reflect teaching effectiveness rather than the feasibility of securing an A.

The Social Status of Islam in Xi'an

Jordan Hughes

Mentor: James Wertsch

I use the city of Xi'an in the Shaanxi province of China as a case study to investigate the social status of Islam in peaceful regions of China. The focus is on young adults and especially students. Research was conducted largely in two parts of the city, the ancient Muslim quarter and the campus of Xi'an Jiaotong University. Research was gathered qualitatively and anecdotally with an emphasis on nuanced comprehension of personal histories. Interviews with students, staff, and community members on and around the university campus provide the bulk of the knowledge found, in addition to conversations and personal observations with local shopkeepers, families, and a group of tourists from Pakistan. My findings suggested no significant social taboo or intolerance of Islam. While a lack of understanding and cohesion between the majority and minority communities exists clearly within young people, it does not appear to be coupled with major animosity of one group towards the other. Significantly more research is warranted, but these findings support a hypothesis that China's national governmental crackdown on the propagation of Islam has had little explicit impact on the perceptions of educated young people, a hypothesis which carries national security implications for both China and the United States at a time when Islam is spreading rapidly throughout East Asia.

Conductive Composite Filaments for 3D Printing

Erica Hwang

Mentor: Julio D'Arcy

As energy demands continue to outpace energy supply, inexpensive and effective energy storage mechanisms have become a necessary component to a long-term solution to this energy crisis. Polylactic acid (PLA), a biodegradable, non-petroleum-derived polymer, can be combined with conductive materials such as carbon black or nanofibrillar polyaniline (PANi), a semiconducting polymer, and extruded to create nanostructure composite filaments for use in 3D printing. The polyaniline and polylactic acid composite filaments can be 3D printed into electrochemical capacitors due to the redox properties of PANi. 3D printing, or fused deposition modeling, is an additive manufacturing process that minimizes material waste and can create objects of complex shapes. Filaments for 3D printing are usually either 1.75 mm or 3 mm in diameter, with filaments of 1.75 mm being the focus of this project due to its increasing popularity. A pressurized mixing extruder consisting of a pressurized reactor chamber and a 1/4" NPT ball valve has been designed and created to facilitate the filament-making process. We heated Ingeo Biopolymer 4043D PLA pellets to about 180°C, which is well above the melting point of PLA—about 140-160°C. Melt mixing PLA enabled filament extrusion, but presented challenges for homogeneous dispersion of additives. The melted mixture was too viscous to stir and adding PANi resulted in nonconductive filaments with visible clumps. To address this issue, PLA and conductive fillers will be dissolved in various solvents such as chloroform, hexaisofluoropropanol, or nitromethane to reduce viscosity and then mixed. The solvent will then be evaporated off, and then the composite material will be extruded.

Exploring Continuity between Schizoid PD and Autism Spectrum Disorders

Pearl Igwe

Mentor: John Constantino

In the second part of a longitudinal study, the Constantino Lab focuses on the continuity between schizoid Personality Disorder (PD) and Autism Spectrum Disorders (ASD). We address whether milder ASD syndromes are an antecedent for schizoid PD in adulthood—specifically, whether milder ASD symptoms is an antecedent for schizoid PD in adulthood. In this study, we examine the second wave of data acquired from the schizoid personality disorder section of the DIGS, SAICA and the SRS. The sample consisted of 75 boys ages 7-25 who were either high functioning, verbal males with clinically diagnosed ASD (n=53) or males who were not diagnosed with ASDs (n=22). In the first part of the study, participants and a parent completed the Diagnostic Interview for Genetic Studies (DIGs). A question was considered to be DSM-IV diagnosable if a score of 3 was reported (always true) and ≥4 symptoms was needed to be clinically diagnosed with schizoid (a relaxed criterion where a score of 2 or "often true" was used for separate analysis). In the second part, SAICA scores from participants and a parent were taken. The SRS score for each of the participants was also reported. Univariate analysis, correlation tables, regression tables and histograms were performed for between-group and within-group analysis of the participants. The results show that when the relaxed criterion was utilized, 13 out of 53 ASD subjects met full DSM-IV criteria for schizoid-PD and an additional 13 met three out of four criteria required for diagnosis. The results also showed that the elevation in the mean score for schizoid-PD traits was due to a shift in the entire distribution, and not a function of excessive trait burden in a subset of ASD subjects. This study shows that there is some continuity between SRS scores and schizoid PD, and further research exploring this relationship is necessary.

Analyzing the Effects of PLD3 on APP Processing

Chimezie Ileje

Mentor: Celeste Karch

Alzheimer's disease is a form of dementia that affects 30 million worldwide. Neuropathologically, AD is defined as neuronal cell death accompanied by amyloid plaque accumulation and neurofibrillary tangle formation within the brain. Current models of AD have several limitations: animal models incompletely simulate the development of AD; cells from deceased AD patients are difficult to isolate and manipulate; and immortalized cells do not display typical neuronal phenotypes observed in human AD brains. Human induced pluripotent stem cells—stem cells created from adult somatic cells—provide a solution to this problem. IPSC technology facilitates in vitro derivation of human neurons to study neurodegenerative diseases like AD. The goal of this study was to use human iPSC to examine a gene that increases risk for developing AD. IPSC-derived cortical neurons were used to investigate the effects of the A442A variant of the phospholipase D3 (PLD3) gene on PLD3 and amyloid precursor protein (APP) metabolism. Sequential APP cleaving generates amyloid beta peptides, some of which accumulate to form the amyloid plaques that characterize AD. PLD3 has no known function but has been found to be a risk factor for AD. Human iPSC were generated by reprogramming dermal fibroblasts from PLD3 risk variant carriers and non-carriers using non-integrating Sendai virus. To ensure the faithful reprogramming of patient derived human dermal fibroblasts into iPSCs, we measured Oct4, TRA, Sox 2, Nanog, and SSEA4 expression using immunocytochemistry. Validated iPSC were then differentiated into cortical neurons, the main cell type affected in AD, and PLD3 and APP metabolism were measured using immunoblotting. APP levels were statistically similar in both lines; however, we found that PLD3, glycosylated and non-glycosylated forms, was higher in cells carrying the PLD3 A442A variant than in control cells. Together, these findings suggest that the AD risk variant, PLD3 A442A, alters PLD3 accumulation in iPSC-derived neurons.

MicroRNA-142 Is Critical for Peripheral NK Cell Homeostasis and Function

Aaron Ireland

Mentor: Todd Fehniger

Natural killer (NK) cells are innate lymphocytes integral in immunity against viral infection and cancer. NK cells are regulated by microRNAs. MicroRNAs (miRNAs) are small, non-coding RNAs that target mRNAs to inhibit translation and initiate mRNA degradation. Next-generation small RNA sequencing has identified miRNA-142 to be highly expressed in murine NK cells, and thus we hypothesized that miR-142 is critical for NK cell development, survival, and/or functionality.

To investigate this hypothesis, we examined the NK cell compartment of miR-142 deficient mice. Flow cytometric analysis of harvested NK cells, tagged with fluorescent antibodies targeting markers of maturation, showed a significant NK cell deficiency despite no observed blocks in maturation. Across peripheral blood, spleen, liver, and lymph nodes, NK cells were decreased between 2-10 fold as compared to controls. Since this deficiency was evenly spread across all stages of NK cell development, we concluded that miR-142 isn't necessary for maturation of NK cells.

To test whether the NK cell deficit in mir-142-deficient mice was cell intrinsic, we performed bone marrow chimera experiments. Here, control and mir-142-deficient bone marrow were co-transplanted into irradiated mice, and the contribution of each to hematopoiesis was assessed. A significantly reduced number of chimeric mouse NK cells were derived from mir-142-deficient bone marrow than control, supporting the cell-intrinsic role of miR-142 in NK cell homeostasis. Additionally, NK cells deficient in miR-142 were found to have no signaling through their IL-15 cytokine receptors due to insufficient STAT5 phosphorylation. This failure to signal led to an observable defect in the production of IFN-γ, an important immune cytokine. Furthermore, miR-142 deficient NK cells have drastically altered integrin expression, which we hypothesize inhibits NK cells from leaving the bone marrow, where NK cells are produced. Thus, we conclude that miR-142 is required for maintaining normal function and homeostasis of peripheral NK cells.

Medical Technology in a Developing Developed World, Mexico City 2016

Isabel Izek

Mentor: Shanti Parikh

Mexico continues to be classified as a developing country. As one of the most advanced developing countries, Mexico has an impressive number of technologically advanced hospitals. Unfortunately, access to medical technology is reserved for those who can pay for private hospital care, excluding much of the nation's population. The purpose of this study was to evaluate discrepancies in medical technology and to unearth barriers that prohibit individuals from receiving adequate medical care. We interviewed medical practitioners and patients within pediatric and neonatal treatment centers to compile varying perceptions on the available medical services. It was determined that although on paper all Mexican citizens have access to basic healthcare services, the level of treatment varies drastically because of the existence of private and publically funded institutions. This inconsistent level of care causes lifelong disabilities for infants who suffer from neurological injuries that require immediate medical attention.

Hypoxic Environments Regulate CXCR4 Expression and Drive Collective Cell Migration

Rachel Jacobsohn

Mentor: Steven George

Approximately 90% of the deaths related to breast cancer are caused by metastatic dissemination of the disease. Furthermore, once a tumor has reached the metastatic stage there is only a 22% chance of 5-year overall survival for the patient. Accumulated evidence has demonstrated that exchange of information between tumor cells and its extracellular matrix environment, such as hypoxia, contributes to cancer metastasis. CXCR4, a G-protein coupled receptor that activates intracellular signaling pathways controlling cell shape, migration and proliferation, is hypothesized to contribute to tumor cell migration away from the primary site. The objective of this project was to investigate the role of hypoxia to regulate CXCR4 expression and drive cell migration. Using a 3D hydrogel system to mimic features of the tumor microenvironment, studies reveal hypoxia leads to up-regulated CXCR4 expression. Furthermore, CXCR4 knockdown via shRNA resulted in decreased CXCR4 expression that did not change under hypoxia. Findings from this study indicate a potential role for CXCR4 signaling that is regulated by hypoxia. These findings are significant as they begin to provide insight regarding escape mechanisms cancer cells use to metastasize to distant tissue.

Using Bacterial Nanocellulose as a Plasmonic Bionsensor

Liz L. Jahng

Mentor: Srikanth Singameneni

Bacterial Nanocellulose (or BNC) is a promising material for a paper substrate because of its cheap price, portability, smooth surface, mechanical properties, and ideal detection properties. This research project focused on developing a multiplex plasmonic biosensor that could detect multiple artificial antibodies on its surface at the same time. By applying wax "wells" to the BNC surface, solutions dropped onto the BNC could be contained in the sealed region, thus ultimately allowing the separation of different artificial antibodies on the same surface of BNC. A successful multiplexing biosensor would be useful in further applications, as most needs for biosensors must detect multiple biomarkers, such as the urine test for kidney cancer, which detects for three biomarkers. The only complication in this research was the difficulty of immobilizing gold nanorod solution on the BNC surface. While many factors could have contributed to this issue, further research needs to be done to determine the correct factor and method, and thus this research will continue.

Towards Discovering Inhibitors of cyt c Biosynthesis in Systems I, II, and III

Shannon J. Jiang

Mentor: Robert Kranz

Cytochrome c (cyt c) is a heme protein found in most organisms (including human pathogens) that plays an essential role in both aerobic and anaerobic growth. The biogenesis of c-type cytochromes occurs by three different systems (Systems I and II in bacteria and System III in humans). Besides requiring different protein systems, their site of synthesis is also different. Systems I and II function in the periplasmic space while System III functions in the mitochondrial inter-membrane space. These differences may allow for selective targeting of bacterial systems using antimicrobial compounds which may be beneficial in combating infectious bacterial diseases. My goal is to develop a robust assay that detects cyt c maturation quantitatively to allow for subsequent analyses of levels of cyt c maturation in the presence and absence of potential inhibitors. In recombinant E. coli, Systems I and II produce cyt c in the periplasm while System III makes cyt c in the cytoplasm. An *in vivo* assay has been developed in the Kranz lab that detects cyt c produced in the periplasm, but cannot detect production in the cytoplasm. Therefore, I have been optimizing an *in vitro* method to extract cyt c from recombinant E. coli grown in small volumes (<5mL) and detect it quantitatively by heme stain. Here I present work showing that the *in vitro* assay can detect differences in the amount of cyt c produced within System III. I also explored the optimal conditions for comparing cyt c biogenesis across the three systems in recombinant E. coli. Future direction is to test known inhibitors of heme biosynthesis and protein biosynthesis to test the effectiveness of this assay.

Studying Competition in the Vegetative State: Using *Dictyostelium discoideum* Sex Locus as a Stable Marker

Daniela Anabel Jimenez

Mentors: David Queller and Joan Strassmann

Dictyostelium discoideum is an excellent model for studying cooperation and control of conflict. When these amoebae starve, they aggregate together to form a multicellular slug and eventually a fruiting body. *D. discoideum* genotypes compete for space in the fruiting body and avoid forming the stalk cells, which will die. Most studies have only focused on competition when these amoebae aggregate together and become multicellular. However, the amoebae spend most of their life in the unicellular stage. Therefore, it is necessary to develop techniques to study interactions between *D. discoideum* during their unicellular, vegetative state. The recently discovered sex locus for *D. discoideum* provides a stable genetic marker to identify a clone throughout its lifetime. By taking advantage of the distinct regions within the sex locus, qPCR primers have been developed to give quantitative information of the results of mixed genotype interactions. This technique will provide an opportunity to fill the gaps in our current understanding of interaction throughout the *D. discoideum* lifecycle.

Rational Radicals: Japanese Foreign Policy in the Twenty-First Century

Syrus Jin

Mentor: Colin Bassett

This research analyzes the foreign policy platform of the Japanese Liberal Democratic Party (LDP) and presents the view that the LDP has continued to seek a middle-course of balancing U.S. and national interests despite the rise of nominally nationalist LDP politicians to positions of leadership. The doctrine of pragmatic policy-making that subordinated national autonomy to economic growth developed among Japanese statesmen immediately after the end of U.S. occupation of Japan in the 1950s, amidst a debate between economic pragmatists and nationalist-orientated revisionists in the LDP, where the revisionists were ideologically characterized as having a more glorified view of Japan's imperial past and muscular notion of providing for Japanese security. Although the turn of the century has seen the rise in popularity and influence of LDP revisionists, the expansion of the Japanese military and the rise in Japanese military operations abroad has been more of a reflection of changes in geopolitical threats and developments in the region rather than pure ideological motivations. Additionally, a number of barriers prevent the implementation of aggressive revisionist policies, including the government bureaucracy and relations with the United States. The full defects of pursuing ideologically-based policies were shown when the DPJ opposition party held power form 2009-2012 and soon showed its inability to deal with institutional moderating factors. Despite the fact that LDP revisionists almost entirely controlled the office of the Prime Minister in the twenty-first century, Japan continues to go down a familiar path of taking pragmatic action devoid of nationalist rhetoric which demonstrates an inherent flexibility for future Japanese policies.

Genes Associated with Subjective Well-Being in a Recent GWAS Are Associated with Decreased Depressive Symptoms: Possible Biological Mechanisms

Mackenzie Jones

Mentor: Ryan Bogdan

Subjective well-being (SWB) is heritable and associated with physical and mental health. A recent genome-wide association study (GWAS) of 298,420 individuals identified 3 single nucleotide polymorphisms (SNPs) associated with SWB. The amygdala is a brain region critical for behavioral vigilance and assigning emotional significance to stimuli. Elevated amygdala response to threat has frequently been observed in stress-related disorders such as depression making it a promising intermediate phenotype through which genetic risk for SWB may emerge. Here, we examined whether polygenic scores (PS) for SWB are associated with threat-related amygdala function.

Genomic, neuroimaging, and self-report data were available for 480 participants who completed the ongoing Duke Neurogenetics Study. Threat-related amygdala reactivity was assayed using an emotional face-matching task while functional magnetic resonance imaging data were acquired. Depressive symptomatology was assessed with self-report. We tested whether PS for SWB are associated with depressive symptoms and threat-related amygdala function. Further, given recent evidence from our lab that the association between amygdala reactivity and psychopathology is moderated by time of day, we examined whether this time of day moderated the association between SWB PS and amygdala function.

We found that polygenic scores associated with increased SWB were associated with decreased depression (significant at 4 of 10 p-value thresholds). There was a significant SWB PS x time of day interaction (significant at 5 of 10 p-value thresholds), such that among participants scanned earlier in the day, lower PS for SWB were associated with heightened amygdala reactivity.

These findings compliment evidence from our laboratory that elevated amygdala reactivity in the morning is associated with stress-related psychopathology as well as prior observations that SWB is reduced among those with late chronotypes. Diurnal-related variation in amygdala function may mechanistically link common genetic variation to SWB and related psychopathology.

The Effect of Negative Allosteric Modifiers on mGluR5 Activity

Sartajdeep Kahlon

Mentor: Karen O'Malley

The metabotropic glutamate receptor, mGluR5, is a G protein-coupled receptor (GPCR) widely expressed in the brain where it is linked to various developmental pathways involved in intellectual disabilities such as autism spectrum disorders. Most GPCRs are located on the surface of the cell where they receive signals from the environment which they convert into signals inside the cell. What makes mGluR5 unique is that most of it is inside the cell where it can also be activated and hence trigger signaling from its position inside the cell. Because cell surface mGluR5 activates different responses than the intracellular receptor, we hypothesized that compounds that inhibit mGluR5 might do so in a differential fashion. Specifically that some mGluR5 inhibitors might only block the cell surface receptor whereas others might block intracellular mGluR5. To test this hypothesis, I used primary cultures of spinal cord dorsal horn neurons which we have previously shown to express high levels of this receptor. When activated mGluR5 leads to increased intracellular calcium which can be conveniently measured in dishes of cells using fluorescent calcium-sensitive dyes. By measuring a range of concentrations of 5 different inhibitors, I was able to deduce that certain drugs were more effective at inhibiting the cell surface vs. the intracellular receptor. This information will be useful in developing new therapies for disorders linked to mGluR5 signaling such as autism spectrum disorder.

Exploring the Role of DCAF1 in HIV Replication: A 2-hybrid Screen in Yeast

Anish Kanesa-thasan

Mentor: Lee Ratner

Viral proteins x and r (Vpx and Vpr) are members of the lentiviral accessory protein family, which function to manipulate native cell machinery and enhance viral replication in differentiated immune cells, including monocyte-derived macrophages. Macrophages, along with CD4+ T cells, are primary targets of HIV infection and crucially important in *in vivo* virus proliferation. Vpr is ubiquitous across all primate lentiviruses, but Vpx is unique to HIV-2 and some Simian Immunodeficiency Viruses (SIVs). Vpr and Vpx both associate with the CRL4 E3 ubiquitin ligase complex via binding to Cul4-associated factor 1 (DCAF1), the complex's substrate receptor. E3 ubiquitin ligases identify target proteins for degradation, and catalyze the transfer of ubiquitin from an E2 enzyme; they are frequent targets of viral infections and cancers, as they control the final step in the ubiquitination pathway. Vpx uses the CRL4 E3 ligase complex to target the restriction factor SAMHD1, which hydrolyzes dNTPs to maintain a cellular concentration below the functioning capacity of HIV-2 reverse transcriptase, for degradation. Vpx-controlled degradation of SAMHD1 removes this block, and allows for viral replication in HIV-2/SIV. Vpr is needed to induce G2 cell cycle arrest, but the exact mechanism and scope of Vpr-mediated inhibition is poorly understood.

We use a yeast 2-hybrid screen to identify DCAF1-interacting proteins, which could provide vital insight into the mechanism of Vpx and Vpr function and inform novel HIV therapies. Our ongoing screen has revealed several interesting candidate DCAF1 interactions, and, we hope, will reveal several more within the semester.

The Mechanisms by Which Smaller Images Provide Beneficial Effects in Category Learning

Madison Kasoff

Mentor: Mark A. McDaniel

Identifying conditions that enhance category learning presents an opportunity for improving science education (e.g., teaching rock categories in geology courses). However, research on this topic is relatively scarce. Past research in our laboratory has suggested that presenting some natural categories, such as tropical fish, as small (100 px) rather than large (1000 px) images is beneficial for learning. The current research is aimed at uncovering the mechanism of this effect. We identified three plausible mechanisms supporting the advantages that smaller images provide for the learner and present several experiments assessing the merit of these hypotheses. *The general desirable difficulty hypothesis* suggests that small images create difficulty in the learning process, which subsequently improves performance. *The attention shift hypothesis* suggests that leaners' attention shifts from the color/pattern of the body to the outside shape (a critical feature for determining the fish category) as the image becomes smaller, a prediction based on a mathematical relationship between perimeter and area of an object. *The ease of shape extraction hypothesis* proposes that shapes are easier to extract for small images because the entire shape is within leaners' visual contour, whereas larger images are not and thus requires gaze shifting during the shape extraction process. Our data is evidence against the *attentional shift hypothesis*. The other two hypotheses remain plausible, although the general pattern of results seem to favor *the general desirable difficulty hypothesis*. Participants made Category Learning Judgments (CLJs) to predict expected success of tropical fish category classification when presented with new images. Across all experiments, we predicted and observed that participants judged that larger pictures aided their learning the most—the opposite of their actual performance.

Functional Role of Nonstructural Proteins in Respiratory Syncytial Virus Mediated Host Immune Evasion

Samir S. Kaveeshwar

Mentor: Gaya Amarasinghe

The genome for Respiratory Syncytial Virus (hRSV) encodes for eleven proteins through ten distinct genes. Two proteins of interest are called Nonstructural protein 1 (NS1) and Nonstructural protein 2 (NS2). These proteins have been shown to evade the human immune system through inhibition and suppression of the signal interferon pathway that, in response to viruses, produces proteins that target the expression of antiviral genes through secondary pathways such as the JAK/STAT pathway. Specifically, NS1 and NS2 have been linked to lower levels of STAT2, which is a key signaling protein in the type 1 signal interferon pathway. The degradation of STAT2 occurs through cellular ubiquitination, a type of degradation accomplished by E3 ligase complexes. Recently, our collaborators have identified several host factors that interact with hRSV NS2. I plan to use *in vitro* pull down and immunoprecipitation studies to validate these hits. Collaborative studies within our group and elsewhere will test the functional significance of these integrators once we validate direct binding. The hypothesis for this study centers on the idea that the direct interactions between hRSV NS2 and host factors modulate the host immune response.

Application of the Dispersive Optical Model to ^{208}Pb

Michael Keim

Mentor: Willem Dickhoff

A review of developments for the application of the dispersive optical model (DOM) to ^{208}Pb is presented. By providing appropriate parameters describing real and imaginary parts of a nonlocal self-energy, connected through a dispersion relation, reasonable reproductions of both scattering and bound-state properties are generated. By fitting these parameters to experimental data, a more accurate description of the neutron skin may be achieved, which would have implications for the physics of neutron stars.

Circadian Expression in Human Tracheal Epithelial Cell

Meaghan Kenfield

Mentors: Jeff Haspel and Erik Herzog

Circadian rhythms are 24-hr oscillations in both behavior and physiology. These rhythms are internally generated by cell-autonomous clocks that depend on clock genes including Period2 (Per2) and Bmal1 to generate rhythms and to entrain to the daily environmental cycle. These clocks modulate events including cerebral activity, heart rate and blood pressure, plasma flow, urine production, electrolyte and water homeostasis, production and secretion of hormones, metabolism, and body temperature with time of day. In health, these clocks are synchronized to each other to produce coordinate daily rhythms in the body. Abnormalities in circadian rhythmicity can result in sleep disorders, such as insomnia, or lead to other conditions such as obesity, diabetes, depression, bipolar disorder, and seasonal affective disorder.

