Socioeconomic Status Links to Children’s Literacy Development
Dina S. Ghosh

Optical Astronomy and Photometry of Active Galactic Nuclei using the Antipodal Transient Observatory
Jordan Raisher

Children’s Intuitions about Physical Ailments and Diseases
Jeremy Winer

Feature Articles

Policy Brief
Children in Poverty: Protecting the Developing Brain
Alison Cesurz

Summaries of Student Work

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is that a paper represent research—contribution of new
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honors, or have been funded by our office. Work need
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the eternal research question “How does that work?” To others, the triangle represents the Greek letter ∆, the
mathematical symbol for change.
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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 to the creation of new knowledge. In many cases their research leads to new questions to be studied by future investigators. The work reported on in this volume represents numerous hours spent in laboratories, libraries, and in the field gathering data and analyzing and interpreting information. Authors have completed Honors Theses, published papers in academic journals, and presented findings at symposia and conferences.

How to address the problems created by illiteracy in the U.S.? Dina Ghosh’s research provides important information on the critical link between print awareness in young children and the socioeconomic status (SES) of the household in which they are being raised. The study finds that in addition to the frequency of literacy-related talk, the nature of the talk influences children’s subsequent print awareness and both factors are directly related to socioeconomic status. Literacy-related activities in low SES families tend to be more structured and possibly less effective in developing a child’s interest in learning to read and write. Dina concludes that educating low SES parents to engage in less structured activities, such as shared book reading, may impact future literacy outcomes.

In his senior honors thesis work, Jordan Raisher used the Antipodal Transient Observatory (ATO) optical telescope to collect data on the extreme environments within Active Galactic Nuclei (AGN) and Gamma Ray Bursts (GRBs). In order to collect meaningful information, the ATO required extensive repairs and improvements to the programs that operated it. Jordan’s work created a specialized system to conduct multiwavelength observations of some of the most interesting objects in the universe. The telescope’s field of view and slew speed were verified, and software that automatically responds to NASA’s GRB alerts was installed. The telescope’s image data from three AGN taken over a period of five months were compared to those made by other telescopes and subsequently used to construct characteristic spectra for
each object. Jordan concludes that after the ATO’s sister telescope in India has been similarly upgraded, the system may become the premier optical GRB apparatus in the world.

When do children begin to understand subtle differences in illnesses and diseases they may encounter? This is the question psychology-neuroscience-philosophy student Jeremy Winer’s research seeks to answer. Children of ages four to seven years were presented with simple vignettes about sickness and then asked to answer a few questions. The questions focused on whether the sickness was chronic and whether it was contagious. Jeremy found that children as young as four years old can properly make predictions on contagious factors and whether a common illness is chronic or not. However children in all age groups tested guessed seemingly randomly at questions about more complex sicknesses such as allergies. The study presents a solid foundation for future researchers interested in children’s understandings and intuitions about sickness and poses many new questions to be answered.

The Summaries of Student Work contained in this volume represent the dedication and effort of students and their faculty mentors at Washington University as well as other institutions at which the authors have worked. We end with an important summary of research on the impact of poverty on brain development in children conducted by Alison Cesarz. The work is being considered as a policy brief to be submitted to the Center for Disease Control and may therefore influence policy decisions at the national level. Finally, the contributions made to the WUURD by the Peer Review Board are gratefully acknowledged by the authors and editor. We invite you to enter the world of research at Washington University through the works herein.

Respectfully,

K R I S T I N S O B O T K A

KRISTIN SOBOTKA

Editor
**ABSTRACT**

By the time many U.S. children begin formal schooling in kindergarten, they already have some understanding of reading and writing. We hypothesize that children acquire this knowledge through conversations with their parents at home beginning at ages as early as two and a half years. However, previous studies indicate that children from low socio-economic status (SES) families do not perform as well on kindergarten reading outcomes (Aikens & Barbarin, 2008). Low SES children’s delays in literacy development can considerably impair their later academic success. The present study examines the differences between low SES and high SES families in early parent-child literacy conversations.

The results of the present study indicate that high SES parents both initiate and engage more frequently in literacy-related conversations with their young children than low SES parents. Additionally, while low SES parents talk more about literacy in structured settings such as memorizing the alphabet, high SES parents more frequently talk about literacy in unstructured contexts.

**KEY TERMS**

- Socioeconomic Status
- Print Awareness
- Phonological Awareness
- Letter Recognition
- Home Literacy Environment
- Early Literacy Talk
- Literacy Conversations
- Literacy Development
- Reading/Writing Development

**FACULTY MENTOR: REBECCA TREIMAN, P.H.D., BURKE & ELIZABETH HIGH BAKER PROFESSOR OF CHILD DEVELOPMENTAL PSYCHOLOGY**

Professor Treiman conducts research on language and language development, focusing on reading and spelling skills. One line of research examines children’s spelling errors and the reasons behind these errors. Other research looks at the linguistic skills and knowledge that children bring to the learning of literacy, including phonological awareness and knowledge about letters. Other lines of research look at the processes involved in single-word reading and spelling in adults and the nature of spelling-sound relationships in English and other languages.