The goal of this project is to conduct and analyze real-time bioluminescent recordings of clock gene expression of human tracheal epithelial cells (hTECs) *in vitro*. Cells from donors with asthma, COPD and normal airway functioning were studied. In order to produce bioluminescent recordings, I made and transduced cells with Luciferase knockin reporter gene lentiviruses of two clock genes, Period2 and Bmal1. In order to ensure synchrony of plated cells, each plate was pulsed with dexamethasone prior to bioluminescent recording using a photo multiplier tube (PMT) in a light-tight, temperature-controlled incubator. Preliminary results reveal rhythmic expression of both Period2 and Bmal1 in hTECs from both wild-type and asthmatic donors.

Ultrastructural Analysis of the Drosophila Larval CNS in Wild-Type and AdamTS-A Loss of Function and Over-Expression Mutants

Prajwal Keranahalli

Mentor: James Skeath

The structures of organs and tissues often determine their function. The morphology of the central nervous system is important in increasing the efficacy of neuronal interactions. Various neurological disorders, such as ALD, arise due to structural defects in the CNS. Therefore it is important to understand the mechanisms that govern tissue structure. In all organisms, the structure of the CNS is regulated in part by the basement membrane or ECM. Understanding the genes and pathways that govern ECM formation and maintenance is essential to elucidate how tissues like the CNS maintain their stereotyped structure as they grow. In Drosophila, the CNS is covered by a thick ECM, the neural lamella, which immediately overlays two layers of surface glia. These three layers are essential to impose structure in the CNS. This research was focused on understanding the function of the metalloprotease AdamTS-A in surface glia. Prior work from the lab indicates that at the end of larval development AdamTS-A is expressed in surface glia, and that reduction of AdamTS-A function leads to massive distortion of the CNS structure. I looked at the expression of AdamTS-A in perineurial and subperineurial glia, the two types of surface glia, in order to determine when AdamTS-A turns on in each cell type and characterize its influence on the distribution of AdamTS-A expressing glia during larval life. Once I mapped the onset of AdamTS-A expression in surface glia and the distribution of AdamTS-A expressing glia as a function of time during development, I conducted a similar experiment in AdamTS-A mutant backgrounds to ascertain how alteration in surface glia function may lead to mass distortion of CNS structure.

Synthesis of Near-Infrared Emitting Quantum Dots for Deep Tissue Imaging

Daniel Khan

Mentor: Bryce Sadtler

Quantum dots are fluorescent nanoparticles that exhibit unique and tunable optical properties due to their small size. Quantum dots can be used for a variety of applications, including LED displays and in medical diagnostics, because of their high brightness, stability, and efficiency. My project focuses on using nanoparticles as contrast agents for deep tissue imaging. Deep tissue imaging has historically been done using ionizing radiation such as x-rays, but this method poses significant health concerns to both patients and health care workers. Visible light is unsuitable for deep tissue imaging because it is scattered and absorbed by tissue and water. Quantum dots, however, can be tuned to emit light in the near-infrared spectrum; this allows for deep tissues to be imaged safely and without radiation scattering. To use quantum dots for deep-tissue imaging, the nanoparticles must be non-toxic, stable, and emit light with high quantum yield in the near-infrared region. The toxicity of quantum dots is determined by the composition of the particles. The stability of quantum dots may be enhanced by a synthesizing a shell around the particle. The fluorescence quantum yield and emission wavelength of a quantum dot are dependent on its composition, morphology, and size. By altering one of these variables, the fundamental optical properties of the quantum dots can be controlled. My project focuses on synthesizing Ag_2S quantum dots that emit light in the near infrared region, from 1100 to 1400 nm. Afterwards, a ZnS shell is generated around the quantum dot to enhance the particle's stability. The Ag_2S nanoparticle is synthesized by heating silver and sulfur precursors in a favorable solvent. To prevent oxidation, the quantum dots have been stored in airfree conditions. This inert environment has caused a unique self-assembly of the nanoparticles in dendric structures, which may be the subject of future research.

Purification Chip for Radiolabeling Antibodies

Minki Kim

Mentor: David Reichert

In recent years, the use of radiolabeled antibodies as positron emission tomography (PET) imaging agents has increased in clinical trials. But, many challenges exist with the conventional labeling method. It requires a large laboratory space and inefficient process of removal of non-specific bound radiometals. In order to accelerate the preparation time and increase efficiency, the Reichert lab has employed microfluidic chips to create an on-demand system for radiolabeling antibodies and peptides.

The lab has successfully prepared single-patient doses of ^{89}Zr-labeled Trastuzumab antibody that is used to target metastatic breast cancer cells, with microfluidic chips. Using their chip, they found the microfluidics approach generated a labeling yield over 2.5 times greater than conventional methods under similar conditions. However, these radiolabeled antibodies and peptides must go through extensive purification processes before they can be administered to patients in order to ensure accurate doses of radioactivity.

This research focuses on developing a purification chip to easily remove non-specifically bound radiometals. The design requires a chip that has tanks with small posts. Since the whole chip is made of polydimethylsiloxane (PDMS), linker silanes can be attached to these posts. These silanes can contain a variety of functional groups; however, we primarily focus on (3-aminopropyl)trimethoxysilane that contains an ammine group. Using peptide coupling reaction, we can covalently bond silanes to bifunctional chelators such as diethylenetriamminepentaacetic acid (DTPA) that binds radiometals. Each post will then have a molecule of DTPA that can bind radiometals. Then, solutions containing radiolabeled antibodies can be passed through the chip, and the immobilized DTPA can remove non-specifically bound radiometals from antibodies. Although preparation of the chip may be more time-consuming than conventional purification methods, the chip can be used multiple times and ultimately reduce the time for purification.

Transient and Single-Particle Sensing of Gold Nanorods for Applications in Biomolecular Sensing

Eshan King

Mentor: Lan Yang

Single molecule biological sensing is of great interest in many areas of science, from pure biological research to integrated lab-on-chip devices. Its applications include medical diagnostics, drug detection, and environmental monitoring. In this project, we seek to create a label-free biomolecular sensor using a tapered optical fiber and functionalized gold nanorod.

Optical fiber waveguides allow for cheap and simple environmental sensors. By tapering the fiber to single mode operation using the flame-pull method, a substantial portion of the electric field exists in the medium surrounding the taper. By monitoring the extinction profile of a light signal propagating in the tapered fiber, particle binding events can be detected.

Gold nanorods near the tapered fiber greatly increase the electric field strength around them compared to the bare fiber. This increases the extinction profile of the nanorod and any molecule that binds to it, increasing the sensitivity of the optical fiber. This setup allows for the detection of single proteins and short oligonucleotide binding kinematics.

Our work has shown transient detection of gold nanorods in a buffered, pH 7 aqueous environment in the form of downward signal spikes. We have also observed step changes in the transmitted signal due to single gold nanorods binding to the fiber when the pH is dropped below the isoelectric point of silica. When the pH is raised again to 7, the nanorods remain bound to the fiber, indicating that the binding of nanorods to the silica fiber is irreversible.

Our future work will build off of these promising results. We aim to functionalize the gold nanorods with human anti-IgG using a simple thiolating technique, bind them to the tapered fiber, and detect single IgG molecule binding events as a "proof of concept" of our platform.

Biodiversity-Ecosystem Function Relationships Are Mediated by the Environment and Functional Trait Assembly

Ashley Knudson

Mentor: Jonathan Myers

There are numerous studies demonstrating that biodiversity should increase the strength of vital ecosystem functions (e.g., biomass production or pollination services). However, most studies manipulate species diversity by randomly assembling communities within small homogeneous environments. There is considerable debate though regarding the extent to which these biodiversity-effects scale up to natural, heterogeneous landscapes where most ecosystem management and restoration actions are targeted. Here, I asked what factors impact the strength of this relationship. Specifically, how is the biodiversity-ecosystem function relationship in naturally assembled plant communities is altered by environmental variation and the distribution of functional traits? I conducted this study in an Oak-Hickory forest landscape at the Tyson Research Center. I censused plant species composition, biomass, and functional traits in 90 1-m¬2 plots distributed across strong soil resource gradients in the forest. Using general linear models, I found species diversity increased productivity across all environments. However, with increasing environmental harshness there was a lesser effect of diversity on productivity. I also found that two components of functional diversity mediated the strength of this relationship. Functional divergence (the degree of niche differentiation among dominant species) increased the biodiversity effect whereas functional evenness (the degree to which species abundances are distributed in niche space) decreased the biodiversity effect. Ultimately, results from this study show 1) the importance of biodiversity for ecosystem functions demonstrated in homogenous, random assembly experiments applies to heterogeneous, naturally assembled communities; and 2) the strength of this relationship depends on both the environmental conditions and distribution of functional traits. These results have important implications for extending current theory to better predict how biotic homogenization and habitat loss will alter the functions of real-world ecosystems.

Does Tau Pathology in the Sublaterodorsal Region Affect Sleep Patterns in Mice?

Vishal Krishnan

Mentor: David Holtzman

Tauopathies are a class of neurodegenerative diseases associated with the aggregation of tau protein including, but not limited to, Alzheimer's disease (AD), frontotemporal dementia, and progressive supranuclear palsy. In addition to neurodegeneration, Tauopathy patients are predisposed to sleep disturbances such as insomnia, excessive daytime sleepiness, and rapid eye movement (REM) sleep disorder. The neurological basis of this observation is largely unknown. In recent studies, it was determined that an injection carrying a cholinergic agonist to the dorsomedial pons induces REM sleep muscle atonia. Within this region, is the area of the brain known as the sublaterodorsal nucleus (SLD). The SLD is a structure thought to be both necessary and sufficient for generating REM sleep muscle atonia. The Holtzman Lab has identified REM sleep disturbances at a point in the lifecycle of P301S mice that coincides with a significantly increased amount of tau pathology in this region. It is unclear if tau pathology in the SLD region has a significant effect on REM sleep patterns. The purpose of this experiment was to better understand the relationship between tau pathology in the SLD region and the sleep patterns in mice (specifically REM sleep). The SLD regions of the P301S htau transgenic mice were directly injected with wild-type or P301S brain lysate. We studied the REM, non-REM, and wake cycles of the mice. The preliminary results indicate that there is little to no significant relationship between tau pathology in the SLD and the sleep patterns of P301S mice.

ROCK Inhibitors Prevent DLK Activation in a Regenerative Context

Trevor J. Krolak

Mentor: Aaron DiAntonio

During development, neurons extend axons across great distances to form a neural network. However, the length of axons makes them vulnerable to injury and disease. Following injury, axons degenerate and must be regrown to restore function.

In the central nervous system, regeneration fails completely. By contrast, in the peripheral nervous system, neurons activate a regenerative response that is capable of achieving limited regrowth. In severe cases, however, this regeneration is insufficient for functional recovery. If the regenerative program could be induced or sustained pharmacologically, functional recovery would be more obtainable.

The DiAntonio laboratory has previously demonstrated that Dual Leucine Zipper Kinase (DLK), a stress-induced MAP triple kinase, is required for activation of the regenerative program following injury. However, the regulatory mechanisms governing DLK remain poorly understood.

Using an *in vitro* assay of DLK activity, we demonstrated that ROCK inhibitors (ROCKi) could block cytoskeletal stress-induced, DLK-dependent regenerative signaling. Because DLK signaling plays an important role in other aspects of the neuronal injury response, including axon degeneration and cell death, we examined the ability of ROCKi to influence these responses. Treatment with the inhibitors did not affect cell death or axon degeneration, suggesting that their capacity to regulate DLK activity is restricted to a regenerative context.

Ultimately, our work has identified novel pharmacological regulators of DLK, a kinase required for activation of the regenerative program, and interrogated their mechanism. An expanded understanding of the program's regulatory mechanisms will provide therapeutic targets to combat neurodegenerative disease and injury.

Impact of Belowground Arthropods and Fungi on Germination Rates and Seedling Survival of Exotic and Native Plant Species in Missouri

Molly Kuhs

Mentor: Scott Mangan

Although biological invasion is one of the largest threats facing our ecosystems today, we still do not have reliable methods to help predict which species will become potential invaders. Belowground arthropods and fungi have been shown to strongly influence species invasion capacity, as well as influence plant community assembly. According to the enemy release hypothesis, exotic plants become invasive by escaping their co-evolved belowground enemies and by being unrecognized or unpalatable to belowground enemies occurring in the introduced range. I tested this hypothesis through an exclusion experiment using three native and four exotic species common to central Missouri. In a greenhouse study, I tested how the exclusion of belowground insects and fungi affected seedling germination, establishment and early development of native and exotic species. I found that removal of belowground insects and fungi significantly altered the germination success of native species, while having no significant effect on exotic species. I also found that above and belowground biomass of the native species significantly increased when soil-borne insects and fungi were removed, while such removal had no effect on plants exotic to the region. These results lend support for the enemy release hypothesis and suggest that belowground insect and fungi communities may play a role in shaping plant community assembly and invasion.

A Deep Network for Predicting the Epoxidation of Drug-Like Molecules Generalizes to an External Test Set

Ayush Kumar

Mentor: S. Joshua Swamidass

Drug toxicity studies cost billions of dollars annually. A major driver of this expense is unexpected adverse drug reactions, which are frequently caused by reactive drug metabolites. Epoxides, a class of potent electrophilic cyclic ethers, are one of the most common types of reactive metabolites, and our study focuses on developing a computational model capable of identifying the site of epoxidation (SOE) and epoxidized molecules in order to provide a rapid screening tool for a key drug toxicity risk.

Our model utilized a deep convolutional network and 702 epoxidation reactions to predict SOE within epoxidized molecules, and predict the likelihood that a molecule will be epoxidized. In order to determine the generalizability of the final model, a cross-validation protocol and external test set were used. The cross-validation protocol contained 389 epoxidized molecules and the external test set contained 13 epoxidized molecules with their labeled SOEs. The average site AUC and top-two metrics were used to evaluate the accuracy of the two models. The final epoxidation model that was developed was able to determine SOEs within the molecules in the cross-validation dataset with an average site area under the curve (AUC) of 95.9%. Similar accuracies were demonstrated by the model for the external test set with a 93.7% average site AUC. Furthermore, the model separated epoxidized and non-epoxidized molecules with 79.4% AUC for the cross-validation and 82.4% AUC for the external test sets. Currently, there is no other epoxidation model reported in the literature, and we have shown that our model not only identifies molecules capable of epoxidation, but also the specific sites of epoxidation, which can direct rational structural modifications to make drugs safer. This novel model can be used for early-drug screening and provide researchers with another tool to limit drug toxicity.

Identifying and Characterizing the Mutational Landscape of Noncirrhotic Hepatocellular Carcinoma

Jason Kunisaki

Mentor: Obi Griffith

Hepatocellular carcinoma (HCC) is the 5th highest diagnosed cancer type worldwide, and with the 2nd highest mortality rate, it contributes to 750,000 cancer related deaths per year. Cirrhotic HCC, which comprises of 80% of all cases, is strongly associated with hepatitis B/C infection, alcohol abuse, and fatty liver disease. Noncirrhotic HCC, making up the remainder 20% of HCC cases, can occur with no known underlying liver disease. Because the liver maintains normal functionality, noncirrhotic tumors are often detected at a more advanced stage, and have a high recurrence rate.

To understand the genomic landscape of noncirrhotic HCC, whole genome and transcriptome sequencing was performed on a discovery cohort consisting of 26 matched tumor/normal noncirrhotic HCC samples, as well as 3 matched tumor/normal cirrhotic samples. Analysis on the discovery set focused on structural variation (SV), gene fusion, copy number variation (CNV), loss of heterozygosity (LOH), and differential expression. Custom targeted capture sequencing was performed on another 87 HCC samples, and the total of 116 samples were analyzed for single nucleotide variants (SNVs) and insertions and deletions (INDELS).

Recurrent losses were observed in 6q, 8p, 13q, and 17p, with LOH of 8p being associated with lymphovascular space invasion (LVSI) and a shorter recurrence free survival. Copy number deletions at 2q were associated with a shorter overall survival. Recurrent SVs occurred at DNA repair genes (*MACROD2*), nuclear receptor signaling genes (*NCOR1*), cell adhesion genes (*CNTN1*), and microtubule organization genes (*CEP57L1*). Novel fusions involving *NR1H4* were found in 2/29 HCC samples, and mutations in *CTNNB1*, *FRAS1*, *RPS6KA3*, *RB1*, and *C5* were associated with shorter overall and/or shorter recurrence free survival.

We conclude that several genes and mutational events are potentially implicated in HCC development and progression. However, these mutational events largely do not appear to be specific to noncirrhotic HCC.

Lead Iodide Crystal Synthesis for Single Crystal Conversion Studies to Lead Perovskites

Craig Laing

Mentor: Bryce Sadtler

We report the synthesis of lead iodide crystals of various sizes grown via solution-phase colloidal chemistry. Different solvent systems were investigated using different surfactants and reaction conditions to develop a lead iodide crystal synthesis for use in single crystal conversion studies to lead perovskites. Different solvent systems involving ethylene glycol (EG) and either isopropanol or 1,4-butanediol were used to precipitate microcrystals of lead iodide from lead nitrate and potassium iodide. Polyvinylpyrrolidone and hexadecyltrimethylammonium bromide were used as a surfactant in an attempt to control the size of the particle in an effort to produce nanoparticles of lead iodide. The conditions of the lead iodide microcrystal synthesis were optimized to produce more uniform crystals of the smallest possible size. These crystals were then transformed to lead perovskite and this transformation was studied using various characterization techniques.

PIK3C2G in Multiform Glioblastoma

Patrick Nils Lasowski

Mentor: Milan Chheda

Multiform Glioblastoma (GBM) is an aggressive, malignant cancer which affects glial cells, most commonly in the brain. There are currently no curative treatments available for GBM. It is thought that GBM tumor initiating cells (TICs) strongly contribute to GBM's aggressive and malignant nature. Tumor initiating cells are known for their plasticity, resistance to treatment, self-renewing capabilities, and tumorigenic properties. Knowing more about the specific genes involved in the genetic pathways common to GBM could provide information beneficial to the eventual development of effective GBM therapies. Previous experiments targeting genes amplified in GBM have shown that the knock down of PIK3C2G results in decreased relative cell counts. Additionally, previous experiments have shown that suppression of PIK3C2G in TICs resulted in cell differentiation and cell death. Other previous experiments have focused on PIK3C2G's role in insulin signaling in hepatic cells. Little is currently known about PIK3C2G's role in the brain or elsewhere in the body outside of in the insulin signaling pathway in hepatic cells. In order to investigate the potential proto-oncogenic properties of PIK3C2G, we designed knock down and over expression experiments in a transformed cancer cell line and murine NIH 3T3 cell lines respectively. The designed experiments involve immunoblotting, immunoprecipitation, quantitative PCR, sub-cloning DNA, and shRNA-mediated gene suppression. Initially, we chose to use the gateway system for the overexpression experiment due to its flexibility. However, after concerns regarding potentially low levels of expression when using the gateway system's destination vectors, we settled on using the retroviral vector pBABE-puro instead. Following previous complications, the final stages of this experiment are still underway.

Geographic Analysis of Weak Educational Institutions and Their Associated Ecological Risk in Missouri

Chase Latour

Mentor: Rumi Price

Goals of secondary educational institutions are to provide students with an education as well as a supportive and engaging environment. However, when they fail to meet the standards to achieve and maintain these goals, students can be at risk for numerous adverse outcomes. To understand individual risk for adverse outcomes, we consider the ecological risk factors associated with schools according to the *Weak Institution* perspective. This perspective holds that the breakdown of social institutions (such as schools, family system, etc.) increases the vulnerability of members in those institutions, thus increasing the probability of adverse behavioral and situational outcomes later in their life course. To understand the ecological risk factors, we empirically examined school system based data and identified the spatial distribution of higher-risk school districts in Missouri. We used performance measures from publicly-available school district data for public school districts (N = 455 school districts). These measures included attendance and rates of dropout, graduation, and discipline as well as free and reduced lunch percentages and student to classroom teacher ratios. Factor analytic techniques were applied to combine these measures to create an aggregated risk score for each school district. Our analysis shows that the variables that carry the most weight for determining the risk scores are attendance, dropout, graduation, and discipline rates. We mapped the risk scores of the school districts in Missouri on a relative scale according to their factor scores. The results are presented in a map format so that law-makers and advocacy groups can more easily identify the districts that may need increased assistance.

The Role of STAT3 in Alzheimer's Disease Associated Amyloid Beta Damages

Molly Lawrence

Mentor: Itender Singh

One of the hallmarks of Alzheimer's disease (AD) is the buildup of amyloid-beta peptide in brain parenchyma and blood vessels. Accumulation of these deposits on blood vessels, known as cerebral amyloid angiopathy (CAA), has been shown to decrease functional reactivity and cerebral blood flow in brain, resulting in cerebrovascular dysfunction and cognitive decline.

Amyloid-beta is also found to cause vascular oxidative stress, suggesting that the toxicity of the protein is related to the production of reactive oxygen species (ROS). Recent studies support this, showing that inhibition of ROS and NADPH oxidase, a transmembrane enzyme that catalyzes production of superoxides, reduces amyloid-beta related deficits in mice. However, the mechanism by which amyloid-beta causes this oxidative stress is not yet well understood.

STAT3 (signal transducer and activator of transcription 3) is known to be a primary regulator of NADPH oxidase and is shown to be activated in higher levels in brains of Alzheimer's patients. We hypothesize that STAT3 is a pivotal upstream regulator of amyloid-beta induced damage.

Our objective for this study was to evaluate the role of STAT3 in behavioral deficits *in vivo*. We used mice bred to express 5 mutations of familial AD, called the 5xFAD model, that are prone to significant amyloid-beta deficits. To inhibit STAT3, 12-month old 5xFAD mice showing CAA were injected with an inhibitor drug, LLL-12, over several weeks. Subsequently, cognitive function was analyzed through novel object location and recognition tests, burrowing behavior tests, and Y-maze tests. We observed improved hippocampal dependent memory in the STAT3 inhibited 5xFAD mice compared to their littermate controls. This suggests that STAT3 plays a key role in amyloid-beta deficits, and could act as an effective therapeutic target for AD patients.

The Effect of Negative Affect on Anxiety Trajectories

Clara Lee

Mentor: Thomas L. Rodebaugh

Individuals with social anxiety disorder (SAD) are known to have significant anxiety surrounding feared social events. Prior research has shown that, compared to healthy controls, those with SAD show higher levels of anxiety in anticipation of and immediately after a speech. However, predictors of anxiety trajectory during a prolonged period after the occurrence of a stressful event and whether anxiety returns to baseline have yet to be explored. In this study, we examined the effect of trait negative affect (NA) on differences in anticipatory anxiety using latent trajectory models (LTMs) of state anxiety prior to a speech and attenuating anxiety after a speech. Participants were randomized into either the induced anticipatory anxiety (IAA) group or a no induced anxiety (NIA) group, and then completed computerized tasks and a speech task. The IAA group received reminders about the speech task prior to the speech, while the NIA group did not receive any reminders. We hypothesized that negative affect would predict higher intercept (baseline anxiety), steeper positive slope 1 (S1; change in anxiety from baseline to speech), and less steep negative slope 2 (S2; change in anxiety post-speech) in the IAA condition compared to NIA. We examined a piecewise LTM with Group x Negative Affect interaction as a predictor. There was a main effect of NA on the intercept, indicating higher levels of baseline anxiety were predicted by greater NA. However, NA did not predict S1 and no significant variance was found for S2, indicating little variation in post-speech rates of anxiety attenuation among subjects. Our results suggest clinical implications regarding interventions for managing anxiety in context of feared events. If post-event rate of decline in anxiety is not variable, perhaps it is more important to instead target the accumulation of anxiety in anticipation of the event.

CFD Performance of Turbulence Models for Flow from Supersonic Nozzle Exhausts

Han Ju Lee

Mentor: Ramesh Agarwal

This research compares the performance of several eddy-viscosity turbulence models for computing supersonic nozzle exhaust flows. These flows are of relevance in the development of future supersonic transport airplane. Flow simulations of exhaust flows from two supersonic nozzles are computed using ANSYS Fluent. Simulation results are compared to experimental data to assess the performance of various one- and two-equation turbulence models for accurately predicting the supersonic plume flow. Results show that the standard eddy-viscosity models can capture the shock structure and shear layer of the plume accurately when the thickness of the shear layer is small compared to plume diameter. However, when thickness of the shear layer is relatively large, a compressibility correction is required for accurate simulation. Compressibility corrections are implemented in simulations with SST k-ω, k-ε and low Reynolds versions of k-ε models which improved the results compared to the baseline models without compressibility correction.