**ACKNOWLEDGEMENTS**

I would like to thank Washington University's Office of Undergraduate Research and Rebecca Treiman for their generous funding of this study. I am indebted to Rebecca Treiman and Kristina Decker for their guidance and supervision in this project through the Reading and Language Lab. I would also like to thank the University of Chicago for making the transcripts used in the present study available through the Language Development Project.

**Author:**

Dina S. Ghosh

Dina Ghosh is a senior at Washington University in St. Louis, majoring in Philosophy-Neuro-science-Psychology. Her interest in children’s literacy development stemmed from the Mind-Brain-Behavior course’s discussion of how human beings acquire language. Dina is currently applying to medical school and hopes to specialize in psychiatry, neurology, or pediatrics.

**Peer Editor:**

Sarah Gallo, a senior majoring in Anthropology
INTRODUCTION

Before children learn to read and write, they acquire print awareness, a basic understanding of the purpose and conventions of text (Evans & Saint-Aubin, 2005). Written language is a second-order symbol because it represents spoken language, which in turn represents objects, actions, etc. in our environment. While spoken language acquisition occurs rapidly with little effort for most children, written language learning is a more complex, gradual process. For example, in order to read and write, children must learn the conventions and formatting particular to a given language. Examples of the conventions of written language in English include writing words from left to right and separating words with spaces.

By the time children enter formal schooling in kindergarten, many of them already have a certain level awareness of print. For example, even preschoolers who cannot read or write yet know that repeated strings of letters or strings of misoriented letters do not make up real words (Evans & Saint-Aubin, 2005). This knowledge can arise from conversations children have with their parents at an early age; these conversations between parents and children about print are an important component of the home literacy environment. Christian, Morrison & Bryant describe the home literacy environment as all of the factors in the home that contribute to children’s literacy such as the number of books in the home and the amount of time spent reading per week (1998). This study found that the mother’s education correlated positively with the home literacy environment. Additionally, the higher the mother’s education, the greater the child’s receptive vocabulary and letter recognition was.

We hypothesize that socioeconomic status (SES), a combination of the education and income level of a family, influences the home literacy environment and subsequently, children’s academic performance. Specifically, studies indicate that children from low SES families have a higher risk of reading-related difficulties in school (Whitehurst & Lonigan, 1998). For this reason, we hypothesize that there are SES differences in the quantity and quality of literacy-related talk in the home prior to children entering kindergarten.

Questionnaire data indicates that poorly educated parents, primarily including non-high school graduates or high school graduates, talk more about literacy in formal settings such as flashcards and workbooks, whereas well-educated parents, primarily including those with a bachelor’s degree or beyond, talk more about literacy in informal settings such as storybook reading (Stipek, Milburn, Clements, Daniels, 1992). The present study uses transcripts of video-recorded conversations between parents and children from high and low SES families in order to investigate the findings from these parent reports in more depth.
METHODS

Participants:
This longitudinal study uses transcripts of home conversations between parents and children recorded while the children are 30 months, 42 months, and 50 months of age. Each conversation recording lasted for 90 minutes. Conversations took place in a natural setting in which parents and children were told to continue with their daily activities. The participants are a socioeconomically diverse, representative sample of 52 parent-child pairs from the Chicago area, all of whom are native English speakers. Although there were originally 60 parent-child pairs, eight were excluded from the analyses because they did not have data at all three time-points.

Information about education and income level of the family was collected categorically through a questionnaire. Because education and income levels were positively correlated ($r = .40, p = .004$), a principal components analysis was used to combine the two variables into a composite measure of SES with a mean of 0 and standard deviation of 1.0.

Many of the previous studies of the home literacy environment relied on questionnaires, which could potentially lead to response bias. For instance, on a questionnaire, parents might claim to read to their children more often than they actually do. However, the present study reduces response bias by directly investigating the home conversations that occur between parents and children.

Procedures:
The transcribed recordings of the conversations contained time stamps distributed approximately once every minute. From these time stamps, the amount of time that parents and children spent talking about letters, general literacy, topics unrelated to literacy, and the alphabet was determined.

Letter talk was defined as talk that either included letters (my name starts with a C) or the word letter (“dog” has three letters). General literacy talk was defined as talk that related to literacy, but not letters specifically (reading is fun). Literacy-unrelated talk was defined as all other talk (let’s make a sandwich). Alphabet-related talk was defined as any mention of the ABCs or the alphabet (say your ABCs).

Within the transcripts, an utterance was defined as any sequence of words preceded and followed by a pause. For instance, “Finish eating first, then we’ll play with blocks” would count as two utterances. The number of utterances in letter talk, general literacy talk, literacy-unrelated talk, and alphabet-related talk were coded.

Each parent-child conversation was categorized into one of four major contexts: shared book reading (storybooks, magazines, etc.), toy play (blocks, trains, etc.), production (writing, drawing, workbooks, etc.), and unstructured activities (eating, cleaning, etc.). The number of utterances and amount of time spent in each context were calculated from the time stamps in the transcripts.