Calculating the Physical Properties of Black Holes

Heather Lee

Mentor: Henric Krawczynski

Using equations and tables made by the physicist Chandrasekhar, our team built a code to potentially calculate the properties of black holes using the polarization of light bent around the black hole. Chandrasekhar's equations, however, leave out some key variables that may have a measurable impact on the outputs. Because of this, I looked at the derivations of equations and tables found in *Radiative Transfer*, in order to understand how Chandrasekhar formulated his calculations and then included some of the variables, notably partial Rayleigh scattering, into the equations to make them more accurate for our intended use.

The first step in this process was understanding Chandrasekhar's results, so I began by recreating them through dissecting his equations and using them to recreate notable tables. The results of this were inconclusive as I was unable to find the base to use interpolation to calculate the H-function: an important part of later calculations. The contents of this essay, however, include the means by which other variables are defined and the iterative process necessary to calculate the H-function. Unfortunately, because of time restraints, I did not make it to the next step: altering the equations themselves.

This is important in calculating the properties of black holes of which there are three: mass, spin, and charge. Because the properties are interdependent, one of the properties must be known to calculate the others. The problem, however, lies in that black holes are not directly observed; we must calculate one of the properties based on something that interacts with it. Using the polarization of photons would make the mass of the black hole readily known and from this we could calculate the others.

Designing Ultrasensitive Responses in Cellular Systems by Introducing Cooperativity into Artificial Riboswitches

Matthew Leong

Mentor: Tae Seok Moon

An interest in synthetic biology is creating systems with higher sensitivity to stimulus, which allows for response thresholds to be achieved in biosensors and systems to behave in a more predictable manner. One way in which nature elicits this response is through cooperativity, the biochemical principle in which the binding of a ligand increases the rate of subsequent ligand binding events. This research focused on introducing cooperativity into the toehold riboswitch, an artificial and versatile post-transcriptional form of gene regulation. Toehold switches are a form of RNA secondary structure that forms upstream of a gene, sequestering the ribosome binding site in the absence of a trans-acting RNA. By introducing cooperativity, we hope to not only achieve higher degrees of stimulus sensitivity, but also to test the limits of how well RNA behavior can be designed through theoretical computer simulations. By using the RNA simulation program NUPACK, additional ligand binding sites were rationally introduced into the original riboswitch design. A model was then generated with parameters taken from literature to show that theoretical results from these modifications would yield higher sensitivity. The riboswitches were then cloned upstream of a fluorescent reporter protein and downstream of a constitutive promoter using inverse PCR. The trans-activating RNAs were similarly cloned downstream of inducible promoters. These two vectors were transformed into *E. coli* and inducer concentration transfer curves were experimentally constructed. These transfer curves were then fitted to the general Hill equation to obtain general Hill coefficients which were used to quantitatively measure cooperativity in the system. It was found that an increase in the number of ligand binding sites decreased the absolute fluorescence but increased the general Hill coefficient, which may be indicative of the presence of cooperativity.

Identification of Genes Essential for Orsay Virus Infection in *C. elegans*

Christian Leung

Mentor: David Wang

The host factors responsible for viral infections remain poorly characterized, in part, due to a lack of systematic approaches that identify such factors in a whole organism. The model organism, *C. elegans*, has proven invaluable in dissecting many biological processes conserved from worms to humans. Study of host-virus interaction was limited in *C. elegans* due to the lack of a natural infecting virus. The Wang Lab has discovered the Orsay virus, a single-stranded, positive sense RNA virus that infects and replicates in a subset of the twenty intestinal cells of the host *C. elegans*.

Through a forward based genetic screen, we have identified three mutant lines that block or inhibit Orsay virus infection. Out of these three, we focus on *viro-133* and *viro-116*, which identify a premature stop codon in the gene *sid-3* and *B0280.13*, respectively. Genome annotation showed that *sid-3* encodes a non-receptor tyrosine kinase and *B0280.13* encodes an ortholog of the human WAS (Wiskot-Aldrich Syndrome) gene. We examine the mechanism of these genes in the context of Orsay virus infection.

To understand these genes, we first confirm that loss of function in *sid-3* or *B0280.13* blocks viral infection by confirming that an independently generated null allele of either *sid-3* or *B0280.13* causes the same phenotype. Second, we assess whether the mutation in these genes block viral entry by examining *viro-133* or *viro-116* worms that possess a heat inducible integrated viral genome. In these mutant worms, exogenous viral infection is blocked, but viral infection through heat induction is successful. Bypassing the entry step allows the Orsay virus to complete its lifecycle, suggesting that *sid-3* and *B0280.13* are involved in an early stage of the viral lifecycle, such as virus entry. These results begin to elucidate the nature and mechanism of these two host factors in Orsay virus infection.

Experiencing Lupus: An Illness Narrative

Jerik Leung

Mentors: Alfred Kim and Rebecca Lester

The aim of this research is to foreground individuals' experiences with Lupus including encounters with diagnosis, treatment, and disease course in order to highlight how social misunderstandings and stigma about this condition affect the delivery of care. An overarching theme of ambiguity plays a prominent role in numerous facets of the individual illness experience. From a biomedical perspective, Lupus is a notoriously ambiguous disease without a concrete method of diagnosis or stable course of disease. While there is a wealth of literature that aims to explore Lupus in the context of its ambiguity, it primarily represents the positions of health care providers who typically lack experiential evidence of living with Lupus. Through in-depth interviews and ethnographic fieldwork, I sought to understand how people with Lupus themselves understand and find meaning in the ambiguity of their illness. In viewing Lupus from these differing perspectives of health care providers and individual suffers, tension between these two parties caused by Lupus' inherent ambiguity becomes clear. Health care providers experience pressure to deliver clinically certain models to an illness in which uncertainty is one of the primary facets of the illness experience. In exploring this tension, I primarily draw on anthropological work surrounding models of chronic illness and social dimensions of immunology in order to contextualize how individuals with Lupus situate themselves in these frameworks. I present potential practical implications of integrating ethnographic findings as a means of improving existing treatment for individuals with Lupus.

Molecular Mechanisms of pH Modulation of Cardiac Sodium Channels ($Na_v1.5$)

Bicong Li

Mentor: Jonathan Silva

During ischemic heart disease, pH drops from 7.4 to 6.0 within 10 minutes of onset, severely affecting ion channel gating. The cardiac sodium channel ($Na_v1.5$) is particularly susceptible to this abrupt pH change, and its altered gating is thought to predispose patients suffering ischemia to arrhythmia and sudden cardiac death. We observed the voltage-sensing domains (VSDs) of $Na_v1.5$ to discover molecular mechanisms of its regulation by pH.

A cysteine mutation was made in each of the four VSDs (DI-DIV) of $Na_v1.5$. Synthesized RNA from these constructs was injected into *Xenopus oocytes*. Once channels were expressing, a fluorophore was tethered to the cysteine via a disulfide bond. By measuring the kinetics and change in magnitude of the fluorescence, we were able to track VSD conformational changes along with the current-voltage relationship.

We found that reducing the pH of the extracellular solution from 7.4 to 6.0 causes I_{Na} to decrease in magnitude by 50%, and shifts in both activation and fast inactivation rightward, consistent with previous results. At a pH of 6.0, time to peak was reduced by 300% while inactivation was only 10% slower. Observation of the VSDs showed that the DII-VSD is not affected by pH, and the DIII-VSD showed a small depolarizing activation shift ~6.65 mV. The DIV-VSD displayed a complex phenotype, not shifting after short pulses, but shifting prominently (23.27 mV) after prolonged pulses. Its kinetics were also slowed by a factor of 2 at a pH of 6.0.

These results suggest an important role for the DIV-VSD in determining regulation of $Na_v1.5$ by pH.

What Types of Flashcards Improve Science Test Performance?

Chelsea Lin

Mentor: Mark A. McDaniel

Flashcards are one of the most popular study methods that students use to study for exams, helping to enhance memory and increase test performance. However, little is known about the mechanism of the benefits of creating flashcards and the type of flashcards that are the most effective. In this experiment, we explore whether self-generated flashcards result in better test performance than company-provided flashcards. We are also interested in illuminating potential methods to create better flashcards. Participants read different passages—a biological anthropology passage about dating methods or a geology passage about tectonic plates—and were in different study conditions. The study conditions included one group that self-generated flashcards, a group that received company-provided flashcards, a group that instructed participants to create conceptual flashcards, and a group that was given paper and pen as a "free study" group. After the study period, the participants took a quiz which included eight multiple-choice questions and five free-response questions. The free-response targeted conceptual information whereas the multiple-choice targeted the retention of the presented information, a mixture common in science exams. We hypothesize that the group who generates conceptual flashcards will perform the best and that in general, generating flashcards will be more beneficial than being provided flashcards. The results should contribute to a more comprehensive understanding of how and what kind of flashcards are useful for students.

Effect of Circadian Rhythmicity on Sensory Reception in Weakly Electric Fish

Anan Lu

Mentor: Bruce Carlson

Mormyrids are weakly electric fish that communicate and navigate through their environment using an electric organ discharge (EOD). Electrosensory neurons in their brains establish a neural network that detects the EODs of other fish, i.e., electric communication signals, in their surroundings. Biologically, nearly all living organisms experience a circadian rhythm that regulates behavior and physiology. I want to know, therefore, whether there are changes in the electrosensory system that mediate variation in behavioral sensitivity to communication signals during the day versus during the night. And, if such changes exist, to identify the pattern of variation throughout the 24-hour cycle. Since mormyrids are largely nocturnal species that are quiescent for most of the day and highly active during the night, I hypothesize that their sensory systems will show greater sensitivity for identical stimuli presented during periods of vigilance (night) than those presented during periods of rest (day). To test this, I measured extracellular evoked potentials in response to a range of natural EOD stimuli presented in 20-minute intervals on 12 randomly selected *Brevimyrus niger*. Each fish's brain activity was recorded for 6 hours straight via an electrode, with a 4-hour overlap between each successive fish in order to cover the entire 24-hour cycle and to minimize inter-fish variance. Results from these 12 fish are inconclusive, as there were possible factors that may have caused the pattern of sensitivity to external stimuli not related to the fish's natural circadian rhythm. Further experiments and data analysis will be needed to assess whether circadian rhythmicity plays a role in sensory perception in mormyrids.

Searching for Extended Halos around TeV Blazars with Fermi LAT

Bohan Lu

Mentors: Manel Errando and Henric Krawczynski

At the center of certain elliptic galaxies, also known as blazars, are super massive black holes that eject jets of ionized material that travel close to the speed of light. Relativistic jets from blazars that have hard spectra in the TeV band are suggested to interact with the proposed extragalactic magnetic fields to produce halo-like extended cascade emission. In this study we analyzed high energy gamma rays based on the data from the Fermi Large Area Telescope (LAT) and attempted to detect the speculated halo-like extended emission around TeV blazars. We extracted and filtered events from the Fermi LAT database and performed maximum likelihood analysis against the null hypothesis that such halos are absent. Although still inconclusive, the results we obtained showed that seven out of ten sources we analyzed exhibit relatively strong patterns that could be interpreted as halo-like extended emission. This interpretation, if verified, would imply the existence of extragalactic magnetic field with a moderate field strength. A further validation of the detection significance of the halos is needed, which, if performed successfully, could establish a preliminary ground for future studies in the origins of extragalactic magnetic field and reveal more information about the very high energy blazars.

Investigating the Role of *actr10* in Schwann Cells of the Peripheral Nervous System

Melissa Lu

Mentor: Kelly R. Monk

Myelin is the lipid-rich sheath surrounding axons that promotes the rapid propagation of action potentials. Myelin is made by oligodendrocytes (OLs) in the central nervous system (CNS) and Schwann cells (SCs) in the peripheral nervous system (PNS). Proper myelination of axons is essential for growth and development, and damage to myelin and/or the myelinating glial cells that make myelin can result in neurodegenerative diseases such as multiple sclerosis or Charcot-Marie-Tooth disease. A forward genetic screen performed by the Monk Lab found a mutant, *stl83*, that has reduced myelin in both the CNS and PNS, as assayed by in situ hybridization for *myelin basic protein (mbp)* expression, which marks the mature myelin sheath. The *stl83* phenotype results from a single nucleotide polymorphism (SNP) in the gene *actr10*, which encodes the protein Arp11. Arp11 forms a component of the dynactin motor protein complex, which plays a critical role in cellular transport by directly binding to the motor protein dynein and facilitating retrograde transport of intracellular cargo along microtubules. We hypothesize that the mutation in actr10 prevents proper formation of the dynactin complex, and thus causes a disruption in transport and trafficking. Methods used include the aforementioned *in situ* hybridization, as well as transgene analysis to observe expression of early SC developmental markers such as *foxd3* and *sox10*. Preliminary data involving the drug forskolin, which rescues *mbp* expression, is also included.

Rodent Herpesvirus Texas (RHVT) Encodes a High Affinity Chemokine Decoy Receptor

Yun Hsuan Lu

Mentor: Daved Fremont

Double-stranded DNA viruses have evolved multiple ways of evading host immune surveillance. Viruses target host cytokines that function as early mediators of host immune response and interfere with cytokine signaling through three mechanisms: viral homologs of cytokines, cytokine receptors, and/or sequence diverse soluble decoy receptors.

M3, encoded by mouse gammaherpesvirus 68 (MHV68), was the first herpesvirus-encoded decoy receptor characterized. M3 broadly recognizes C, CC, CXC, and CX3C chemokines, but exhibits high affinity for certain CC and CXC chemokines. Functionally, M3 inhibits chemokine signaling by binding chemokines through the same determinants as their endogenous receptors, but with a higher affinity. Another chemokine-binding protein from herpesvirus Peru (RHVP) has been identified and characterized. RHVP-encoded R17 shares little sequence similarity with M3, yet is structurally similar to M3 and specifically binds certain CC and C chemokines. R17 also interacts with cell surfaces via cell-surface glycosaminoglycans (GAGs). Functionally, much like M3, R17 antagonizes chemokine signaling.

The sequence of another rhadinovirus, rodent herpesvirus Texas (RHVT), has recently become available. RHVT encodes a protein, T17, that shares 32% sequence similarity with R17. Is T17 also a chemokine-binding protein, and if so, what is its binding specificity? This project focuses on comparing R17 and T17 through a systematic analysis of their GAG and chemokine-binding abilities, and the subsequent effect on chemokine-guided transmigration. Cell staining experiments show that T17, like R17, interacts with GAGs. Direct binding experiments reveal that T17, like R17, recognizes specific CC and C chemokines, but can additionally bind certain CXC chemokines. Functionally, my preliminary data suggest that T17 inhibits CXCL12 and CCL2-mediated transmigration of Jurkat T cells and THP-1 cells, respectively. Having demonstrated that T17 is a chemokine-binding protein, we can now focus on the molecular determinants responsible for its different chemokine-binding specificities, and their effects on the modulation of the host immune system.

Cognitive Effects of Hiding Emotion in a Social Situation

Sean Lydon

Mentor: Tammy English

Expressive suppression (i.e., active efforts to minimize emotional expression) has been shown to impair explicit and episodic memory in delayed recall tasks, but it remains unclear how this regulatory strategy influences cognitive processing in a socially stressed environment. Past studies have focused on testing cognitive performance using less interactive stimuli, such as video clips and pictures, to elicit emotion. Research suggests that cognitive processing in a realistic, social atmosphere will have a discriminating effect on attentional resources in suppressors compared to non-suppressors. In the present study, cognitive performance was measured with three types of tasks: immediate recall, verbal fluency, and arithmetic processing. Undergraduates were randomly instructed to hide emotion (suppression condition) or uninstructed (control condition), then participated in a mock job interview. Self-reports of emotional experience, use of emotion regulation, and state social anxiety were collected following the interview. The interviews were filmed to allow for behavioral analysis. We hypothesized that suppressors would show decreased cognitive performance as well as experience higher levels of stress and anxiety compared to uninstructed participants. Analysis showed that participants reported equal usage of expressive suppression and cognitive reappraisal. Within these strategies, results suggest that attentional resources are equally unaffected in high stress social situations. Additionally, cognitive reappraisal and expressive suppression were both equally effective at regulating positive and negative emotional experience. This study incorporates strong emotional and social factors in measurements of immediate cognitive processing to provide a new direction for the study of cognitive performance in emotion regulation.

Grey Matter Volume and Functional Connectivity of the Frontoparietal Network in Schizophrenia

Anita Mahadevan

Mentor: Deanna Barch

Schizophrenia is a chronic psychiatric disorder that afflicts approximately 1% of the population. A particularly debilitating symptom of schizophrenia manifests as cognitive deficits, which contribute to struggles in everyday functioning; however the neural mechanisms underlying these deficits remain unclear. Past research suggests cognitive impairment may be associated with abnormalities in prefrontal brain structure such as reduced grey matter volume, while a separate line of research has implicated abnormal functional connectivity of the frontoparietal network (FPN). Importantly, the association between structural and functional abnormalities, and their relationships with cognition, have not yet been explored. In this study, we analyzed data from193 healthy controls and 146 schizophrenia participants. We assessed group differences in grey matter volume and resting-state functional connectivity of frontal nodes within the FPN. We predicted reduced volume and connectivity in schizophrenia participants compared to controls. Furthermore, we studied the relationship between grey matter volume and functional connectivity of regions within the FPN, and predicted that reduced grey matter volume of these regions would correlate with reduced functional connectivity. Finally, we assessed the relevance of these brain measures to cognitive ability. Contrary to our hypotheses, we found that grey matter volume and functional connectivity of our regions of interest were not significantly different between diagnostic groups. However, functional connectivity of two nodes within the frontal gyrus were significantly associated with grey matter volume of the inferior, orbital, and medial frontal gyri, though this relationship did not differ significantly by diagnostic group. Finally, FPN functional connectivity did not predict cognitive performance on tasks. These data suggest that in schizophrenia, grey matter volume of the prefrontal cortex does not relate to the functional connectivity of FPN nodes in this region, and furthermore that the communication of these FPN nodes does not account for the global cognitive deficits observed with schizophrenia.

Theory of Mind Priming Pilot: Rating the Ambiguity of Revised Line of Sight Probe Task Stimuli

Julia Mandel

Mentor: John Pruett

Theory of mind (ToM) is the ability to reason about the mental state of another agent, as in considering another agent's beliefs and intentions. While we know that humans possess ToM based upon self-report methods, there is presently no definitive objective test for ToM use. While many approaches have been used to test ToM, they all fail to eliminate the possibility that performance can be explained by proximal causal variables, rather than ToM. We believe ToM can be tested objectively by priming ToM in subjects prior to performing a probe task involving line-of-sight judgments that are likely influenced by ToM under conditions of varying ambiguity. This experiment was necessary to norm the varying ambiguity levels of the stimuli used in this probe task. The stimulus images depict a man in a room looking out a window at a UFO. The height of the man, UFO, and shade on the window differ, creating combinations of varying ambiguity regarding whether or not the man can see the UFO. Responses from sixteen valid participants were recorded. On a computer, each subject viewed each stimulus image ten times, thus completing 270 trials of the line-of-sight judgment task. Ambiguity was defined both by the average number of times a subject deemed the UFO seen for a particular stimulus image (percent called seen), as well as reaction time for each image. The average percent called seen and mean median reaction time was determined for each stimulus image, plotted, and then analyzed using a hierarchical cluster analysis. This cluster analysis was combined with experimenter judgments of ambiguity, and it was found that the data are best fit into seven clusters representing five different levels of ambiguity. With this knowledge, stimulus images from each ambiguity level can be presented at optimal rates during the probe task.

Coding Political Preferences for Commissioners of the European Commission

Bradley Mankoff

Mentor: Matthew Gabel

The European Commission is the body responsible for initiating all legislation in the EU. It is checked by the European Parliament and Council, but only it can initiate change. Political scientists refer to any actor similar to the Commission as the 'agenda-setter,' which they argue has immense sway over outcomes, especially relative to bodies like the Parliament that have no agenda-setting power.

Selected by the heads of state of the 28 EU member states, otherwise known as the European Council, the President of the European Commission receives a list of 27 politicians or technocrats, one nominated by each member state other than his or her own, and assigns each of them to a portfolio in the Commission. These portfolios serve a similar purpose to the various agencies in the Executive Branch of the United States Federal Government. The President is given no legal guidelines as to how he may assign portfolios, and the member state cabinets that nominate their country's prospective commissioner are theoretically unsure as to which portfolio their nominee will ultimately be assigned. In reality, however, larger member states continually nominate bureaucrats specializing in economic or financial issues that qualify them for major posts involving agriculture, financial regulation, taxation, and other important issues.

The purpose of this research is to update Fabio Franchino's 2009 research to include the three most recent Commissions in his data sample. Franchino introduces his paper by proclaiming that, "The share of portfolios that each Member State is assigned, through its Commissioners, is strongly related to its resources and voting power, as predicted by the proportionality norm and bargaining theory, respectively."

Longitudinal Study of *Saguinus weddelli* and *Saguinus imperator* in Southeastern Perú

Annie Marggraff

Mentor: Mrinalini Erkenswick Watsa

Few primates are more visibly and genetically identical than callitrichids, which have an astonishing rate of twin births (≥80% of births). This phenomenon, termed genetic chimerism, is an incredible illustration of abnormally high genetic relatedness, making the research of callitrichids important in studying the evolution of primate reproductive systems. I assisted in this longitudinal investigation by gathering morphological, physiological and health data on two species of individually identifiable saddleback (*Saguinus fuscicollis*) and emperor (*Saguinus imperator*) tamarins in southeastern Peru at the Los Amigos Conservation Field Station. The goal of this collected data is to analyze group structure, reproductive success, and individual growth and development in these species. We used a unique capture and release system to gather individual physiological, morphological, and health data about each individual. A recently completed meta-analysis using the gathered data showed that adult females and group size, not the number of adult males, significantly correlates with group reproductive output. These results will help predict future reproductive growth, allowing researchers to track fluctuation in group sizes, possibly relating this data to environmental changes.

Transposon Mutagenesis: The Key to Discovering the Genetic Factors Behind the *Dictyostelium discoideum* and *Burkholderia* Symbiosis

Rory Mather

Mentors: David Queller and Joan Strassmann

The interaction between the bacterium *Burkholderia* and social amoeba *Dictyostelium discoideum* has become a model for both symbiotic relationships and even agriculture within microorganisms. However, one major obstacle preventing a full understanding of the relationship between these two organisms is what are the genetic factors that cause it. Our lab used transposon mutagenesis to singularly mutate every gene with the genome of *Burkholderia fungorum*, a strain of *Burkholderia* known not to engage in a symbiotic relationship with *Dictyostelium discoideum*. Our future plan is to then grow the mutants with the social amoeba and isolate knockouts that develop a symbiotic relationship. By creating a library of genes that promote this specific symbiotic relationship, we can use it to search for analogs within other symbiotic organisms and further our understanding of what general genetic factors lead to these relationships as a whole.

Expanding Our Understanding of Photoautotrophic Iron Oxidation on Earth

Beau McGinley

Mentor: Arpita Bose

Iron is critical for all living organisms as both a nutrient, and as an electron donor or acceptor for microbial metabolism. Fe(III) can serve as a terminal electron acceptor for iron-reducing bacteria and Fe(II) can serve as an electron donor for iron-oxidizing bacteria. Phototrophic Fe(II)-oxidation (photoferrotrophy) is a special form of iron oxidation through which some bacteria can use the energy of light and electrons from Fe(II) to fix carbon dioxide to biomass. The mechanisms underlying photoferrotrophy are relatively unexplored. This is largely because we only have one model organism to study this process, a freshwater purple nonsulfur bacterium (PNSB) named *Rhodopseudomonas palustris* TIE-1. Given the abundance of iron on Earth, the significance of photoferrotrophy may extend beyond our current understanding. For example, we don't fully appreciate the role of photoferrotrophy in marine environments. Using a collection of natural isolates of marine PNSB, we investigated the prevalence of photoferrotrophy in marine ecosystems. We used an unbiased approach to isolate PNSB from a brackish estuary near Woods Hole, MA. We sequenced the genomes of all these isolates, and using comparative genomics, we determined these isolates consist of *Rhodovulum sulfidophilum*, *Rhodobacter sphaeroides*, and *Marichromatium spp*. Of the 22 organisms isolated, 18 were capable of Fe(II)-oxidation, including each of our *Rhodobacter* and *Rhodovulum* isolates. The Fe(II) rates demonstrated by these isolates was faster than any other known photoferrotroph. We are currently generating a knockout for genes to play a role in photoferrotrophy. Overall, our data suggests photoferrotrophy may be prevalent in PNSB and points to a novel photoferrotrophy mechanism in *Rhodobacter* and *Rhodovulum* isolates.

Fast *K*-mer Counting Using the Bi-Directional Burrows-Wheeler Transform

Rishil Mehta

Mentor: Jeremy Buhler

With faster DNA sequence analysis techniques, biologists and clinicians will be able to analyze more DNA in a shorter period of time, allowing them to conduct faster research and better serve their patients. I focused on increasing the speed and lowering the RAM usage of a DNA analysis tool called *k*-mer counting (enumeration of the number of distinct substrings of size *k* within a text). Unlike traditional alignment-based sequencing techniques, *k*-mer counting allows rapid estimation of the similarity between large genomes and/or large unassembled sequence read sets. One of the most efficient counting implementations uses hashing strategies that are fast but require 10 to 100 gigabytes of RAM for genome-sized sequence comparisons. An alternative data structure, the suffix tree, may achieve better running times. Although suffix trees are also memory-intensive, the bi-directional Burrows-Wheeler transform of a DNA string can emulate the behavior of a suffix tree without the overhead of storing the entire tree in memory. I investigated whether *k*-mer counting using virtual suffix trees and the bi-directional Burrows-Wheeler transform could achieve better speeds and/or more efficient RAM usage. My implementation achieved competitive runtimes versus the top competitor program. I also recognized a number of optimizations that will improve the running time/lower RAM usage even further. My virtual suffix tree implementation is indeed a promising candidate to improve the efficiency of *k*-mer counting.

The Jackson Site Is Back! LiDAR-Based Mound Construction and Viewshed Analysis of the Coles Creek Era Poverty Point Landscape

Joy Mersmann

Mentor: T. R. Kidder

The area surrounding Poverty Point in northeast Louisiana is a culturally rich archaeological landscape with a deep chronology linking thousands of years. One of the later occupational features, the Coles Creek era Jackson Place mound group (ca. 700-1200 A.D.), was leveled for farming outside of state park boundaries. Using LiDAR basedata, historic aerial imagery, and descriptions by C.B. Moore, topographic relief of the earthworks is reconstructed in GIS. With these new analytical surfaces, a viewshed analysis from the Jackson Place Mounds suggests the earlier Archaic earthworks, here called heritage structures, were part of the visible Coles Creek landscape.

Machine Learning Psychometric Function Testing

Nikki Metzger

Mentor: Dennis Barbour

Psychometric functions resulting from psychophysical tasks relate physical stimuli to perception. Current methods of psychometric function testing have been designed to be robust and precise, at the expense of efficiency and explanatory power. The Barbour Lab has developed a novel form of psychometric inference that can trade any of these properties for another, thereby yielding an extremely flexible estimator. The current study assessed the agreement between psychometric function thresholds obtained through the lab's novel machine learning (ML) audiometric testing procedure and those obtained from the conventional method of constant stimuli in fifteen participants. Test-retest reliability of the two methods was evaluated in each ear, totaling four tests per ear and eight tests per participant. The ML audiogram tested frequencies from 1,000 Hz to 4,000 Hz, while the method of constant stimuli tested solely 2,000 Hz. The estimated hearing thresholds of these two methods were compared at 2,000 Hz. The hearing thresholds estimated by the lab's ML audiometric testing procedure were very similar to those estimated by the method of constant stimuli: the mean absolute difference between the two different estimates was 4.15 dB SPL. Additionally, the mean absolute difference between repeated measurements of the ML audiogram was 3.80 dB SPL, while the mean absolute difference between repeated measurements of the method of constant stimuli was 2.17 dB SPL. The lab's ML audiometric testing procedure therefore appears to accurately estimate hearing thresholds at 2,000 Hz, suggesting that it also accurately estimates the hearing threshold at all frequencies within the tested range.

Survival of the Fittest: Comparing Synthetic and Clinical Variants of TEM Beta-lactamase

Katelyn Miyasaki

Mentor: Greg Bowman

TEM beta-lactamase is an enzyme produced by bacteria that confers resistance to a number of common antibiotics, such as penicillins. Many variants of TEM exist. Some are seen clinically, while some are synthetic and seen only in laboratory settings. *In vitro* and *in vivo* studies show similar function in synthetic variants as in natural variants. We hypothesize that small differences in fitness are responsible for the synthetic variants not appearing clinically, so we are developing an assay in order to measure these small differences. We are constructing bacterial strains in which TEM expression is linked to expression of a fluorescent protein in order to compete them head-to-head and determine which variants have a competitive advantage. Using strains that express different colors of fluorescent proteins and different TEM variants, we can compare growth by comparing the fluorescent intensity of the different colors. We would like to follow up this study with a series of directed evolution experiments on TEM, using several different variants as starting points. This may shed more light on why some variants are not seen clinically—for example, they may be evolutionary dead ends. We may also encounter novel mutations.

Analyzing Molecular Pathways between Maternal Obesity and Risk of Endometrial Cancer in F1 Mice Generations

Zeel N. Modi

Mentor: Kelle Moley

The incidence and mortality of endometrial cancer have risen by approximately 1.5% and 3.2% respectively in 5 years; 10,470 deaths and 60,050 new cases are anticipated this year. In recent studies, there have been interactions between obesity and Type I endometrial cancer. During pregnancy, if the viable offspring is nurtured in a maternal obesogenic environment, there's a high chance that they would inherit the malfunctioning mitochondria or deregulated epigenetic signatures. These germline modifications result in passing of defective organelles to offspring gametes and can lead to hyper proliferation characterized by hyperplasia and nuclear atypia.

We aim to determine how maternal obesity has contributed to endometrial cancer in offspring by focusing mainly on mice at 72-week time point. To observe whether maternal diet contributed to higher risk of cancer, the mice were fed a control or high fat high sugar (HFHS) diet. After a few weeks, these mice were dissected, and their uteri were collected. We looked for difference in the expression of proteins that have been associated with cancer such as phospho-Pten, Pten, phospho-AKT and AKT of mice on HFHS diet using Western Blotting techniques. We performed Immunohistochemistry to confirm any pathology seen by Hematoxylin and eosin staining (H&E). A pathologist performed pathologic assessment on the stained slides. We observed that offspring exposed to maternal HFHS diet had increased uterine to body weight ratio. Additionally, H&E staining in all cohorts showed neutral phenotype. Lastly, there was no significant different between phospho-AKT or AKT and Phospho-Pten or Pten levels in mice exposed to HFHS diet. In conclusion, maternal diet or direct exposure to HFHS diet mice did not lead to endometrial cancer in initiation by 72 weeks in wild-type C57B/6J offsprings.

Designing β-lactamase Inhibitors to Restore the Efficacy of Existing Antibiotics

Katelyn Moeder

Mentor: Greg Bowman

We use a combination of computer simulations and biochemical experiments to discover druggable pockets in proteins that are not present in their crystallographic structures, which we call cryptic sites. TEM-1 β-lactamase is an enzyme that degrades common β-lactam drugs, rendering bacteria resistant to common antibiotics such as penicillin. By developing β-lactamase inhibitors that bind cryptic sites, we will restore the efficacy of many existing antibiotics. A high-throughput screen was developed and used to discover an inhibitor and two activators, and we are currently trying to verify that these compounds bind in their predicted cryptic pockets by mutating key binding residues identified by computational docking experiments. Through the mutation of these residues, we have been able to alter the effects of one of the compounds on the enzyme, giving strong evidence that the compound binds in the predicted site. We are currently collecting more data on the binding of the other two compounds, and there is evidence both of these compounds bind in their predicted cryptic sites. We are also working on obtaining structural data in the form of NMR and crystallography to compare against our docking and experimental results.

Isolating Different Pools of Tau in the Brain

Paul Moiseyev

Mentor: Randall Bateman

Alzheimer disease (AD) is a debilitating neurodegenerative disease. One of the proteins implicated in this disease is Tau, a microtubule associated protein. It normally binds to and stabilizes the microtubule but, in AD, it becomes hyper-phosphorylated, breaks off from the microtubule, and forms aggregates. While the general mechanism is known, it has not been quantitatively analyzed. Using a tandem Liquid Chromatography/ Mass Spectrometry procedure, along with the highly sensitive MS instruments, the phosphorylation of Tau can be more thoroughly quantified. This is done by comparing the ratio of signal strengths of phosphorylated residues to non-phosphorylated residues of Tau, giving us a phosphorylation probability for each residue. In the brain, Tau can be separated into two pools: Non-aggregate and Aggregate. Thus, by comparing phosphorylation ratios, different quantitative profiles of the different pools of Tau can be established. In order to obtain an accurate quantitation, it is necessary to find a procedure to separate the pools of Tau in the brain; that is the goal of this portion of the project. In particular, this project seeks to find the optimal method for separating Aggregate Tau from Non-Aggregate Tau. This relies on the fact that the different pools of Tau have enough of a difference in solubility in certain reagents that, under ultracentrifugation, aggregate Tau may successfully pellet from the *solution.* Based on protocols in the literature, we tested a series of different protocols using an MES buffer or the detergent Sarkosyl to separate the dissociate and aggregate Tau. The aggregate Tau is then re-solubilized and purified through a second series of buffers and centrifugation steps. Finally, Tau is Immuno-precipitated, trypsinized, and run through an LC/MS procedure. The signal strengths of the peptides and the differences in phosphorylation ratios are used to compare protocols. From this, a quantitative profile of Tau can be established.

Brain Structure in Children and Young Adults with Phenylketonuria

Devante Morgan

Mentor: Desiree White

Phenylketonuria (PKU) is an inherited disorder in which metabolism of the amino acid phenylalanine is disrupted. Previous studies in pediatric populations suggest structural brain differences between (1) individuals with PKU relative to controls and (2) typically developing females relative to typically developing males. However, it remains unknown whether group (i.e., PKU vs. control) and gender interact to influence brain structure during development. To address this gap in the literature, two-way factorial ANOVAs were run evaluating the respective and interactive influences of group and gender on gray matter volume, whole brain surface area, and average cortical thickness in individuals with PKU (aged 7-18 years; N = 42, 24male) and controls (aged 7-21 years; N = 69, 31 male). Structural brain data were obtained using high-resolution magnetic resonance imaging (MRI) and semi-automatic cortical reconstruction in FreeSurfer. Results of analyses designated a main effect of gender, wherein gray matter volume and whole brain surface area were significantly greater in males relative to females. No other effects were significant. Further work is needed to clarify whether these results are stable across the developmental period.

Synthesis of the N4 Tetradentate Ligand

Emily Morgan

Mentor: Liviu Mirica

In today's industry there is a high demand for the ability to synthesize large organic molecules for use as drugs or fuel sources. Metal catalysts represent one powerful method thru which two hydrocarbons are fused together via a cross-coupling reaction. Our group focuses on the catalysts for these reactions, specifically those of palladium and nickel varieties. Much work has been done on palladium catalysts in their 0 and +2 oxidation states. The +3 and +4 oxidation states of Pd and the +3 state of nickel also appear to catalyze these coupling reactions, but the mechanisms thru which they do so are poorly understood.

In order to clarify the mechanisms thru which Pd^{III-IV} and Ni^{III} catalyze these reactions we use the N4 tetradentate ligand which interacts with and stabilizes the metal ions and allows us to study their properties. This ligand is well-suited for our investigations for several reasons. The ligand is flexible and macrocyclic which allows it to stabilize the octahedral geometry of the Pd^{III}, Pd^{IV}, and Ni^{III} ions. Additionally, we are able to add various functional groups to the ligand, and by studying the effects of the addition of these functional groups we can infer certain properties of the metal complexes.

One current limitation on our research is the labor and time-intensive nature that the synthesis of the N4 ligand requires several steps. Thus, one goal is to increase the efficiency of the N4 tetradentate ligand synthesis. Additionally, we will be investigating other reactions that involve modifications of the ligand.

Assessing Differences in Boldness, an Evolutionarily Important Personality Trait, among Rural and Urban Box Turtles

Madeleine Mullen

Mentor: Stephen Blake

Personality is not unique to humans, but also occurs in a wide range of animal species. In some species, individuals that display bold behavior may be more alert to feeding and social opportunities or may be better at warding off predators. As a trade-off, boldness may expose them to higher risk of being detected by predators or other potentially dangerous situations. Depending on the cost-benefit trade-offs in different environments, natural selection may favor boldness over timidity or vise-versa. We investigated boldness in two populations of box turtles in St. Louis, Missouri; "rural" turtles at the Tyson Research Center and "urban" turtles in Forest Park. We hypothesized urban turtles would be bolder than rural turtles due to their increased exposure to human-induced disturbances. During summer 2016, we searched for box turtles at each site. On finding a turtle, it was immediately placed in a black nylon bag for three minutes, after which the turtle was set free. Two observers hid from the turtle and recorded the time the turtle took to 1) expose its head and 2) begin walking. The behavior before handling, size, and sex were recorded, as well as each turtle's behavior inside the bag. We found no difference in boldness by site, however, females exhibited significantly greater boldness than males at both sites. We conclude that the selective pressures that influence boldness are likely consistent across sites, despite the demonstrably higher likelihood of traumatic injury in the urban site. Differences in boldness related to sex are harder to explain, but could be related to differences in reproductive strategies between sexes. Female turtles have the ability to store sperm from multiple males to ensure genetic diversity for their clutch. The desire to mate with multiple males makes females bolder, but further research is needed to explore this hypothesis.

Circadian Regulation of Microglial Function in Alzheimer's Disease

Collin Joseph Nadarajah

Mentor: Erik Musiek

Alzheimer's Disease (AD) is the most common form of dementia and carries age as its number one risk factor. Neuronal damage caused by inflammation and oxidative stress are consistent hallmarks of AD. Microglia, the chief immune cells of the central nervous system, are principal contributors to, and under certain conditions can exacerbate, these effects. Furthermore, disruption of circadian rhythms and the molecular clock of CNS cells have been linked to the development and progression of AD. Thus, investigating circadian rhythm dysfunction in microglia and its impact on AD could elucidate the role of microglia in the neurodegeneration seen in AD.

To disrupt the microglial circadian clock, we used a microglial specific (Cx3cr1-linked) Cre recombinase to excise and knock out microglial *Bmal1*, a core clock gene, causing total loss of microglial molecular clock rhythms throughout the CNS. This Cre lineage was crossed to AD model mice (PS1/APP transgenic) and all mice were aged to 16-18 months. We quantified gene expression of various inflammatory and oxidative stress markers in cortical tissue via RT-qPCR. We then measured astrocyte and microglial activation and evaluated amyloid beta (Aβ) plaque load via immunohistological staining of brain tissue slices. In the PS1/APP-Cre+ mice, there was elevated expression of cytochrome b-245, beta chain (Cybb or NOX2), an oxidative stress marker, relative to that of the PS1/APP-Cre- mice. This suggests a potential role for the microglial circadian clock in regulating the oxidative stress response in AD.

Studying the Synthesis of Cupprous Oxide Nanocrystals

Andrew Novick

Mentor: Bryce Sadtler

Nanocrystals are playing an increasingly significant role in society. Platinum nanoparticles are used in catalytic converters (most widely known for their application in cars) to convert carbon monoxide, other hydrocarbons, and nitrogen oxides into less hazardous gasses with lower greenhouse effects. Gold nanoparticles have been used to allow for targeted drug delivery, as well. Morphology can play an important role in the performance of nanoparticles, particularly in catalysis. Different crystal shapes result in different crystal facets being exposed at the surface. Reactants can adsorb to the different facets based on the facets' surface energies and manner in which its atoms are arranged on the surface. In order to optimize nanocrystal performance, further work is necessary to better understand the effects of morphology on catalytic performance for specific reactions and catalysts. Cuprous oxide, a well-established nanocrystal catalyst that has demonstrated the ability of oxidizing carbon monoxide and producing hydrogen gas from water, was chosen as the subject of our work. The effects of a variety of factors including atmospheric composition and type of surfactant on the size and morphology of cuprous oxide were determined. An argon atmosphere was shown to smooth the edges of the particles, relative to their synthesis under atmospheric conditions. The surfactant PVP was shown to stabilize the [111] crystal facet, leading to an octahedral shape, while ascorbic acid led to cubic nanocrystals with [100] facet on their surface. An increased concentration of reducing agent (both glucose and ascorbic acid) allowed for a decrease in nanoparticle size. With these results, cuprous oxide nanocrystals can be reliably produced in a variety of shapes and sizes, allowing for further work to be conducted on evaluating the effects of different morphologies—and their resultant crystal facets—on catalytic activity.

Synaptic Dependent Amyloid-β Generation *in vivo* in Alzheimer's Disease Mouse Model

Derrick Ogola

Mentor: John Cirrito

Alzheimer's disease (AD) is the most common cause of dementia and is pathologically characterized by toxic amyloid-β (Aβ) oligomers and plaques. Extracellular accumulation of Aβ peptide in the brain appears to precipitate disease onset and the cognitive AD-associated pathogenic cascade. In humans and transgenic models of AD, brain regions with the highest levels of synaptic activity show the greatest amount of Aβ plaques, suggesting Aβ production is closely linked to synaptic transmission. To determine the relationship between Aβ generation and synaptic activity, our lab has developed novel microimmunoelectrode (MIE) technology that detects Aβ in the brain ISF with high temporal resolution in the hippocampus of living mice (measures Aβ *in vivo* every 60 seconds over several hours), allowing us to examine Aβ kinetics on the order close to which peptide generation occurs (seconds to minutes). We custom designed a 3D-printed adaptor to connect the MIE to an injection port which enables us to measure Aβ and locally deliver drugs directly to the dentate gyrus. With these technologies, we pharmacologically manipulated synaptic activity by delivering picortoxin, a $GABA_A$ receptor antagonist, and tetrodotoxin, a sodium channel blocker, increasing and decreasing excitatory transmission, respectively. Large increases in synaptic activity rapidly brought forth higher Aβ levels in the mouse brain, while inhibition of nonspontaneous synaptic activity decreased Aβ levels *in vivo* in a concentration dependent fashion. These findings highlight a close temporal relationship between synaptic activity and Aβ generation in the brain.

Defining Neuronal Subtype Specification in Reprogrammed Striatal Neurons

Hannah Olsen

Mentor: Andrew Yoo

The ability to reprogram human skin cells into neurons has greatly enhanced our understanding of human neuronal function and disease processes. We recently developed a protocol to reprogram human skin fibroblasts directly into striatal medium spiny neurons (MSNs). This class of neuronal subtype is further specified into DRD1- (dopamine receptor 1) or DRD2-expressing MSNs, which are differentially affected in Huntington's disease (HD). In our study, ectopically expressing brain enriched microRNAs, miR-9/9* and miR-124 and striatum transcription factors CTIP2, DLX1/2, MYT1L (referenced hereafter collectively as miR-9/9*-124+CDM), converted human fibroblasts into MSNs comprised in the majority by DRD1-expressing cells, with approximately 70% of MSNs expressing DRD1. DRD2-MSNs are of great clinical interest as they are amongst the first cells to die in HD, with the number of DRD2-MSNs rapidly reducing with increasing pathology severity. In addition, other studies have shown that the cellular expression of DRD2 mRNA is dramatically reduced in HD while DRD1 mRNA levels are relatively stable. Therefore, the ability to generate a homogenous population of DRD2-expressing MSNs from HD patients would give us an unprecedented platform to model HD in culture. Through a comprehensive screening of over 30 genes, I found the transcription factor LHX8, when transduced in conjunction with miR-9/9*-124+CDM, consistently produced an approximately ten-fold increase in transcript levels of DRD2 without affecting DRD1 expression. Similar results were observed in both wild type and HD cell lines, indicating that LHX8 robustly affects cellular fate specification independently of disease status.

A New Route to the Synthesis of a Triplet Silylene

Dawa Michael O'Sullivan

Mentor: Peter Gaspar

Silylenes, the silicon analog of carbenes, are neutral divalent molecules with an sp2 hybridization. Silylenes can exist in a spin paired, singlet, or spin unpaired, triplet, ground state. While many singlet silylenes have been synthesized and studied, no reactive triplet silylenes have been studied. Previous work on synthesis of triplet silylenes has yielded molecules too sterically hindered to undergo the reactions required to perform mechanistic studies. This project attempts to synthesize a non-sterically hindered disilene stabilized silylene utilizing previous syntheses of stable singlet silylenes. The synthesis of the target molecule was designed using computational calculations performed by previous Gaspar group members. While the synthesis is not complete several steps have been successfully completed with 1HNMR and GC-MS data corresponding with published literature values.

Technology for Drug Development to Eradicate HIV/AIDS

Rahul Oza

Mentor: Alexander Barnes

Worldwide 36.9 million people live with HIV; 2.6 million are children under the age of 15. There is still no cure for HIV, but effective treatment with antiretroviral drugs can control the virus so that patients with HIV reduce the risk of virus transmission while enjoying healthy lives. Our laboratory seeks to design targeted drugs that reverse HIV latency; enabling the immune system to identify and destroy HIV-infected cells. One promising therapeutic strategy is to activate the latent reservoirs of HIV within infected T-cells. The viral production will directly induce cell death, leading to the eradication of HIV/AIDS within patients.

To achieve this goal, we are developing bryostatin, a powerful activator of Protein Kinase C (PKC), as a method to reverse HIV latency. PKC activation is a common pathway that upregulates HIV expression. Bryostatin 1, a specific PKC activator, increases virus production. Viral reactivation performed in combination with HAART, which suppresses HIV replication, would help eradicate latent viral reservoirs while simultaneously depleting the active virus, essentially curing infected patients.

The goal of this research is to enhance a NMR DNP probe to increase the sensitivity and resolution of our solid-state NMR experiments in order to enhance our ability to design derivatives of Bryostatin that more effectively activate HIV. A drastic gain in sensitivity will allow us to determine biomolecular structure of molecules, such as PKC, with less than a milligram of sample. Through enhanced visualization of the biomolecular structure of PKC, we will be able to develop better Bryostatin analogs that can selectively activate different pathways downstream of PKC known to drive HIV activation, allowing us to more effectively reverse HIV latency and thus help rid patients of HIV.

Pediatric Applications and Usefulness of 3D Printed Prosthetic Arms

Ilan Palte and Mark Sullivan

Mentor: Dominic Thompson

Children with congenital limb deficiencies or limb amputations need to use prostheses from an early age to meet crucial developmental needs. For example, acquiring and refining motor skills through errors, as well as generalization and adaptation to changing environments occur in this time period. Hence, when a child missing a limb undergoes these motor and brain development stages without a prosthesis, they will acquire compensatory movements that are different from those of children growing up intact. Unfortunately, the majority of young amputees considers daily use of their prosthesis difficult, and they abandon it. There are many reasons for this including the typically rudimentary prostheses available for a growing child and their utilitarian aesthetic appearance. A three-dimensionally printed prosthetic that is customized to the patient in both fit and aesthetic could improve functionality and alleviate both the unpleasantness experienced in donning the prosthesis and the costs surrounding periodic replacement of the device. The goal of this project is to create an inexpensive, customized upper extremity, myoelectrically controlled or mechanical prosthetic arm/wrist/hand that is aesthetically pleasing to the patient using 3D printed parts and inexpensive, non-3D printed components. Once the protheses are fabricated and fitted to the patients, they will be evaluated for usefulness/effectiveness to the user using a battery of manual dexterity tests administered by a certified prosthetist.

Genetic Variation Linked to Neuroticism Is Associated with Amygdala Function

William W. Pan

Mentor: Ryan Bogdan

Neuroticism is a heritable personality trait characterized by emotional instability and psychological stress that places individuals at risk for psychopathology. The amygdala is a brain region that plays a critical role in behavioral vigilance and assigning emotional significance to stimuli that may contribute to the expression of neuroticism. A recent GWAS of 180,911 individuals identified common genetic variation associated with neuroticism. Here, we explored whether single nucleotide polymorphisms (SNPs) that were associated with neuroticism at genomewide levels of significance are associated with threat-related amygdala function.

Genomic, neuroimaging, and self-report data were available for 448 non-Hispanic European-American participants who completed the ongoing Duke Neurogenetics Study. Threat-related amygdala reactivity was assayed using an emotional face-matching task while functional magnetic resonance imaging data were acquired. Neuroticism was assessed with self-report. We tested whether 11 genome-wide significant single nucleotide polymorphisms (SNPs) were associated with neuroticism through GWAS. Covariates in analyses included sex and ancestrally-informative principal components.

We found that the risk alleles of three (*TYRP1* rs10809559, *SBF2* rs13923776, *PAFAH1B1* rs12938775) SNPs were associated with elevated amygdala reactivity (all $\beta>0.032$, all $p<0.04$). The *PAFAH1B1* rs12938775 allele associated with neuroticism in the GWAS was also associated with neuroticism in our dataset ($\beta=3.31$, $p<0.016$), however, neither *TYRP1* rs10809559 nor *SBF2* rs13923776 were (both $p>0.68$). We conclude that common genetic risk for neuroticism is associated with elevated threat-related amygdala reactivity. Increased threat-related amygdala response may be a genetically influenced neural mechanism conferring neuroticism and risk for psychopathology.

A Novel, Facile Method for the Synthesis of pH-Modulating Inorganic Carbonate Nanoparticles

Krishna Sarma Paranandi

Mentor: Samuel Achilefu

Many biological systems need to strictly maintain the acid/base homeostatic balance (pH) of their cellular environment. In humans, several pathological conditions, including cancer and diabetic ketoacidosis, are characterized by dysregulation or failure of pH maintenance mechanisms. Treatment of such conditions has focused on modulating pH to appropriate physiological ranges. Prior studies show that nanoparticles of inorganic carbonates, particularly of calcium carbonate, are effective in achieving this. Thus, inorganic carbonate nanoparticles are pursued as a possible therapy for many pH-based disorders, but have faced significant difficulties associated with reliably synthesizing stable inorganic carbonates at sub-micron size scales. To address this problem, a novel, dessicator-based method of synthesizing a wide variety of inorganic carbonate nanoparticles using metal chlorides and ammonium bicarbonate was studied. Six nanoparticle preparations synthesized with this method were subsequently analyzed for particle size, morphology, pH-modulating properties, and optical characteristics. Results show that this method is capable of producing uniform, spherically shaped particles in the 50-150 nm range. In addition, while all the carbonates demonstrated an alkalization effect relative to their respective chlorides, the extent to which pH was increased depended on the specific cation associated with the carbonate. Also, all the nanoparticle solutions exhibited a distinct fluorescence emission peak at approximately 500 nm. These findings suggest that such particles can have a wide range of potential therapeutic applications in biomedical environments. The pH-modulating effects and optical properties, along with the inherent advantages of the nanoparticle platform, will be extremely useful in the management of a variety of diseases.

Identities at Stake: How Empathetic Virtual Reality Reshapes Personal Identity

Jin Seok Park

Mentor: Pannill Camp

A common understanding of virtual reality (VR) places emphasis on its function as a machine that builds empathy. Current academic research relies on behavioral science to back this claim, which is insufficient in that its conclusions are heavily based on external observations, such as experiments where VR experiences led to a display of empathetic behavior. In order to understand how the mind motivates such action, I attempt to evaluate VR's potential to generate empathy with a more theoretical approach by analyzing the frameworks of the mind proposed by two different philosophers: David Hume and Edmund Husserl. Although they formulated their ideas in the eighteenth and twentieth centuries, respectively, their works provide valuable insights into how the mind reacts to external perceptions. By applying the ideas of Hume's empirical ego and Husserl's transcendental ego to VR experiences, I posit that VR has the potential to reshape our notion of personal identity, particularly when the experience is geared towards building empathy. Specifically, the empirical ego helps us understand that personal identity is a collection of perceptions that are easily susceptible to change when new perceptions are introduced. On the other hand, the transcendental ego shows that the idea of personal identity is made up of the stances that we have intentionally formed regarding our experiences, which are less affected by individual experiences. By applying these frameworks to real and imagined VR experiences, I conclude that VR has the potential to reshape our personal identity and that the increase in empathetic behavior is not the sole effect of the technology but one of the many manifestations of such reshaping. Ultimately, I hope to demonstrate the value of philosophical frameworks in seeking to understand how a new technology may affect how we act but also how we think and define ourselves.

Cyclophilin A Mediates Blood-Brain Leakage and Edema after Subarachnoid Hemorrhage

Devin Patel

Mentor: Itender Singh

Subarachnoid hemorrhage (SAH), a unique form of hemorrhagic stroke, remains a serious health problem with a 32% mortality rate in the United States. Of those surviving the initial hemorrhage, more than half deteriorate in the days following SAH due to early brain injury or EBI (which occurs 1-3 days after SAH). The predominant vascular deficit leading to EBI is blood-brain barrier (BBB) disruption, along with the release of cytotoxic agents and inflammatory mediators. Recently, a causal link between metalloprotease 9 (MMP9) and EBI after SAH has been suggested in rodent studies. A correlation between serum MMP9 levels and vasospasm in human SAH has also been noted. While a major contributing role of MMP9 in SAH-induced brain injury is rapidly being established, the upstream molecular events leading to its upregulation and the downstream molecular events by which it causes EBI are poorly understood. Cyclophilin A (CypA) is a proinflammatory molecule that is known to drive MMP9 expression via the transcription factor NF-κB p65. Previously we discovered that CypA plays a causal role in AD-induced cerebrovascular deficits, including APOE4-linked BBB disruption and CBF deficits. CypA is secreted from cells in response to inflammatory stimuli, such as hypoxia and oxidative stress. Whether CypA plays a role in EBI and/or DCI following SAH, however, is not known. We found that MMP9 activity in the brain increases following SAH. We got the first hint that CypA contributes to EBI when increased CypA levels in CSF were found in SAH patients and mice after experimental SAH. We found that both pharmacological and genetic inhibition of CypA significantly attenuates BBB leakage, as assessed via Evans blue BBB permeability assay. This evidence suggests that CypA is a key mediator of blood-brain barrier dysfunction after SAH.

Emotion Regulation Goals and Strategy Use in Romantic Relationships

Taylor Pitcher

Mentor: Tammy English

Little is known about why people regulate their emotions using different strategies. This matters because strategies can have important emotional and social consequences. The purpose of this study was to see whether emotion regulation goals, motivation behind using strategies, could predict emotion regulation strategy use during a conflict conversation between romantic partners. Based on previous research, we expected that self-oriented goals, such as impression management goals (i.e., managing impression on partner) would predict more suppression; relationship-oriented goals, such as eudemonic goals (i.e., gaining meaning from the conflict) would predict more rumination; and that other-oriented goals, such as rapport goals (i.e., maintaining the relationship) would predict more masking. To test these hypotheses, we had 113 romantic couples, ages 17-55 years, engage in a conversation about a topic they mutually disagreed on. Couples then filled out questionnaires about their emotion regulation goals and strategy use during the conversation. The results indicated that impression management goals and eudemonic goals were positively associated with suppression and rumination, respectively. Rapport goals were not associated with masking. Such results broadly suggest that different types of goals might be associated with different strategies. More specifically, these results suggest that more self-oriented goals (e.g., impression management) might motivate suppression, while relationship-oriented goals (e.g., eudemonic) might motivate rumination. Future research could examine what types of goals predict masking, as well as, how other types of goals predict other strategies.

A Possible Role for the microRNA-276 Gene Duplication in Specifying Sex-Related Neuronal Functions

Nathan Pomper

Mentor: Yehuda Ben-Shahar

MicroRNAs (miRNAs) are short, non-coding, pleiotropic RNAs, which play a role in post-transcriptional regulation of protein coding genes. Genomic data suggest that novel miRNA genes often evolve via genomic duplication events. However, the phenotypic significance of most miRNA gene duplications are still unknown. One example is the miR-276 gene, which is represented by a single copy in most arthropod genomes. However, a gene duplication found in *Drosophila* and other muscomorpha genomes (e.g., the house fly) has resulted in two *miR-276* paralogs, an ancestral *miR-276a* and a derived *miR-276b*, which differ by only a single nucleotide. I tested the hypothesis that the *miR-276* gene duplication plays a functional role via the regulation of novel genetic networks. To test the hypothesis, I utilized a combination of genetic, imaging, and behavioral approaches in *Drosophila* to determine whether the two *miR-276* genes play independent roles in regulating neuronal and behavioral phenotypes. Insights gained from our studies have the potential to uncover an explanation for why some miRNA gene duplications have been retained in certain phylogenetic clades, and the role these duplications play in the emergence of novel phenotypes.

Do Endotoxins Directly Injure Red Blood Cells?

Jaya Prakash

Mentor: Allan Doctor

This project examined the role of bacterial endotoxin (lipopolysaccharide, LPS), in the red blood cell (RBC) damage and abnormal oxygen delivery that is commonly observed in severe infection. Specifically, we are testing the hypothesis that LPS activates proteases involved in eryptosis (a special form of RBC death) and that these proteases damage proteins involved in energy metabolism. It has been demonstrated in the Doctor lab that in RBCs exposed to endotoxin, caspase (an enzyme involved in eryptosis initiation) is activated; however, the mechanism for this is not well understood. We predicted that the activation of caspase 3 and mu-calpain—after endotoxin exposure—would directly injure RBCs in lieu of operating through elements in plasma or white blood cells (WBCs). To test this, an endotoxin exposed human RBC model used whole blood from human volunteers and separated it via centrifugation into its components (washed RBCs, plasma, and WBCs), and samples from each subject were divided into three experimental groups: (1) unaltered whole blood, (2) washed RBCs, (3) washed RBCs + plasma. Each experimental group was incubated with LPS at varying concentrations. Samples from the three groups were evaluated with SDS PAGE and a western blot specific for procaspase 3, caspase 3, and mu-calpain to assess the injury caused by LPS exposure. After repeated trials, caspase 3 seemed to be activated most readily in whole blood where cleaved caspase 3 bands tripled the densitometry readings of those in washed RBCs. Similarly, mu-calpain was most readily activated in whole blood where the cleaved products had densitometry readings nearly 5 and 1.5 times those of the respective bands in washed RBCs. These differences in band densities between the experimental groups for mu-calpain and caspase 3 suggested that the mechanism of RBC injury through these enzymes might depend on signaling through the humoral immune system.

Local Adaptation and the Role of Carried Symbionts to Thermal Stress in a Social Amoeba *Dictyostelium discoideum*

Xinye Qian

Mentor: Joan Strassmann

Environmental stress can result in strong ecological and evolutionary effects on natural populations. In this project, we study adaptive divergence of thermal tolerance in the social amoeba *D. discoideum*. In addition, we test the hypothesis that some of the amoeba symbionts, such as the *Burkholderia* bacteria, could help amoeba survive the thermal stress.

D. discoideum generally lives best at a temperature around 22 degrees Celsius. It is very sensitive to thermal stress and most cannot function well or even fail to survive at higher temperatures. However, some types of amoebae were found in many places with high temperatures across the country, including Texas. To get insight into the difference among the heat-tolerance of populations, we took samples from two populations that differ in climate (Virginia, VA and Texas, TX). We tested them under moderate and thermal conditions and measured their fitness (using spore counting). We found that TX population had higher fitness than VA population under thermal condition, while there was no difference between them under moderate condition. These results suggest that Texas population has locally adapted thermal stress.

When *D. discoideum* clones are collected from the wild, some carry bacterial symbionts (farmers) while others do not (non-farmers). There are benefits and costs of carrying symbionts. In this project, we are currently testing the hypothesis that the *Burkholderia* bacteria, one of the major symbionts, could help amoeba survive the thermal stress.

Biosynthesis of Bi-functional Products from the FASII System

Jimmy Qiao

Mentor: Fuzhong Zhang

This project explored synthesizing long chain carbon structures with two functional groups using E. coli. We utilized the FASII system that normally produces long chain fatty acids and a previously engineered system that we created that allows us to modify the products of the FASII system. There were two methods that we explored in our research: attaching a second functional group after synthesizing a mono-functional molecule using pathways that we already have engineered using the genes pimA, alkJ, aftA, and LACS2, and introducing a precursor molecule that already contains a functional group to the previously engineered system. In addition, we explored an alternative method to synthesize bio-molecules called the cell-free system. This system takes advantage of the cell lysate that contains functional enzymes to bypass the theoretical constraints of working with living cells. Our results showed that the endogenous FabH does not tolerate precursor molecules that contain a functional group. Gas Chromatography Mass Spectrometry (GC-MS) data indicated that no molecules of interest were produced, however the cells continued to grow, showing that the FabH only took in endogenous precursor into the FASII system. In addition, the results showed that the LACS2 gene does not function well in our transformed cells, inhibiting the addition of a second functional group after the FASII system. Finally, the cell-free system also did not produce any fatty acids, signifying that there are still technical problems with the preparation of the lysate. Although the experiments were not successful, we were able to pinpoint the problems of each system, allowing us to return to this project at a later time to trouble shoot the issues.

MIR142 Loss-of-Function Mutations Promote Leukemogenesis via Derepression of ASH1L Resulting in Increased HOX Gene Expression

Rahul Ramaswamy

Mentor: Daniel C Link

Mutations of *MIR142* have been identified in approximately 2% of *de novo* AML and in 20% of diffuse large B cell lymphoma. In AML, the mutations in *MIR142* disrupt both miRNA-142-3p and miRNA-142-5p function, suggesting that loss of *MIR142* plays a role in leukemic transformation. To test this hypothesis, we first characterized hematopoiesis in *Mir142*$^{-/-}$ mice, and reported that loss of *Mir142* results in an expansion of myeloid progenitors with impaired erythropoiesis and lymphopoiesis.

We examined several putative miR-142 target genes, eventually focusing on *ASH1L*, a histone methyltransferase that has been recently implicated in MLL-associated leukemogenesis. The 3' UTR of *ASH1L* contains 4 putative binding sites for miRNA-142-3p, indicating that this miRNA is critical in its post-transcriptional regulation. Indeed, Ash1L protein levels were 3-fold higher in *Mir142*$^{-/-}$ mice bone marrow compared to control mice. Since ASH1L is a known regulator of HOX gene expression, we examined *HoxA9* and *HoxA10* expression in *Mir142*$^{-/-}$ hematopoietic progenitor subsets. While *HoxA9* and *HoxA10* expression were not different in hematopoietic stem cells, they were markedly upregulated in myeloid progenitors. For example, in granulocyte-macrophage progenitors (GMPs), *HoxA9* and *HoxA10* expression were increased 2.86-fold and 34.4-fold, respectively in *Mir142*$^{-/-}$ versus control cells. Likewise, in megakaryocyte-erythroid progenitors (MEPs), *HoxA9* and *HoxA10* expression were increased 5.3-fold and 21.4-fold. Dysregulated *HoxA9* and *HoxA10* expression have been implicated in enhanced self-renewal capacity, and *HoxA9* overexpression has been shown to cooperate with mutant *IDH1* to induce AML in mice. Collectively, these data suggest a model in which *MIR142* mutations contribute to leukemogenesis by de-repressing *ASH1L* expression, which, in turn, increases expression of *HoxA9/10* and enhances self-renewal. Inhibitors targeting ASH1L may have therapeutic benefit in AML characterized by increased HOX gene expression.

Development of Igor Pro Based Data Analysis Programs for Use in the Study of Atmospheric Chemistry

Charles Rapp

Mentor: Brent Williams

The Atmospheric Chemistry and Technology (ACT) lab is primarily focused on the study of organic species in suspended particulate matter. The particulate matter contains a large number of organic species, which leads to large, detailed datasets. The datasets are difficult to work with due to their large size and high level of detail. To aid in further study of these particles, several instruments are often used simultaneously for measurement and data collection. While data analysis techniques exist for many atmospheric chemistry instruments, the large size of the datasets can make these methods prohibitively time-consuming. In an effort to reduce this time burden, software programs that rapidly analyze this data are essential. To this effect, programs were developed or improved in Igor Pro (WaveMetrics, Inc., Lake Oswego, Oregon) for several instruments and general functions: the AE-33 Aethalometer (Magee Scientific, Berkeley, California), which allows for the measurement of the absorption of particles, the Scanning Mobility Particle Sizer (SMPS; TSI Inc., Stillwater, Minnesota), which is used to measure the mobility diameter of particles, Thermal Desorption Aerosol Gas Chromatogram (TAG) and Volatility and Particle Separator (VAPS), which separate organic components of particles based on their volatility and/or polarity, and a preexisting Binning Method program that analyzes TAG/VAPS data using positive matrix factorization (PMF), which is a popular source apportionment technique. The above programs offer the user many different tools for data manipulation and visualization for each of the mentioned instruments. Additionally, these tools will prove beneficial to the further study of organic particles and general atmospheric science due to their ability to efficiently work with and provide visualization for the large amount of data generated from these widely used instruments.

Effects of Effort on Neurocognitive Performance of HIV+ Individuals

Gina Rhee

Mentor: Beau M. Ances

Suboptimal effort confounds cognitive performance in healthy individuals and patient populations. The impact of poor effort during cognitive testing is particularly relevant to human immunodeficiency virus infected (HIV+) individuals. Specifically, concerns have been raised with regards to effort as it may confound diagnosis of neurocognitive impairment in HIV+ individuals. We examined effort and cognitive performance in 131 HIV+ individuals and 96 HIV– controls free of substance use disorder, major psychiatric illness, or neurological confounds. Participants completed a neuropsychological battery and an effort measure (Test of Memory Malingering (TOMM)). Global deficit scores (GDS) were calculated to measure cognition. TOMM did not differ between HIV+ individuals and HIV– controls. TOMM did not differ according to level of cognitive impairment for either HIV+ or HIV- groups. Finally, both TOMM performance and neurocognitive impairment did not correlate with clinical variables (CD4 or viral load) in HIV+ individuals. These results suggest that cognitive impairment in HIV+ individuals is independent of the potential confound of suboptimal effort. Future studies are needed to determine critical determinants of HIV-related cognitive impairment, with a focus on viral-host dynamics that occur during acute and early infection.

Effects of Salinity, pH, and Scale Inhibitor on the Wettability and Stability of Biotite

Gabriella Riek

Mentor: Young-Shin Jun

Geological CO_2 sequestration (GCS), the underground injection of supercritical carbon dioxide ($scCO_2$) more than a mile underneath the surface of the earth, is an up and coming environmental technology that would drastically reduce carbon dioxide emissions. This research was completed with the purpose of better understanding the conditions of rock formations that are used for various underground technologies such as GCS. Biotite, a mica mineral found mostly in the cap-rock layers of underground rock formations ideal for GCS, is used to understand better the mobility and transport of $scCO_2$ through studying the wettability of the basal and edge surfaces and the stability of biotite particles under different conditions. Different basal and edge surfaces were prepared and contact angles were measured to determine the wettability trends of different biotite surfaces with changes in salinity and pH. Furthermore, the stability of biotite was studied by UV/vis spectroscopy using biotite suspensions in solutions of different salinities, pH values, and concentrations of DTPMP (Diethylenetriamine penta(methylene phosphonic acid)), a scale inhibitor. It was found that basal surfaces showed lower contact angles at higher salinities and fairly constant contact angles with varying pH conditions. Edge surfaces showed a trend of increasing contact angles as salinity increased, although the angles were higher than that for basal surfaces, and no discernable trend could be found for varying pH. The stability tests showed that solutions of high salinities destabilize the suspension so that aggregated particles could clog small pores in the geologic formations. Also DTPMP has a stabilizing effect on biotite suspensions and suppresses the effects of pH on stability. While these results provide some promising conclusions, it is evident that the conditions need to be tested for reproducibility and further understanding of the system.

Significance of the Feminization of Eating Disorders

Rachel Rothman

Mentor: Colin Bassett

Today, many individuals develop eating disorders; however, eating disorders are typically associated with women. In this work, I declare that male eating disorders are stigmatized due to the feminization of eating disorders. I explain that the stigma exists in part due to the way males are portrayed in the media as muscular, bold, and strong. Individuals in society value men who look and act in this way, which is what causes men to become insecure about the way they look and increases their likelihood of developing eating disorders. Professionals who adopt socially constructed, gendered views of men are unable to conduct objective research on male eating disorders and diagnose them correctly. I illustrate how the stigma prevents men from recognizing their own unhealthy behaviors and can deter individuals from recognizing eating disorder-related behaviors in other men. Throughout the essay, I provide my own analysis regarding how to combat the stigmatization of eating disorders, which can be accomplished by altering the way we view men in the public eye, research male eating disorders, diagnose male eating disorders, and treat men with eating disorders. I conducted my research by using wide variety of scholarly articles as well as a book on male eating disorders. However, much of my research involved critically analyzing scholarly articles on eating disorders as a whole. I hope to provide a better understanding of the stigmatization of male eating disorders and the implications of doing so. In the coming years, I hope to see significant progress made in reducing the stigmatization of male eating disorders.

Influence of *Dictyostelium Discoideum* upon Species Diversity within *Pseudomonas fluorescens*

Erica Ryu

Mentor: Joan Strassman

Biodiversity is vital for maintaining the ecology of the world. Interactions between organisms can be crucial for survival, as they can help species to coexist. One possible example is the symbiotic relationship between two strains of *Pseudomonas fluorescens* and *Dictyostelium discoideum*. The selfish bacterial strain PF2 takes advantage of the cooperative strain PF3 by absorbing essential iron-carrying siderophores without producing more siderophores, allowing it to devote energy towards growth and outcompete PF3. Previous studies suggested the strains coexist in field conditions and that *D. discoideum* closely associates with the bacteria. This research studies the fitness of *P. fluorescens* in conditions with and without *D. discoideum* to determine whether the amoeba contributes to the strains' coexistence. We found that the fitness of PF2 decreases and that of PF3 increases in the presence of the amoeba. Images taken using a confocal microscope show that the strains are present in the amoeba spores, supporting that *D. discoideum* plays a crucial role in the coexistence of both strains. These findings will provide novel insights into how communities function and how symbiotic relationships evolve.

Investigating the Impact of Auxin on Pseudomonas Metabolism

Saryu Sanghani

Mentor: Barbara Kunkel

Pseudomonas syringae is a bacterial pathogen that infects *Arabidopsis thaliana,* tomato, and many other plants. We know little about how *P. syringae* strain DC3000 survives and grows within its hosts. During pathogenesis, *P. syringae* populates the apoplast of plant tissue, where it must tolerate the stress from defense mechanisms and also import and metabolize the available nutrients to survive and grow. Auxin is a plant hormone that has been shown to play a role in increasing disease symptoms caused by *P. syringae.* Our research seeks to clarify the metabolic pathways that *P. syringae* uses to grow in its hosts and to see whether auxin regulates these pathways.

In many contexts, auxin is a growth and development hormone that contributes to disease by increasing plant susceptibility to infection or by making nutrients available for pathogen growth. Auxin, however, inhibits growth of *P. syringae* on various carbon sources in culture and inhibits expression of specific *P. syringae* virulence genes. To decipher these seemingly paradoxical results, we want to elucidate the metabolic pathways and carbon sources used by *P. syringae.* We hypothesize that *P. syringae* uses auxin as a switch or a signaling molecule that turns off early virulence genes and turns on late virulence genes. These latter genes could be involved in metabolic shifts since different organic compounds could be made available at later stages of infection.

Having fed *P. syringae* various different carbon sources in culture, we saw that the levels of growth were very similar for all carbon sources (minus the negative control) except fructose—which cannot be metabolized as well due to a lacking enzyme. Regardless of carbon source, we did see the inhibitory auxin effect in each media. There was variation in the magnitude of inhibition, but not enough to make significant conclusions.

Toward a Better Understanding of...

Cross-Cultural Happiness

Audrey Schield

Mentor: Tim Bono

I initiated this research to investigate the question, "What makes you happy?" Based on existing research in the fields of personality and positive psychology, I understood the underlying contributing factor to be subjective wellbeing, but I found that the opportunity to answer an open-ended question created many new interesting areas for study. After studying this question in India and Chile I was excited to bring my work back to Washington University in St. Louis and investigate how undergraduates at Washington University articulate happiness and what affects the way we communicate what makes them happy.

Role for Ventral Nucleus Accumbens Dynorphinergic Neurons in Reward

Gavin Schmitz

Mentor: Michael Bruchas

Dynorphin (Dyn) is a key peptide involved in the neural mechanisms underlying motivated behaviors. Dyn is contained in axon terminals and cell bodies located in the nucleus accumbens (NAc), an area associated with the brain's reward circuitry. Recently, two distinct dynorphin-containing subregions within the NAc shell which drive opposing behaviors were identified. Dorsal NAc dyn cell activity is consistent with reward behavior and ventral NAc dyn cell activity mediates aversion. Release of dynorphin in both these areas, activates kappa-opioid receptors (KOR) within both dopaminergic and serotonergic nuclei and their ventral striatal targets; however, the endogenous sources of dyn in these circuits remain unknown. To investigate this, fluorescently tagged retrograde viruses were injected into either the dorsal or ventral areas of the NAc. Retrograde rabies virus travels upstream thereby fluorescently labeling the neurons that synapse onto the dyn-containing cells within either subpopulation of the NAc. Additionally, non-cell type specific canine adenovirus and cholera-toxin B viruses were used to further interrogate projections in the dorsal and ventral NAc shells. These neurons were imaged using confocal fluorescence microscopy following tissue perfusion and immunohistochemistry. From these studies, a GABAergic neuronal projection from the ventral tegmental area (VTA) to the ventral NAc has been identified. This projection drives a robust preference behavior as measured in a real time place testing paradigm and operant self-stimulation. These results increase our understanding of how the distinct populations of dynorphin neurons in the NAc are engaged, recruited, and altered in certain motivated behaviors.

Cardiac Macrophage Composition Determines Dilated Cardiomyopathy Patient Outcomes

Caralin Schneider

Mentor: Kory Lavine

While heart disease represents a leading cause of death, heart failure remains poorly understood. Looking at the immunology of chronic heart failure, specifically the monocyte derived CCR2+ and embryonic derived CCR2- macrophage populations, we have found that macrophage composition is associated with and predictive of clinical outcomes including cardiac function, pathological remodeling, and coronary angiogenesis. We focused on patients with dilated cardiomyopathy (n=55) who underwent placement of a left ventricular assist device (LVAD). Normal donor hearts were used as controls (n=10). We used clinical data and an immunostaining assay I designed using CD68 (pan-macrophage marker) and CCR2 antibodies to identify the macrophage populations. We showed that patients with increased numbers of monocyte derived CCR2+ macrophages display higher mortality rates and deterioration of cardiac function over time. The findings from these experiments demonstrate that manipulating macrophage composition within the diseased heart has the potential to improve the intrinsic capacity for the adult heart to heal following injury and a rationale to design novel heart failure treatments targeting cardiac macrophage subsets.

Reaction Mechanisms of Planar Disilenes

Alex Seim

Mentor: Peter Gaspar

We have recently discovered many novel planar disilenes and have computationally modeled the structures of the molecules. Additionally, we have modeled the reaction mechanisms for a few of these planar disilenes and have shown that these molecules react in concerted 2+4 cycloadditions with reasonable activation barriers like their olefin counterparts. We are now looking to experimentally confirm our computational findings to answer the question of whether or not planar disilenes react via a concerted mechanism in 2+4 cycloadditions.

The Impact of E-cigarette Use in Inflammatory Bowel Disease

Jasmine Serpen

Mentor: Alexandra Gutierrez

E-cigarettes represent a novel method of nicotine inhalation that is growing in popularity and has been studied as a tool for smoking cessation in the general population; however their effect on disease activity, smoking cessation efficacy, disease course, and response to therapy in Inflammatory Bowel Disease (IBD) is unclear. This study attempts to better define and characterize e-cigarette (e-cig) use in the clinical context of patients with IBD. E-cig users were identified from a retrospective database of smoking behaviors in an IBD population. Medical records were reviewed for clinical assessments of disease activity, medication changes, endoscopies, MREs, and surgeries during the year prior to beginning e-cig use, the period when e-cigs were used, and the year after e-cigs were stopped if applicable.

Baseline characteristics of the 27 study participants revealed no significant differences in age, gender, or disease subtype between current and former e-cig users. Use of e-cigs was found to reduce cravings for regular cigarettes in 21 of 27 people but sustained smoking cessation was only seen in 17 of the 27. The primary motivation for choosing e-cigs over other methods of smoking cessation was that other methods were unsuccessful for the patient, in addition to the appeal of the hand to mouth habit and resemblance to regular cigarettes afforded by the e-cigs. Disease activity via subjective and objective measures were recorded but not evaluated for significance due to a small sample size.

We conclude that e-cig users experienced a lessened craving for regular cigarettes while using e-cigs but did not experience significance in sustained smoking remission. Limitations of the study included a small sample size and recall bias. However, this preliminary data offers insights into e-cigarette use in a vulnerable population. Understanding the impact on disease activity will allow for improved disease management as well as counseling on appropriate smoking cessation methods.

A Genetic Study of Heterochromatin Formation Mediated by a Triplet Repeat in *Drosophila melanogaster*

Sukruth Shashikumar

Mentor: Sarah C. R. Elgin

Packaging DNA into heterochromatin is a mechanism used in higher eukaryotes to silence repetitive DNA, remnants of transposons, etc. Genome integrity depends on effective silencing of transposable elements, as their mobilization can lead to gene disruptions, deletions, and translocations. Heterochromatic regions are generally inaccessible to elements of the transcriptional machinery and are thus transcriptionally silenced. The human disease Friedreich's ataxia is caused by expansion of the DNA nucleotide triplet repeat GAA from 10-66 copies in the first intron of the gene *FXN* to 66+ copies, resulting in silencing of *FXN* via heterochromatin formation. To characterize DNA triplet repeat-mediated heterochromatin formation in *Drosophila melanogaster*, we built a transgenic construct with a DNA fragment of 310 copies of the triplet GAA (originating from a Friedreich's ataxia patient) inserted upstream of an *hsp70-white* reporter. (The *white* gene is required for red pigmentation in the fly eye.) The transgene was incorporated at the base of chr. 2L at a site within the actively transcribed gene *nesd* but in close proximity to a heterochromatic block. At this location, *hsp70-white* yields a red-eye phenotype. When GAA_{310} is upstream of the reporter at this site, we observe *hsp70-white* silencing (variegating phenotype). Eye pigment assays were used to quantitatively evaluate the dominant impact of gene mutations on GAA_{310}-*hsp70-white* silencing. Genetic analyses indicate a role for histone deacetylation, H3K9 methylation, and HP1a binding in maintenance of silencing, in common with transposable element (TE) silencing. In contrast to TEs, the RNAi system does not appear to play a role in targeting GAA_{310}-induced silencing. When GAA_{310} was inserted into another site in the euchromatic arm of chr. 2L, transformants did not show a silencing phenotype. We are continuing to investigate the importance of genomic context in heterochromatin formation triggered by insertion of the repetitious GAA sequence.

Exploring Space Weathering Effects on Asteroid Regolith Breccia

David Shaw

Mentor: Ryan Ogliore

In this work we study space weathering effects on asteroid surfaces returned from the Weston, Fayetteville, and Kapoeta meteorites. We first used a freeze-thaw technique to break up the sample, by submerging it in water and repeatedly freezing then thawing. Over many cycles, we managed to obtain pristine sample dust. We then mounted the dust into a scanning electron microscope to examine the surface closer. In particular, we wanted to look at the effects of solar ray irradiation on the asteroid surface, as well as micrometeoroid flux. The second process involved scanning millions of square microns' worth of surface areas, searching for craters that would signal evidence of micrometeoroid impacts. We researched previously found crater densities on lunar surfaces and attempted to make a comparison with our sample asteroid crater density, but despite searching millions of square microns' worth of pristine surface, we have yet to find convincing evidence of micrometeoroid impacts. We also utilized x-ray spectroscopy to look at the mineral compositions of our meteorite sample, and compared it to known elemental ratios of earth-bound olivines and pyroxenes.

The Association between Baseline Pupil Size and Cognitive Function

Jeffrey Shi

Mentor: Julie Bugg

While many studies have been done on what affects cognition, research on the role of the locus coeruleus still remains fairly novel. The locus coeruleus is a nucleus inside the brainstem that is the major producer of the neurotransmitter norepinephrine, and has been linked to various cognitive functions. This study examined the relationship between baseline pupil diameter, which is a non-invasive measure of locus coeruleus function, and various cognitive functions that include fluid intelligence, crystallized intelligence, and attentional control. As one ages, fluid intelligence and attentional control tends to decline and crystallized intelligence tends to increase or stay the same. Since pupil diameter and locus coeruleus function decrease as one ages, it was hypothesized that pupil diameter is positively correlated with fluid intelligence (Gf), not correlated with crystallized intelligence (Gc), and negatively correlated with two attentional control variables: the Stroop and Simon effects. While this study was intended for 60 participants, only 30 participants could be tested in time. While the correlation with Gf was in the right direction, there was not enough power to make a decisive conclusion. The same was observed for the attentional control variables, as there was not enough power to detect a statistical effect, and fatigue may have influenced the data. Interestingly, Gc was the only statistically significant positive correlation. These findings showed promise, but ultimately more data and specific research, such as focusing on one specific variable at a time (i.e., Gc), are needed in order to come to a more reliable conclusion.

Rewarding Effects of Opioidergic Projections from the Ventral Pallidum to Substantia Nigra

Yu Jin Shin

Mentor: Michael R. Bruchas

Opioid addiction has reached epidemic levels recently, but the role of endogenous opioid circuits is still poorly understood. The rewarding effects of opioids are believed to be due to inhibition of tonic GABAergic inputs to midbrain dopamine neurons, releasing these neurons from inhibition and increasing dopamine release. The ventral pallidum (VP) is one the strongest projections to the midbrain dopamine neurons and expresses the opioid peptide enkephalin at high levels. We hypothesized that stimulation of VP enkephalin projections to the substantia nigra pars compacta (SNc) would be rewarding and mediated by enkephalin. We used Penk-IRES-Cre mice, which express Cre recombinase exclusively on enkephalin neurons for optogenetic and chemogenetic manipulations in the VP. Cre-positive mice and littermate controls were injected either with a cre-dependent channelrhodopsin virus or with a Cre-dependent inhibitory chemogenetic actuator in the VP. We used optically-evoked real time place preference (RTTP) and intracranial self-stimulation (ICSS) to measure reward. For our chemogenetic experiments we used conditioned place aversion and operant sucrose self-administration as behavioral readouts. We found that enkephalin-positive VP-SNc projection bidirectionaly controls reward. Stimulating Enk VP-SNc terminals was rewarding in both RTPP and ICSS. Chemogenetic inhibition of these same neurons resulted in a conditioned place aversion. Local infusion of GABAA antagonists, mu and delta antagonists, and glutamate antagonists at a range of concentrations in the SNc did not block the light-induced preference in RTPP. We conclude that enkephalin-positive projections from the VP to the SNc bidirectionally control reward and aversion. Our preliminary results suggest that these effects might not be mediated by enkephalin, GABA or glutamate, although more experiments need to be done, including electrophysiology recordings. Understanding how endogenous opioid peptides modulate reward is crucial for understanding the mechanisms of opioid addiction.

Vocal Communication to Facilitate Dispersal in *Saguinus imperator* and *Saguinus weddelli*

Alessandra A. Silva

Mentor: Mrinalini Erkenswick Watsa

Emperor (*Saguinus imperator*) and saddleback (*S. weddelli*) tamarins live in groups of two to nine adult and subadult males and females. Since each group's primary (and only) breeding female tends to maintain her role in the group for many years, most offspring, upon reaching sexual maturity, must leave to find a group in which they stand a chance to become a breeder. We believe they do not encounter potential mates simply by chance, but rather through communication, such as vocalizations. The Los Amigos Biological Field Station in Peru has run an annual capture and release program for eight years, and is able to identify the age, sex, and reproductive status of every individual in the area. The primary breeding female of each group was fitted with a radio collar; by tuning, changing the gain, and adjusting the frequency on a radio telemeter receiver, we used an antenna to locate the group. Remaining individuals were identified by a bleaching pattern and unique bead collar. Researchers trekked on and off trails through primary and secondary forest for eight hours at a time following an assigned tamarin group, recording behaviors via focal and scan methods. Two-minute scans—regular behavior censuses—were run every five minutes; focals were also recorded regularly, in which one reported (into a voice recorder) a randomly selected individual's behavior continuously for 15 minutes. A more specialized voice recorder captured all vocalizations from the focal individual or any other identifiable members. We tracked the location of the group whenever possible with our GPS, and noted the coordinates of any feeding trees or sleep trees visited that day. Finally, detailed descriptions were noted for any observed scent-marking and mating. This data was collected in the hopes of revealing any trends in behavior within the group, especially in recently mature tamarins.

Shooting for Answers: Bullying, Masculinity, and School Massacres

Bonnie Simonoff

Mentor: Greg Ott

This work examines the complicity of various factors in incidents of gun violence, particularly school shootings, through psychological character analysis of Jodi Picoult's *Nineteen Minutes* and investigation of real-world case studies. Specifically, I evaluate the role of hegemonic masculinity in perpetuating a culture of violence. Amidst escalating rates of school shootings in the U.S., understanding the root causes of this violence becomes increasingly important. With a psychosocial approach, I found that past bullying of the perpetrator remains relevant when it comes to school shootings. However, exploring merely this connection to interpersonal bullying interactions—and to commonly-considered influences of the media and mental illness—fails to encompass a more fundamental correlation; interwoven within the majority identities of the overwhelmingly young, white male perpetrators is their masculinity. In making sense of this contemporary, complex issue, these other factors become more telling when we acknowledge a pervasive, practiced ideal of masculinity as an often-overlooked yet closely associated contributor. Through review of pertinent sociological, psychological, and legal positions and an interview with a gender studies expert, I localized my research to Washington University in St. Louis (WUSTL) positions regarding gun violence. I concluded that WUSTL violence-prevention programming should include discussions of how violence and masculinity intersect in order to prioritize student and community well-being, preparedness, and safety.

Targeted Gene Deletion using Intrinsic Deletion Machinery in *Tetrahymena thermophile*

Urvi Sinha

Mentor: Douglas Chalker

The ciliate *Tetrahymena thermophila* eliminates nearly one third of its genome from the developing somatic nucleus. The goal of this work was to optimize the targeted deletion of genes by exploiting this intrinsic DNA deletion machinery, a method known as "co-deletion." Generating knockouts is an important strategy for determining the function of genes, and co-deletion had the potential to generate knockouts more easily or to knock out multiple related genes at once. Co-deletion occurs when a DNA sequence normally retained in the developing somatic genome is imbedded within an eliminated sequence and the chimeric sequence is introduced into developing *Tetrahymena* cells. The genomic copies homologous to the imbedded sequences are induced to undergo deletion. To attempt to induce co-deletion of multiple genes efficiently, I used Gateway-mediated recombination vectors that contained a recombination cassette flanked by internal elimination sequences into which cloned genes of interest could be inserted. These vectors were transformed into *Tetrahymena* using electroporation and biolistic transformation protocols to determine whether one or both methods promoted co-deletion. Experimental conditions were altered to optimize the efficiency of the transformation, as quantified by the number of drug resistant cell lines generated, and to increase the efficiency of gene deletion, which was demonstrated through PCR analyses and verification of deleted regions by DNA sequencing. I was able to induce co-deletion of several genes, but this method does not appear useful, for several reasons. Deletions occur only in the somatic genome, so they are not heritable. Phenotypic analysis of one gene appeared to indicate that for this particular gene, deletion from the somatic genome alone is insufficient to stop expression during development, when the gene is expressed. Results indicate that co-deletion is not an easier or more efficient method than standard homologous recombination to generate gene knockouts.

p62 Deficiency Leads to the Disruption of Mitochondrial Function in Macrophages

Eric Song

Mentor: Babak Razani

Protein and organelle turnover is critical for cellular homeostasis and is predominantly mediated by autophagy. Disruptions in autophagy lead to the accumulation of dysfunctional organelles, such as the mitochondria. p62 (SQSTM1) is a selective autophagy chaperone protein which targets protein aggregates and damaged organelles to autophagosomes for degradation. Specifically in macrophages, p62 deficiency leads to the improper degradation of unnecessary material, leading to an inflammatory response through IL-1φsecretion and apoptosis, which are phenotypes characteristic of atherosclerosis. Herein we hypothesize that the accumulation of dysfunctional mitochondria in p62 deficiency is a mechanism which drives these phenotypes. In p62 knock-out (p62 KO) macrophages, we observed increased mitochondrial size, lower oxygen consumption, and decreased ATP production, suggesting a vital role for p62 in proper mitochondrial function. Our current focus is to define the changes in mitochondria-related cellular pathways, such as mitochondrial fusion/fission, glucose metabolism, mitochondrial protein transport, and apoptosis in p62 KO macrophages. We examined mRNA levels of proteins involved in those pathways using quantitative PCR. Our preliminary analysis suggests that p62 KO macrophages express glycolysis and mitochondrial fission genes at lower levels. In future experiments, we will validate our results on the protein level by Western blotting and test whether observed mitochondrial deficiency is the cause of induced IL-1β secretion and apoptosis in p62 KO macrophages. Taken together, our data suggest that p62 facilitates maintaining healthy mitochondria, and we hypothesize that mitochondrial dysfunction is the main cause of induced inflammation and apoptosis in p62 KO macrophages.

Total Synthesis of a Library of Unnatural Derivatives of Lingzhiol

Emma Streff

Mentor: Vladimir Birman

Lingzhiol, a tetracyclic meroterpenoid, has an unprecedented structure and exhibits selective inhibitory activity toward p-Smad proteins, which is relevant to the treatment and prevention of renal fibrosis, a common and often fatal final pathway of chronic kidney disease. Discovered by Cheng and colleagues, lingzhiol was isolated in minute quantities from *Ganoderma lucidum*, a tropical fungus commonly used in traditional Chinese medicine under the name ling-zhi (靈芝). Dr. Vladimir Birman and Krishna Sharma Gautam have recently published a novel 9-step synthesis of lingzhiol, which utilizes an acid-catalyzed semipinacol rearrangement of a glycidyl alcohol intermediate. Using variations on this flexible scheme, a library of unnatural lingzhiol derivatives are being synthesized, with particular focus on altering the substitution pattern on the benzene ring. These derivatives will be sent to the Washington University School of Medicine for further investigation of their antifibrotic and neurotrophic activities.

Personality and Biomarkers for Predicting Brain Volumes in Older Adults

Maya Strod

Mentor: Denise Head

Aging of the brain progresses in similar ways throughout the human population, with variation depending on multiple factors including personality and presence of neuropathology. The proposed work will examine the interactive effects of personality traits (i.e., neuroticism and conscientiousness) and AD biomarkers on regional brain volumes in cognitively normal individuals. Higher conscientiousness, combined with lower AD biomarkers, may be related to larger brain volumes, while the combination of higher neuroticism and higher AD biomarkers may be related to particularly smaller brain volumes. CSF measures of AB_{42}, tau, and ptau will be obtained from the ADRC. Measures of neuroticism and conscientiousness will be derived from the NEO Personality Inventory. MRI scans from the ADRC will be processed using FreeSurfer to derive regional brain volume estimates. The results of the statistical analysis suggest that the interaction between neuroticism and tau culminates in larger hippocampal and parahippocampal gyrus volumes. The results also suggest that the interaction between neuroticism and amyloid plaque (AB42) culminates in larger hippocampal volumes, although not larger parahippocampal volumes. This suggests that with the presence of higher neuroticism in a subject, there are a higher amount of AD biomarkers as well as larger brain volumes related to neuropathology. The relationship between specific brain changes and personality in normally aging individuals may predict symptomatic AD earlier than current diagnosing practices.

Establishing the FGFR1 Downstream Signaling Pathways Responsible for Regulating the Differentiation of Cochlear Hair Cells

Yutao Su

Mentor: David Ornitz

Hearing loss affects a large portion of the population and results from the loss or damage of the cells that sense sound. These cells, called hair cells, lack regenerative capabilities in mammals. However, by elucidating the mechanisms that regulate hair cell differentiation during developmental stages we may inspire pro-regenerative therapies applicable in adult auditory systems to restore hearing. Previous studies have shown that a vital component of hair cell differentiation is Fibroblast Growth Factor (FGF) signaling and that it acts through FGF Receptor 1 (FGFR1) in the undifferentiated sensory epithelium. However, the signaling pathway downstream of FGFR1 that is required for hair cell differentiation is not known. There are four candidate pathways that FGFR1 is known to activate: MAPK, PLCγ, AKT, and STAT. We use cochlear explant cultures given specific pathway inhibitors that block each pathway individually to determine which pathway(s) affect hair cell differentiation: U-73122 inhibits PLCγ, LY-294002 inhibits AKT, and U-0126 and SB-203580 inhibit the p38 and MEK1/2 branches of the MAPK pathways, respectively. Our preliminary results show that treating explants with the inhibitors U-0126 and SB-203580 resulted in a decreased number of hair cells. Other inhibitors tested yielded hair cell counts similar to their vehicle controls. These results suggest that the ERK and p38 MAPK pathways could play a crucial role in the development of hair cells. As this is an ongoing project, additional trials and studies are needed to further validate these results.

Exploring Experimental Parameters for the Realization of a One-Photon and One-Qubit Heat Engine

Caroline Sullivan

Mentor: Kater Murch

Quantum systems are deeply influenced by thermodynamics on the microscopic level. A common macroscopic system, the heat engine, uses a thermodynamic cycle to produce work. A macroscopic quantum heat engine can be created by coupling a resonant microwave cavity to a single superconducting transmon qubit and varying the magnetic flux over the system, which uses the coupled eigenstates of the cavity and qubit as the work-generating "stroke" of a thermodynamic cycle. This study examines the theory behind such a system, as well as examples of quantum heat engines using other techniques such as trapped ions, for the purpose of determining a useful and realizable set of parameters to create a one-photon one-qubit heat engine in our own laboratory environment. Further, operating the cycle in reverse would create a heat pump, which under appropriate conditions could have the ability to pull energy from a secondary system in a thermally observable way.

Genetic Mapping of Midbrain Pain Circuitry

Saranya Sundaram

Mentor: Robert Gereau

The periaqueductal gray (PAG) has been shown to be a critical center in mediating endogenous pain modulation. Though the mechanism by which PAG mediates descending pain modulation has been well studied, it is not clear how sensory information coming from different brain regions is incorporated into the PAG and communicates with the downstream brainstem targets. To understand the input/output (I/O) anatomical organization of PAG information processing, we used viral-genetic tracing tools to visualize and quantitatively characterize connections to the PAG.

To determine the inputs coming into the PAG we injected retrograde transsynaptic virus canine adenovirus 2 Cre (Cav2 Cre) into the PAG in Ai32 transgenic mice (express ChR2-EYFP in a Cre-dependent manner). In our preliminary studies using this approach, we observed the robust ChR2-EYFP labelling in several brain regions and spinal cord suggesting these regions make monosynaptic input to the PAG. In our future studies we will be able to stimulate these input regions using blue light and determine the functional role of these inputs to the PAG. To determine the functional role of the PAG outputs to RVM, we used an intersectional genetic strategy that allowed us to specifically target PAG→RVM neurons and manipulate their activity using ChR2. In Vglut (glutamatergic) and Vgat (GABAergic) Cre mice, we injected CAV-FLEx^{loxP}-Flp virus in the RVM and we injected Cre and Flp dependent ChR2-EYFP into the PAG.

This approach allows us to express ChR2 selectively in the Vglut2^{+} or Vgat^{+} PAG→RVM neurons and manipulate their activity to dissect their role in pain processing. In our preliminary studies, we were able to genetically isolate the Vglut2^{+} PAGàRVM neurons.

Optogenetic stimulation of ChR2 expressing Vglut2^{+} PAG→RVM neurons resulted in robust analgesia in a $_{persistent}$ pain model. These results reveal the essential role for I/O organization of the PAG in processing pain information.

Graphene Oxide Nanomaterials for Active Biosensing

Corban Swain

Mentor: Pratim Biswas

Metabolites consist of biological molecules utilized in metabolic processes, i.e. adenosine triphosphate (ATP). Detection of metabolites s valuable on two fronts: 1) Clinically, metabolites can report on the development of specific diseases;¬ 2) While those found in environmental samples can indicate toxicity and the activity of specific organisms.

However, most currently available medical diagnostic tests require extensive resources—large instruments, specialized technicians, etc.—that are inaccessible in developing countries and too expensive for continuous monitoring. To address this need, there is a push to develop medical diagnostics and environmental tests that can be used outside of a complex clinical laboratory and can present results in a simple format (e.g. a visual change or digital readout). Personal glucose meters and pregnancy tests are well-known examples of existing accessible diagnostic tests. Despite these limited examples, there is still a need to create a broader range of accessible diagnostics and, more importantly, to develop a toolbox of materials that can be used in the rational design of equipment-free sensors for any biological analyte. Herein, we interrogate the capacity of graphene oxide nanomaterials for point of care detection and *in situ* sensing of metabolites.

The Role of Lipin 1 in Cardiac Metabolism and Function

Alison Swearingen

Mentor: Dr. Brian Finck

Lipin 1 is an intracellular protein that dephosphorylates phosphatidic acid (PA) to generate diacylglycerol, which is an important step in lipid metabolism. Exercise, which affects cardiac metabolism, has been shown to increase lipin 1 expression in mice, while heart failure or hypertrophy has been shown to cause decreased lipin 1 expression. We have hypothesized that accumulation of PA in failing heart contributes to cardiac hypertrophy and dysfunction, and thus, the overexpression of lipin 1 in failing hearts will alleviate cardiac dysfunction by reducing PA accumulation. To test this hypothesis, we generated transgenic mice with cardiac specific overexpression of lipin 1 (cs-lipin 1 OE) by using a cre-inducible transgene to examine the effects of this protein on cardiac metabolism and function. The cs-lipin 1 OE mice appear outwardly normal, and H&E staining did not show any architectural abnormalities or inflammatory infiltrates.
Additionally, echocardiographic studies revealed no functional abnormalities in the hearts of cs-lipin 1 OE mice compared to littermate control mice. However, the cs-lipin 1 OE mice have increased heart weight to body weight ratios and increased expression of several genes associated with ventricular hypertrophy. While contrary to our original hypothesis, these data provide novel evidence that lipin 1 may influence cardiac hypertrophy and function.

Host-Parasite Interactions: Effects of Larval Habitat on *Ascogregarina barretti* Infection in *Aedes triseriatus*

Brenden Sweetman

Mentor: Kim Medley

Throughout human history, mosquitos have been effective vectors of some of the most virulent human pathogens. In response, much research has investigated the relationship between mosquitoes and the pathogens they vector, but little is known about the role of parasite infection on mosquito fitness, which can indirectly influence vector competence. Parasite infection is fundamentally an ecological process; thus, we investigated the role of key ecological factors influencing pathogen infection rates and fitness in the native treehole mosquito, *Aedes triseriatus.* In their larval habitat, they can become infected by a non-lethal gregarine parasite (*Ascogregarina baretti*) that requires the mosquito to complete its life cycle to reproduce. We evaluated the effect of nutrient level and type on *Ae. triseriatus* larval survival, development time, and *A. baretti* infection by placing 30 individual larvae per level in 12 ml of water infused with 3 levels of ground crickets or leaf detritus. These nutrient resources mirror natural detritus present in larval aquatic habitats. Data collected provided insight into three aspects of the observed host-parasite relationship: First, in habitats with low concentrations of animal and leaf infusion, mosquito fitness declines and pathogen infection rate is low. Second, in high concentration animal infusion, mosquito fitness is high and pathogen infection rate is low. Third, in high concentration leaf infusion, although larvae mortality is rare, pathogen infection rate is significantly higher. These interactions indicate higher complexity pathogen/larval interactions such as a larval immune response in low nutrient environments where stress is high. Exploring how mosquitos interact with pathogens under different ecological and environmental conditions is fundamentally important to understanding how these ecological factors can effect mosquito and pathogen distribution and how vectored disease is spread. The relationship between *A. triseriatus* and *A. barretti* can act as a model to further understand how ecological factors influence pathogen-host interactions.

The Effect of Framing on Mind-Wandering in Young and Late Adulthood

Benjamin Talisman

Mentor: Julie Bugg

Research on mind-wandering has usually found that older adults report lower levels of mind-wandering than younger adults, but objective measures on the Sustained Attention to Response Task (SART), such as PostError slowing and PreError speeding, reveal that they experience similar levels of mind-wandering. Previous experiments, in particular Jackson & Balota 2012, have created some evidence that this may result from the subject's perception of mind-wandering, so this experiment was designed to investigate whether framing mind-wandering in a positive light can eliminate some of the biases that cause older adults to report lower levels of mind-wandering. The results indicate that while our manipulation encouraged more reports of mind-wandering, there was no interaction between age and how mind-wandering was framed. This suggests our manipulation may not have been significant enough to encourage more accurate mind-wandering reports in older adults, or that perceptions of mind-wandering inherently cause lower levels in older adults.

LTL1 Protein Regulates DNA Rearrangement Boundaries in *Tetrahymena thermophila*

Marta Taye

Mentor: Douglas Chalker

The somatic genome of ciliated protozoan, *Tetrahymena thermophila* undergoes extensive reorganization during development to allow for efficient gene expression. *Tetrahymena* possess two functionally different nuclei, a micronucleus and a macronucleus. The transcriptionally silent micronucleus, or germline nucleus, contains five pairs of condensed chromosomes. The macronucleus, or somatic nucleus, is transcriptionally active, providing for all gene expression. During sexual development, new somatic and germline nuclei differentiate, which for the somatic genome requires thousands of site-specific deletions of DNA segments called internal eliminated sequences (IESs). Removal of IESs eliminates approximately 30% of the genome from over 10,000 individual loci to create a streamlined somatic nucleus that drives gene transcription. We identified a protein, encoded by *LTL1*, required for precise excision of a specific subset of IESs. Wild-type cells exhibit reproducibly accurate excision of IESs; however, in Δ*LTL1* cells, this subset of IESs, which includes IES D, is excised with aberrant and heterogeneous boundaries. Thus, *LTL1* appears to determine the position of deletion boundaries for specific IESs. To establish that loss of *LTL1* alone is responsible for the observed defects in IES excision, I introduced a wild type copy of *LTL1* into Δ*LTL1* cells and found that excision accuracy of IES D was restored. I attempted to pinpoint the specific cis-acting sequences required for accurate IES excision of IES D by introducing site-specific mutations in the region flanking this IES and assessed the impact on excision boundaries. Mutagenesis of sequences upstream of -75bp resulted in aberrant excision boundaries, indicating that *LTL1* requires these to precisely excise IES D. This work provides clear evidence that *LTL1* regulates the excision boundaries of specific IESs through recognition of sequences within the flanking region. Investigating the role *LTL1* plays in reorganizing the *Tetrahymena* genome sheds light onto the complexity by which chromatin domains are established in eukaryotes.

The Genetic Basis of Alzheimer's Disease: Phenotype-Genotype Relationship in Autosomal-Dominant Alzheimer's Disease

Carmen Toomer

Mentor: Tammie Benzinger

Autosomal Dominant Alzheimer's Disease (ADAD), the rarest form of Alzheimer's disease (AD), leads to early onset dementia and is due to a mutation within Amyloid Precursor Protein (APP), Presenilin-1 (PSEN-1), or Presenilin-2 (PSEN-2) genes. Each mutation alters the metabolism of β-amyloid (Aβ)—the protein considered to be a driving force in the physiopathogenic cascade of AD—and guarantees AD development. Like the more common, sporadic form of AD, abnormalities observed in ADAD are cerebral microbleeds (CMBs) and severe white matter hyperintensity (WMH), which are detected with imaging tools. The aim here is to evaluate these two features and their relationship with ADAD genotypes.

The Dominantly Inherited Alzheimer Network (DIAN) enrolls participants at risk for ADAD, and performs clinical, cognitive, imaging, and biochemical assessments. The symptom onset in ADAD is approximated by the afflicted parent's age of disease onset, and is termed estimated years to onset (EYO). CMBs and WMH can be observed even before symptom onset, and are indications of vascular abnormalities. Studies have shown that AD individuals with severe WMH have more CMBs.

Among ADAD mutations, the expression of the imaging biomarkers is variable. The PSEN-1 mutation is the most common mutation and has exhibited severe AD pathology. Using the DIAN data, I will correlate the participants' WMH volumes with CMBs counts, using factors such as EYO, cognitive impairment and the mutation type. I hypothesize that PSEN-1 carriers have more severe WMH and CMBs when compared to the other two mutations. I aim to further establish the trend outlined by previous studies. Further understanding ADAD pathology will increase our ability to devise therapies to control and combat AD as a whole.

The Effects of Arterial Tortuosity on Aneurysm Progression

Lien Tran

Mentor: Jessica Wagenseil

Thoracic aneurysm and dissection (TAAD) is a condition that puts the thoracic aortic wall under unnecessary stress. A number of new reports have suggested that arterial tortuosity may be a telltale key in predicting TAAD progression. Tortuosity, which is defined as the ratio of the actual length of the artery to the geometric length, has been shown to be proportional to aneurysm diameter. Although previous clinical studies have been conducted with a limited pool of participants and varying tortuosity indices, we plan on increasing the number of participants as well as compare various methods of tortuosity measurement to find the best indicator of TAAD progression.

Mouse models with arterial tortuosity and TAAD have been used successfully to better our understanding of aneurysm growth and intervention. Therefore, we will again use them to follow longitudinal changes in tortuosity. This project specifically focuses on three syndromes that are associated with TAAD and arterial tortuosity—Marfan Syndrome (MFS), autosomal recessive cutis laxa type 1B (ARCL1B), and Loeys-Dietz Syndrome type 1 (LDS1). We propose to determine if arterial tortuosity is predictive of aneurysmal disease outcomes in mouse models of MFS, ARCL1B, and LDS1. We will then compare our new method of monitoring TAAD progression with traditional methods. We also aim to investigate the role of TGF-φAT1r signaling and MMP activity in arterial tortuosity and aneurysm pathogenesis using mouse models of MFS, ARCL1B, and LDS1 and compare the predictive value of different measures of arterial tortuosity and length for disease outcomes in TAAD through retrospective analyses of clinical data. This involves examining MRI images of over 200 clinical patients who have MFS or LDS whose disease outcomes are known, in order to quantify the predicative value of arterial length and tortuosity.

Carriage of Symbiotic *Burkholderia* spp. Changes the Number of Innate Immune Cells in Social Amoebae

Stacey Uhm

Mentors: David Queller and Joan Strassmann

Innate immunity is the first line of defense for eukaryotes. This non-specific immune response targets agents of harm such as toxins and pathogens. The innate immune mechanism has been studied in depth in many organisms, especially humans, and now in the social amoeba *Dictyostelium discoideum*. The innate immune cells in *D. discoideum* called sentinel cells phagocytize harmful material inside multicellular aggregates of *D. discoideum* during the social stage. These spent sentinel cells are left behind in trails as the multicellular slug migrates and can be counted using fluorescent confocal microscopy.

Some *D. discoideum* clones known as farmers carry symbiotic *Burkholderia* spp. We have previously reported that farmers have fewer sentinel cells than non-farmers and thus their innate immunity could be impaired. We also reported that farmers exposed to a toxic environment gained protection from Burkholderia spp. while non-farmers were significantly harmed even with greater number of sentinel cells.

Here, we determine if fewer sentinel cells in *D. discoideum* farmers are a consequence of the symbiotic relationship with *Burkholderia* spp. If true, these data suggest that *Burkholderia* spp. are able to manipulate the innate immunity of their host farmer to reduce the possibility of clearance during the multicellular stage and possibly facilitate the symbiotic relationship with their host farmer. Further study of this simple system could lead to insights in how bacteria are able to interact and manipulate the innate immunity of their eukaryotic hosts.

Conduct Disorder Genomewide Association Study and Extension to Affective Brain Function

Namrata Vakkalagadda

Mentor: Ryan Bogdan

Conduct disorder (CD) is a moderately heritable childhood externalizing disorder associated with substantial personal and societal burden. The current study sought to examine its molecular genetic architecture and neural mechanisms that may underlie associations between genetic risk and disorder expression. The authors performed a genomewide association study (GWAS) of retrospectively reported CD among Australians of European ancestry who completed the Comorbidity and Trauma Study (ncases=680, ncontrols=995). They then tested genetic risk factors identified from the GWAS for association with self-reported psychopathy and regional differences in neural activity to an emotional face-matching task in an independent sample of 406 non-Hispanic U.S. undergraduate students of European ancestry. The authors find that the major A allele of the intergenic rs12536973 polymorphism was associated with increased risk for CD (OR=2.00, p=3.74E-08), and gene-based analyses revealed an association with GOLM1. The A allele of rs12536973, as well as genomewide polygenic risk scores (PRS) developed from the discovery GWAS, were associated with increased self-reported psychopathy in the independent college sample. CD PRS were negatively coupled with left anterior insula activity to emotional faces in whole-brain analyses. Post hoc conjunction analyses showed that both CD PRS and self-reported psychopathy were associated with reduced activation in overlapping clusters within the bilateral anterior insula and supramarginal gyri. Collectively, these results provide insight into the genetic architecture of CD risk and suggest that blunted neural responses to affective social stimuli in regions previously linked to empathy may represent a neural mechanism through which genomic risk may promote its expression.

Physiognomy Predicts Local Tick Abundance in Ozark Forests

Thomas Van Horn

Mentor: Kim Medley

Amblyomma americanum (L.) (Acari: Ixodidae) is a common tick species in the mid-western United States that is emerging as an important human disease vector. While some recent studies have modeled broad-scale (regional or county-level) distribution patterns of *A. americanum*, less is known about how fine-scale habitat characteristics drive *A. americanum* abundance. Such fine-scale information is vital to identify targets for tick population control measures within land management units. We investigated how fine-scale habitat features predict host-seeking *A. americanum* adult and nymph abundance within a 12-ha section of oak-hickory forest in Missouri. We trapped ticks using CO_2-baited traps at 40 evenly-spaced locations for three 24-hour periods during the summer of 2015, and we measured biotic and abiotic variables surrounding each location. A total of 2,008 *A. americanum* were captured, of which 1,009 were nymphs and 999 were adults. We observed large fine-scale variation in local abundance (min=0 ticks, max=112 ticks, mean=16.7 ticks/trap night), which we visualized using interpolation techniques. Using generalized linear mixed models, we identified variables that best predicted nymph and adult abundance. The best models determined by AIC for both nymphs and adults used aspect to predict abundance and had negative relationships with slope. Nymph abundance was negatively related to temperature variance, while adult abundance had a negative relationship with elevation. These results demonstrate that managers can predict local tick abundance through simple physiognomic factors and use these parameters for targeted management action.

Decision Making and Psychotic-Like Experiences

Gina Vellequette

Mentor: Deanna Barch

Individuals with schizophrenia have been shown to make decisions differently than healthy individuals, and often in ways that are less effective or accurate. These individuals often make decisions based on their previous experience rather than thinking based on planning for the future. In psychology, these different types of learning are called model-free and model-based learning systems. A model-free learning system is a habitual learning system that is based on prior experience and a model-based learning system is goal-directed that relies on prospective information. Previous studies have found that people with schizophrenia show intact model-free learning, but a reduced model-based learning system. This study examined whether this same pattern of learning was true for individuals in the general population who experienced psychotic like experience, but did not have a clinical diagnosis of schizophrenia. This was achieved by asking 57 healthy participants to complete tasks and questionnaires. The study had participants perform a "space-alien" task that has been used in previous research to measure model-based and model-free learning decisions. The task asks participants to first choose a spaceship to take them to one of two planets, and then pick an alien for a chance of a reward. This measures decision making by looking at what the person would decide to do once they either received a reward or did not receive a reward. The participants also filled out questionnaires asking about depression, hedonic experiences and psychotic-like experiences. We found that those individuals that experienced psychotic-like experiences showed intact model-free learning, but impaired model-based learning, with a similar pattern to that seen among individuals with schizophrenia. This means that in a healthy population, individuals that have psychotic-like experiences make decisions in a similar fashion to those with schizophrenia.

Building Non-Monogamies: Race, Quare Sexual Politics, and the (Im)possibilities of Non-monogamy

Jordan Victorian

Mentor: Shanti Parikh

Scholars of race, feminism, and queer theory have long challenged compulsory monogamy as a regulation of desire and bodies who desire. Yet while the effects of monogamy have been discussed, its assumptions still limit the politics we imagine to be possible. Literature on the consensual non-monogamy often under-analyzes how structures of power affect intimacies. Racial and ethnic studies often reinforce normalizing ideas of monogamy and 'appropriate' sexual behaviors, stifling queer potential within these deviant practices. Moreover, queer theory and politics often gloss over how racism, as part of heteronormativity, makes people of color into sexual "others." Attempting to bridge conversations across these fields, this project seeks an intersectional analysis of power exploring non-monogamous desire within a larger sexual economy of inequality and (im)possibility. Through critical theory and ethnography, the project engages consensually non-monogamous people of color, particularly in St. Louis, to highlight the sexual politics and sexual cultures they interact with. Ultimately, it works toward destabilizing the sociopolitical mandate toward "The [White] Monogamous Couple" and building toward a more liberated future for all of us feeling and enacting desires—whether through monogamous sexual and intimate couplings, multi-partner arrangements, or something beyond.

Epimorphin Regulates the Mouse Intestinal Stem Cell Niche via the Stromal Microenvironment

Courtney Vishy

Mentor: Deborah C. Rubin

Intestinal resection for disorders such as Crohn's disease may result in short bowel syndrome, with nutrient malabsorption and parenteral nutrition dependence. There are few effective treatments. Stem cell therapies represent a novel therapeutic approach. Epimorphin (Epim) regulates growth factor secretion from intestinal subepithelial myofibroblasts. Although Epim is not expressed in epithelial cells, we previously showed that primary cultures of *Epim*$^{-/-}$ enteroids have increased surface area and budding compared to wild type (WT) enteroids. Our aims are to understand the mechanisms for this increase and determine whether this reflects stromal environmental effects on the stem cell niche.

Crypts were isolated from WT and *Epim*$^{-/-}$ mouse small intestines and cultured *in vitro*. Enteroids were imaged after 6 days and analyzed for surface area, budding, and epithelial differentiation by staining. Enteroids were then passaged two more times, reimaged, and harvested for RNA. RNAseq was performed to determine the effect on global epithelial gene expression.

In primary crypt stem cell cultures, *Epim*$^{-/-}$ enteroids had significantly larger surface area and more buds vs. WTs ($p<0.001$). At the second passage, enteroid area and budding in *Epim*$^{-/-}$ vs. WT enteroids were no longer significantly different (p=NS). The percentage of goblet and Paneth cells per enteroid was significantly increased in *Epim*$^{-/-}$ enteroids ($p=0.01$). Stem cell marker expression was significantly increased in *Epim*$^{-/-}$ vs WT enteroids by qRT-PCR ($p<0.05$). RNAseq analysis revealed significant differences in 86 genes. We conclude that Epim regulates mouse intestinal epithelial and stem cell proliferation and gene expression via stromal contributions to the niche microenvironment.

Classification of Hippocampal Interneuron Types Using Optical Clearing and Immunostaining

Elena Waidmann

Mentor: Edward Han

Although hippocampal neuronal activity is required for spatial navigation and learning, little is understood about how the pyramidal neuronal network is controlled during these behavioral states. The wide anatomical and molecular diversity of hippocampal interneurons suggests that these neurons play a critical role in shaping network activity and plasticity. To better understand the role of interneurons during ongoing behavior, we recorded the calcium activity of identified interneuron types from head-fixed animals performing a spatial navigation task in virtual reality. By using cre-driver lines to drive calcium indicator expression, we can study the activity patterns of broad classes of interneurons; however, more precise tools are required to further subdivide these categories so that function can be mapped onto individual interneuronal cell-types. To do this, we performed post-hoc brain clearing and antibody staining using the AbSca*l*e method. AbSca*l*e uses urea, sugar alcohols, and various ionic detergents to wash out lipids and clear intact tissue. We are able to preserve genetically encoded calcium indicator fluorescence while using immunofluorescent labeling to stain for markers of different subtypes of interneuron. These technical advances will allow us to assign functional activity to specific subtypes of interneurons in order to elucidate how diverse interneuron types interact to regulate hippocampal activity during movement and learning.

A Grassroots Revolution? Imagining Change in St. Louis Food Landscapes

Joselyn Walsh

Mentor: Peter Benson

This work engages with the formation of a burgeoning alternative food movement in St. Louis, MO by examining the conditions under which it arises as a response to dissatisfaction with conventional food. Through situating ethnographic interviews with St. Louis residents into a broader context of the problematization of U.S. food and eating outlined by Julie Guthman in Weighing In: Obesity, Food Justice, and the Limits of Capitalism and Susan Greenhalgh in Fat-Talk Nation, I discuss how people come to internalize dominant cultural narratives of food system problematization as their own. I draw on arguments from Guthman and Greenhalgh as well as from my own research with individuals and organizations in St. Louis to discuss points where the explanatory power of dominant cultural narratives of personal responsibility for health and nutrition and a focus on the consumer as a locus of intervention fall short. I provide evidence that the strength of these flawed narratives is pervasive enough to change the agendas of local organizations which would typically challenge the environmental and health effects of industrial agriculture to ones which seek to promote health and sustainability without challenging powerful economic interests. I argue that we need to be attentive of the power of reproducing these narratives, as a move to emphasize these types of initiatives may result in managing rather than addressing harm caused by powerful industries.

The Next Generation of Wireless Cyber-Physical Simulator

Xinghan Wang and Kevin Xu

Mentor: Chenyang Lu

In order to make Wireless Cyber-Physical Simulator (WCPS) more accessible to people in the research community, and also to improve its accuracy of representing real industrial models, we worked on the dockerization of WCPS, and implemented the multi-rate feature for WCPS, enabling the simulator to have different network rate and plant rate when running a simulation. We created a new version of WCPS by dockerizing run-time libraries and the Tossim server and also embedding the multi-rate feature in the old version. Our report includes the introduction and dockerization of WCPS, and shows the results of using the new generation of WCPS on a specific linear system.

Adding Insecurity to Injury: Risk Factors for Disordered Eating among Competitive Runners

Sophie M. Watterson

Mentor: Eileen G'Sell

Running has a reputation for improving physical and mental health. However, competitive runners experience both elevated rates of injury and disordered eating behavior, which indicates that competitive running may have some detrimental impacts. Is there a connection between competitive running, injury, and eating behaviors? Could injuries be a potential trigger for disordered eating in runners? I found extensive data had been published on injury and disordered eating as they relate to running, but not in conjunction with one another. To explore this potential connection, I conducted a survey of 136 Division III college runners in the University Athletic Association who had experienced injury in their collegiate careers, which addressed changes in social behaviors, moods, self-perception, and eating behaviors while injured. An alarming 9.2% of those surveyed reported that they experienced disordered/restrictive eating behavior while injured that was not pre-existing. My research found that competitive runners and individuals with eating disorders tend to base their self-esteem upon external validation. In the case of a runner, this validation comes from athletic performance. When an injury challenges the athlete's ability to perform, it may also challenge her self-esteem, which can lead to disordered eating. Additionally, restrictive eating behaviors may be intensified by cultural pressure to attain an ultra-lean "runner's body."

Pathological Biomarkers and Cognitive Change in Parkinson Disease

Alexandra J. Weigand

Mentor: Meghan Campbell

Although Parkinson disease (PD) is primarily considered a movement disorder, there are also cognitive problems associated with this disorder that cause significant impairment to quality of life. There is, however, a high degree of inter-individual variability in cognitive dysfunction in PD, necessitating prognostic tools that can predict the trajectory of cognitive decline for a given individual. The current study investigates the utility of various biomarkers associated with the pathological progression of PD and their ability to predict cognitive change across different domains and time intervals. Data were obtained for 174 PD participants who were either cognitively normal (N = 93) or cognitively impaired (N = 81) at baseline. Regression analyses were conducted to determine associations between baseline biomarkers (including cerebrospinal fluid (CSF) amyloid-beta 1-42 ($A\varphi_{42}$), tau, and alpha-synuclein (α-syn); amyloid-beta deposition measured with Pittsburgh compound B (PiB); and regional gray matter volumes (GMV)) and reliable change indices (RCIs) for five cognitive domains across one, two, and three year intervals. Results indicated that CSF and PiB measures of amyloid-beta pathology predicted cognitive change across longer time intervals, whereas regional GMVs predicted more imminent cognitive change. Further, the timing of cognitive change varied based on the location of amyloid-beta deposition such that brainstem and posterior cortical amyloid-beta deposition was predictive of distant future cognitive change and anterior cortical amyloid-beta deposition was predictive of more imminent cognitive change, suggesting that amyloid pathology follows a caudo-rostral progression similar to Lewy body pathology in PD. These findings may have prognostic value, such that the presence of certain biomarkers and the location of pathology may predict which PD patients will develop cognitive impairment and when the decline will begin.

Lighter Than a Feather: MEMS Scale with Attogram Sensitivity

Zack Weinstein

Mentor: Erik Henriksen

An ongoing project in the Henriksen lab explores the effect of adding isolated osmium atoms to the surface of devices based on flakes of graphene. This is done in order to determine if osmium can induce a spin-orbit coupling in graphene, in the hope of eventually creating a 2D topological insulator. There is much current interest in the study of topological insulators, which exhibit bulk insulator and conducting edge states, very similar to the Quantum Hall Effect but occurring at zero magnetic field instead of the quantizing fields required in the QHE.

In this process, it is critical to know the density of atoms added to the graphene, but directly measuring such a tiny added mass is difficult. For atoms that interact electronically by donating charge to graphene, the number of atoms added to the lattice can be easily determined by measuring the shift in the charge neutrality point of graphene against an applied gate voltage, but this technique cannot work for atoms that remain neutral. Therefore, in order to measure the density of added atoms, we attempted to construct microelectromechanical (MEMS) resonators from silicon-on-insulator wafers. Such resonators, in a parallel plate capacitor configuration, exhibit resonant frequencies that can be measured electronically. When atoms are added to the silicon device layer, the resonant frequency of the device changes due to mass loading, and this change in resonant frequency can be directly related to the change in mass. By placing this resonator some distance from a source of mass (in this case, a small thermal evaporator located near the sample stage in the measurement cryostat), the mass flux from the source can be measured, and the number of atoms added to the graphene can be determined. These resonators have sizes on the order of magnitude of about 500 microns.

Photoluminescence of CdTe Quantum Wires

Sarah Willson

Mentor: Richard Loomis

The main objective of this research was to investigate the photoluminescence (PL) properties and the dynamics of excitons prepared in CdTe Quantum Wires (QW). Specifically, I measured the PL spectra as a function of position along single CdTe QWs to investigate the uniformity of the energy band gap along them. Deviations occurred due to small changes in the diameter of the QW or to variations in the organic ligands that are bound to the surface of the QW. I also measured the PL lifetimes, which are inversely proportional to the electron and hole radiative recombination rates. I worked towards preparing these measurements under low temperature settings as well to investigate the role translation kinetic energy has on the dynamics and lifetimes of the excitons. I used photo/thermo-enhancement techniques created by the lab to increase PL and quantum yield (QY). I accumulated a collection of wires that were successfully imaged with a consistent photoluminescence peak. The individual wires consistently emitted photons at a higher frequency than the ensemble batches. Additionally the quantum yields maintained consistently above the QY throughout the summer, which indicates that, the photo-enhancement methods were successful. The data collected can provide information regarding the limits that can be expected in semiconductor QWs, but also general insights into how the specific properties of a QW and the potential energy landscape along it effect the momentum of excitons and the nature of radiative recombination.

Mechanical Testing of Mice Achilles Tendons

Alexander Wirtz

Mentor: Spencer Lake

The Achilles tendon is one of the strongest tendons in the human body, yet this tendon accounts for a significant amount of injuries in athletic activity. A significant fraction of these injuries result in surgery for proper rehabilitation, with most surgical patients no longer participating in athletics post-operation. Understanding the dynamics loading mechanics of the Achilles tendon is an essential and initial step in improving the surgical and rehabilitation processes. Recent studies have shown that, due to the viscoelastic nature of the tendon, the response of the tissue to varying loading conditions can cause strain patterns to be unusual. These strain patterns are analyzed by observing the elastic fibers within the interfascicular matrix. Because it is crucial that tissue dynamics are understood, a successfully reproducible mechanical testing procedure must be conducted to determine the role of elastic fibers in multiscale mechanics. Achilles tendons were harvested from available mouse models and various uniaxial tensile testing techniques were observed. These techniques include incorporating a stability frame made of sandpaper, inducing various clamping intensities, altering the dissection procedures, compression in a phosphate-buffered saline bath, adding adhesives, and incorporating strain-tracking techniques. Various outcomes were observed and successful procedures were developed to be introduced in sensitive experimental procedures.

Transparent Conducting Sulfides

Sondra Wouch

Mentor: Cynthia Lo

Researchers are constantly looking for new transparent conducting materials for applications in photovoltaics and flexible electronics (photochromic windows, flexible solar cells for satellites, and cell phone screens). This projects focuses on analyzing a large group of binary sulfide compounds as potential transparent conducting materials (TCMs). Through ab initio computations, the electronic properties of 186 binary sulfides will be examined.

The sulfides for this project were found through Materials Project with restrictions on the energy above hull (less than 0.01 eV) and band gap (greater than 0.5 eV). The sulfides were also selected to not contain any oxygen. A program was written to identify and list all the binary sulfide compounds with information in Materials Project that fit the previous requirements. This program gave a list of the materials' names and their Materials Project ID number. The ID number is what is used to call the information from the Materials Project website to be run through the calculations to obtain the electronic properties. All of the chosen sulfides were run through density functional theory (DFT) calculations performed by Vienna Ab Initio Simulation Package (VASP).

The first and foremost electronic properties that were collected from the DFT calculations are mobility and conductivity. This is because these two properties are the most comprehensive indicators that a material will make a reasonable transparent conducting material.

Mobility decreases as carrier concentration increases because more electrons result in a greater electronic field, which then results in less electron mobility. Similarly, conductivity increases as carrier concentration increases because a greater number of electrons increases the conductivity of the material. As such, these are the sought after trends for potential transparent conducting sulfides.

Annotation of Contig19 in *Drosophila eugracilis*

Hang Xue

Mentor: Sarah Elgin

Heterochromatin domains are regions found in the genome where DNA is densely packaged. In most cases, genes in these regions are silenced, presumably due to limited access of the transcriptional machinery. The small fourth chromosome of *Drosophila*, also known as the dot chromosome or F element, is unusual in exhibiting many characteristics of heterochromatic domains, and at the same time maintaining some euchromatic properties. There are 80 genes actively transcribed on the F element. To examine the regulation of these genes and the evolution of this unusual domain, a comparative study is being undertaken by manually curating gene models and identifying motifs specific to the F element using phylogenetic footprinting for species diverged recently (10-15 Myr) from *D. melanogaster*.

This project focuses on contig19, a 40 kb region of the dot chromosome in *D. eugracilis*. The *D. melanogaster* genome has been used as a reference to annotate all features. A variety of bioinformatics tools and databases were used during annotation, including UCSC Genome Browser GEP Mirror, FlyBase, BLAST, ab initio gene predictors, TopHat, RNA-seq data, DHS data, RAMPAGE data, BG3 and S2 data on DH sites, and RNA PolII CHIP-seq data. Four genes on this contig, *Zyx, PlexA*, *ATPsynbeta*, and *CaMKII*, were annotated. Comparative analysis indicates that *PlexA*, ATPsynbeta, and *CaMKII* are highly conserved between *D. eugracilis* and *D. melanogaster* while *Zyx* is less conserved and might have a new isoform. The transcription start site, repetitious elements, synteny and potential regulatory elements of each gene are being examined in this project, looking for any special characteristics of genes within the F element. These data can help us understand how genes in densely packaged DNA can be expressed when typical genes are generally silenced in such a heterochromatic environment.

Synthesis of Bismuth Vanadate Nanocrystals for Methane Oxidation

Alicia Yang

Mentor: Bryce Sadtler

Since methane is the main constituent of natural gas and biogas, it is important to develop a more cost-effective, efficient method of transporting methane for fuel using intermediate chemicals. One major obstacle in industrial chemical processes has been converting methane gas into liquid methanol. Methane activation by heterogeneous catalysis will play a key role to secure the supply of energy and chemical fuel in the future. We report the synthesis of bismuth vanadate nanocrystals for the photochemical oxidation of methane. Accordingly, we varied reaction conditions such as temperature, reaction time, pH, surfactants, and methodology in order to regulate the growth and structure of their surface crystalline facets. We used electron microscopy, X-ray diffraction, and absorption spectroscopy to characterize the structure and properties of the reaction products. We developed a system for gas chromatography in order to characterize the selectivity and activity of the nanocrystals for methanol production.

The preliminary results we obtained included bismuth vanadate nanocrystals of various morphologies: thick and thin platelets, nanorods, and bipyramids. Based on the results, the bipyramidal nanocrystals appear to be most effective for methane conversion. We will continue to alter and refine the procedures to better control their morphology and learn more about the corresponding photocatalytic properties using absorption spectroscopy, density functional theory, and etching.

Investigating the Relationship between Cell Size and Biosynthetic Capacity in *Bacillus subtilis*

Zhizhou (Jason) Yang

Mentor: Petra Levin

It is known that nutrient availability is a primary determinant of cell size in Bacillus subtilis. Cells cultured under nutrient-rich conditions are up to three times larger than cells cultured under nutrient-poor conditions. These variations in cell size arise from changes in the relative rates of cell cycle progression and cell expansion. Several nutrient-dependent regulators modulate cell size in bacteria by impacting the cell division machinery to retard cell cycle progression, but relatively little is known regarding the relationship between nutrient availability, cell expansion and cell size. We reasoned that nutrient availability impacts cell size by altering the biosynthetic capacity of the cell, but it is unclear whether size is a function of global biosynthetic capacity, or of the activity of specific biosynthetic pathways. To answer this question, we treated *B. subtilis* with subinhibitory concentrations of antibiotics targeting multiple biosynthetic pathways (transcription, translation and fatty acid synthesis) and quantified cell size. We found that size decreased most dramatically when cells were cultured in the presence of fatty acid synthesis inhibitors, and that this decrease in size was reversed to a certain degree when the cultures were supplemented with exogenous fatty acids. After narrowing down our focus to the fatty acid synthesis pathway, we are trying to determine how the expression of particular genes in this pathway impact cell size. Fatty acid synthesis in *B. subtilis* is regulated by FapR, a transcriptional repressor that down regulates expression of multiple genes involved in fatty acid synthesis. As an alternative means of modulating fatty acid synthesis, we will determine the impact of deleting or overexpressing fapR on cell size. Future work will be focused on the role of individual genes in the FapR regulon in cell size control.

지문 (jē•mōōn): Exploring Equality in South Korea

Caroline Yoo

Mentor: Lori Watt

How in the twemty-first century, can one strive to understand inequality? In a world that places importance on being individual and unique, where does that place equality in our society? What makes people universal?

During the months spent in South Korea in the summer of 2016, my research focused on how to address these questions by studying the intolerances in South Korea through art in a way that showcased equality over all the inequalities. Every individual is unique and a person of their own. Hence although people are not equal, I was looking at equality in a way in which humans are made up of the same building blocks – we are all of one race, we are all human, we have the same flesh, bone, and beating heart. Therefore I decided to create a piece that enhanced the importance of the human-ness of each individual that blurred the line of the discriminated and the discriminator to show how in the end the two groups were not all that different.

I decided to work the 지문 (*jē•mōōn*) which translates to "fingerprint" from Korean to English to accentuate the human aspect of each individual. A fingerprint is unique to the human kind but also individual to that specific person. A fingerprint is able to identify a person through a database when scanned, but without a scanner, a fingerprint is simply a fingerprint, a print that reveals that a person is human and nothing more. I collected stamped ink thumbprints from all types of peoples from a myriad of backgrounds in hopes to showcase the universality of human beings. In highlighting the fundamental core of our being, my goal was to show how to move towards a future with less intolerance in South Korean society by focusing on essence that makes people equal.

Category Learning with Actual Samples and Its Effect on Memory Performance

Jae Un Yoo

Mentor: Mark A. McDaniel

Category Learning is a process of establishing knowledge of categories that enable learners to identify novel items from the learned categories. While it is a widely studied subject in psychology, research in category learning almost always used pictures to learn categories, and very few studies used actual samples. In order to examine how using actual samples affect category learning, we looked at the learning of rock categories as often taught in college level geology courses. To compare learning with rock images and learning with actual rocks, participants were given a set of rock items from different categories, either in pictures or actual samples, and were later tested on their ability to classify novel items into their corresponding categories. By including both rock images and actual rocks in the classification task, we also examined transfer appropriate processing which suggests that learning and memory performance is best when the type of item used in the encoding process match the type of item used at test. The generalization task had two conditions; immediate test and a 48-hour delay. While cue-dependent theory of memory predicts the actual sample condition to be better at delay because of the greater number of cues (e.g., tactile cue), prototype theory of category learning predicts the picture condition to be better at delay because memory for specific items fades as time passes, but prototypical representation endures delay. Our results may not only be of theoretical interests but also can have implications in how we may optimize category learning instruction.

The Molecular Mechanisms of Sensory Synapse Formation

Judy Yoo

Mentor: Robert W. Gereau

Estimated to cost the country over 635 billion dollars per year, in both treatment costs and lost productivity, pain is an extremely exigent issue in society today. Therefore, it is critical to develop a more comprehensive understanding of the mechanism with which these pain signals are processed, potentially opening up new ideas for possible treatments. Studies have shown that two classes of proteins, neurexins and neuroligins, play a large role in the specificity of synaptic connectivity, leading to the hypothesis that the expression patterns of these neuroligins and neurexins create a code for connectivity. With this in mind, we propose the hypothesis: β neurexins in sensory neurons influence interactions with neuroligins, in turn altering aspects of synapse formation. Utilizing a co-culture of sensory neurons, cultured from mouse dorsal root ganglia, and fibroblast COS7 cells transfected with purified neuroligin DNA adhesion molecules and presynaptic terminals were be immunostained and then imaged—allowing for quantitative analysis of synapse formation utilizing the images from the confocal. To isolate the effects of the neurexin gene, a conditional gene knockout technique using viral vectors was implemented in order to knockout the genes coding for β neurexins. Under the premise of our hypothesis—that β Neurexins in sensory neurons influence interactions with neuroligins, there would be distinctly increased synapse formation in sensory neuron cultures containing the Neurexin gene than those with the genes knocked out. This would be visually indicated by the number of stained adhesion molecules and presynaptic terminals in the contrasting confocal images, showing that trans-synaptic interactions of neurexins and neuroligins play a large role in the specification of synaptic connections.

Geometric Algorithms for Identifying Protein Structures

Dan Zeng

Mentor: Tao Ju

Understanding the structures of macromolecular assemblies is necessary to describe the mechanics of a wide variety of cellular processes. Such assemblies often consist of hundreds of proteins and nucleic acid, each with a unique shape. Modern imaging techniques, including electron cryo-microscopy, create 3D density maps to portray the shapes of these assemblies. However, computational methods for deriving structural models from these images are not fully developed because structural geometry varies depending on the image resolution. To address this issue, we developed geometric algorithms in Gorgon, a molecular visualization software. First, we created an interface for Pathwalking. This algorithm determines protein backbones by first creating a predetermined number of pseudo-atoms at regions with high densities, then determining a path through these pseudo-atoms with a travelling-salesman heuristic. As long as structural features are resolvable, Pathwalking accurately constructs models even at resolutions as low 7-8 °A. Our interface allows for biomedical researchers to adjust parameters for an algorithm which was previously restricted to the command line. To address the cases in which parameters for Pathwalking are not known and when maps are of higher resolution (<5 °A), we also developed Extremal Curve Skeletonization. Skeletonization uses the geometric profiles of locally maximal density curves and surfaces to identify α-helices and β-sheets. Such secondary structures (SSEs) play in pivotal role in protein interactions. We found that the SSEs which could be accurately obtained through skeletonization can be used as anchors for identifying the rest of the protein structure. Our future work involves creating algorithms that will detect the resolution and automatically adjust the algorithm accordingly. Such resolution-aware algorithms will reduce the labor involved in converting density maps into structural models and reduce the human bias that often results from this process.

Empresas Legales? Argentine Recovered Restaurants and the 2011 Bankruptcy Law

Ben Zeno

Mentor: Rebecca Clouser

In Argentina, workers occupied bankrupt businesses and created horizontal cooperatives in order to keep working and producing. This movement of empresas recuperadas ("recovered businesses") has long outlasted the economic turmoil that produced its initial prominence after Argentina's 2001 sovereign debt default. In the years since, legal reforms have gradually legitimized the practice under certain circumstances, culminating in 2011 reforms to Argentine bankruptcy law which create a legal path for recovery within the bankruptcy system. Initial survey results from 2014 showed the bankruptcy system to be underutilized and ineffective. The goals of this project, combining field interviews with workers, lawyers, and academics in Buenos Aires and analysis of survey data, are: 1) To characterize the practical application of the 2011 Argentine bankruptcy law on newly-recovered businesses after 2011, focusing on six Buenos Aires restaurants, and to determine the effect this has on "institutionalization" of the movement by the state; and 2) To study work in restaurant cooperatives, which have been under-studied in recent years, and compare with organization and work in previously-studied cooperatives in the movement. Preliminary findings show that the bankruptcy law has been negatively interpreted, but precedent-setting favorable decisions have begun to come from higher appeals courts, and that more companies find success in recovering the business and purchasing the goods necessary to keep their business functioning than were suggested by the first studies of the law's effect.

Biochemical Characterization of AldA, a Novel Enzyme in *Pseudomonas syringae* Indole-3-acetic Scid Biosynthesis

Kaleena X. Zhang

Mentors: Joseph M. Jez and Barbara Kunkel

Plant pathogens can devastate agricultural systems by reducing crop yield and undermining crop integrity. To attenuate the negative impact of plant disease, it is critical to understand how pathogens utilize signaling pathways, regulatory mechanisms, and virulence factors to bypass plant host defenses. *Pseudomonas syringae* is a pathogenic bacterium that causes necrotic lesions and leaf coloration loss (chlorosis) in susceptible plants, including tomato and peach. Recent literature has shown that *P. syringae* has the ability to endogenously produce a key plant hormone, auxin (indole-3-acetic acid; IAA), likely as a means of concealment while infecting the plant. Initial studies indicate that *P. syringae* strain DC3000 uses a tryptophan-dependent IAA biochemical pathway in this process. To elucidate how microbial IAA confers pathogenicity, we have analyzed the NAD(H)-dependent indole-3-acetaldehyde dehydrogenase (AldA) that catalyzes the final indole-3-acetaldehyde (IAAld) to IAA conversion step in the *P. syringae* strain DC3000 IAA biosynthetic pathway. Based on the AldA X-ray crystal structure and known aldehyde dehydrogenase behavior, we hypothesize that a catalytic cysteine residue performs an essential nucleophilic attack on the aldehyde moiety in IAAld. A subsequent hydride transfer from the covalent intermediate to NAD+ and nucleophilic attack by an activated water molecule releases the final IAA product. To test this catalytic mechanism proposal, we have determined the activity profiles of AldA active site mutants, and compared them to initial velocity studies on wild-type enzyme. This study has identified two active site residues, Cys302 and Glu267, that are absolutely essential for AldA function. Further research directions could involve generating and characterizing minimally active AldA varieties that retain normal catalysis but have attenuated substrate binding. Knowing AldA structure and activity can direct us to novel ways to counteract pathogen virulence, including designing targeted inhibitors that act on essential residues.

Extracting Lignin Using Deep Eutectic Solvents

Wilson Zhong

Mentor: Marcus Foston

The conversion of biomass into fuels and other products is a costly and inefficient process. Lignocellulosic biomass contains carbohydrates such as cellulose and hemicellulose which can be converted to fuels such as ethanol. However, it also contains lignin, a complex polymer that has the potential to be a renewable resource for a wide variety of high value products, such as aromatic chemicals. Unfortunately, current biomass fractionation methods degrade the lignin's structure, making it unusable for conversion into high value products. If lignin can be successfully extracted from biomass, with its desirable structure intact, we can increase the economic viability of biomass refineries, putting us a step closer to renewable energy. Initially ionic liquids were examined for their use in biomass fractionation to successfully extract lignin with its structure relatively intact. However, these ionic liquids were found to be too toxic and expensive for industrial use. Currently, we are testing the ability of deep eutectic solvents (DES) to extract lignin from dry poplar flour. DES are mixtures of two substances, that when combined in specific ratios, have a significantly lower melting point than either of the individual substances. DES have similar physiochemical properties to ionic solvents; however, they are safe, cheap, and more environmentally friendly. Our research is dedicated to determining whether biomass fractionation is possible using DES, and if so to identify which solvents are the most effective at extracting lignin from biomass. One of the solvents we tested, Choline Chloride and Urea in a 1:2 ratio, was found to be significantly better at extracting lignin than the other DES, and even the ionic liquid. Moving forward we wish to test more DES combinations and to determine the structure of the extracted lignin to see if it is usable as a feedstock for lignin-derived products.

Annotation of the Genomic Landscape on Contig29 of the *D. eugracilis* Dot Chromosome

Kristina Zudock

Mentor: Sarah Elgin

Most *Drosophila* have a small chromosome known as the dot chromosome (F element). This chromosome is unusual because it appears to be almost entirely heterochromatic, yet its 1.3 Mb-long arm has a normal gene density and three times the number of repetitive elements on euchromatic chromosome arms. The ~80 genes found on the F element are expressed and function in heterochromatin at the same levels as is typical of euchromatic genes. The genomic landscape of the *D. eugracilis* dot chromosome was examined in this study. *D. eugracilis* was selected because it is more recently diverged (10-15 million years) from a common ancestor with *D. melanogaster* than other *Drosophila* previously analyzed, meaning its dot chromosome regulatory motifs likely share enough similarities with *D. melanogaster's* to be recognizable. This study focuses on the annotation of contig29, an ~56 kb region of the *D. eugracilis* fourth chromosome. One goal of this project is to identify the most parsimonious gene model for the two features on contig29 as compared to the *D. melanogaster* ortholog. Each gene model was required to have appropriate stop and start codons, coding exon boundaries, and splice sites that do not lead to phase shifts across an intron while being in congruence with transcription data. Using a mixture of bioinformatics tools and genomic databases along with *D. eugracilis* expression data (including RNA-Seq analysis in embryos, adult male, and adult female flies), the coding spans for two genes and their isoforms were identified—*MED26* (two isoforms differing in their 5' UTRs) and *bt* (five unique isoforms). Additionally, genomic data for *D. melanogaster*, *D. biarmipes*, and *D. eugracilis* was examined for evidence of transcription start sites for the two features on contig29. Ultimately, annotation of these conserved regulatory motifs will provide insight into how gene regulation functions on the dot chromosome.

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