The initiator of each conversation (parent or child) was coded. The level of engagement or interest in each conversation was measured based on the number of utterances that the parent and child contribute.
RESULTS

Statistics and Data Analysis:
The relationship between SES and literacy-related talk in the home was investigated using a bivariate correlation analysis in SPSS (Statistical Product and Service Solutions) statistics.

There is a significant correlation between SES and proportion of parent-initiated conversations out of all literacy-related conversations when collapsed across all ages. Higher SES was correlated with a higher proportion of parent-initiated conversations \( r(52) = .30, p = .032 \).

There is a significant correlation between SES and proportion of parent utterances out of the total literacy-related utterances when collapsed across all ages. Higher SES was correlated with a higher proportion of parent utterances in literacy-related conversations \( r(52) = .29, p = .035 \).

There is a significant correlation between SES and proportion of literacy-related talk out of total talk in unstructured contexts when collapsed across all ages. Higher SES was correlated with a higher proportion of literacy-related talk out of all unstructured talk \( r(52) = .43, p = .002 \).

There is a significant correlation between SES and proportion of literacy-related talk out of all talk at 42 months. Higher SES is correlated with a higher proportion of literacy-related talk \( r(52) = .30, p = .032 \). This correlation was not significant at the other two time-points, 30 and 50 months.

There is a marginally significant correlation between SES and proportion of alphabet-related utterances out of all literacy-related utterances at 42 months. Lower SES is correlated with a higher proportion of alphabet-related utterances \( r(46) = -.29, p = .052 \). This correlation was not significant at the other two time-points.

DISCUSSION

The objective of the present study was to determine whether the quantity and quality of literacy-related talk in the home between parents and young children varies by SES. The results support the hypothesis that low SES parents talk less about literacy in the home, and that the quality of literacy-related talk differs between low and high SES families.

When collapsed across all ages, results suggest that low SES children initiate a larger proportion of literacy-related conversations than high SES children do. Although this may seem counter-intuitive, the converse is that low SES parents initiate a smaller proportion of literacy-related conversations than high SES parents do. If low SES parents do not initiate as many of the literacy-related conversations as high SES parents, low SES children may have less exposure to talk about print concepts early on. This may help explain why low SES children tend to acquire language and reading skills more slowly (Whitehurst & Lonigan, 1998).

In addition to low SES parents initiating a smaller proportion of the literacy-related conversations than high SES parents, low SES parents contribute fewer utterances to literacy-related conversations than high SES parents when collapsed across all ages.
Though low SES children are just as likely as high SES children to initiate and contribute to literacy-related conversations, low SES parents are not as likely as high SES parents to reciprocate their children’s interest. This could limit low SES children’s exposure to reading and writing-related talk early on. This finding supports the claim that high SES parents tend to be more responsive in general to their children in conversations (Hoff, 2003), and may help explain the lags in literacy development for low SES children (Whitehurst & Lonigan, 1998).

The present study was one of the first to break down daily activities into four major contexts: shared book reading, toy play, production, and unstructured activities. When collapsed across all ages, results indicate that high SES families have a higher proportion of literacy talk than low SES families in unstructured contexts such as doing laundry, singing, and making lunch. This finding is in line with the claim that well-educated parents tend to emphasize reading and writing-related words in more informal settings such as book reading (Stipek et al., 1992), which might make literacy-learning more interesting for young children. Yet less educated parents emphasize reading and writing-related words in more formal settings such as flashcards and workbooks (Stipek et al., 1992), which may make literacy-learning more tedious for young children.

A major difference at 42 months is that low SES parents do not spend as much of their time talking about literacy with their children as high SES parents. Out of all the topics that parents and young children talk about at home, literacy is a more common topic of conversation in high SES families. Talk that is rich in literacy-related words such as read, book, and write could help children better understand print concepts at an early age. Reduced exposure to literacy-related talk at home can lead to low SES children having fewer opportunities to learn about reading and writing before beginning formal schooling. This finding supports the claim that children from low SES families have a higher risk of reading-related difficulties such as lags in developing phonological awareness and letter recognition (Whitehurst & Lonigan, 1998).

A potentially surprising finding at 42 months is that when low SES parents and children talk about literacy, they focus more on alphabet-related words (ABCs, alphabet) than high SES parents and children. Using more alphabet-related words could mean that low SES families emphasize learning the alphabet more, and other literacy-related activities less. Yet, memorizing the arbitrary order of the alphabet does not teach children the function of letters or which letters correspond to which shapes and sounds. While learning the alphabet is important for learning to read, it is not sufficient for literacy because children must also learn the function and conventions of letters (Evans & Saint-Aubin, 2005). Other types of literacy-related activities such as shared book reading and toy play may be more helpful for this purpose.

Overall, these results indicate that there is a considerable difference in the home literacy environment of children from low SES families and high SES families. High SES parents initiate and engage more often in conversations about literacy, even with children as young as two and a half. Furthermore, high SES parents talk more about literacy in unstructured contexts than low SES parents, which may help foster children’s interest in learning to read and write. Because the ability to read and write is an integral component of a child’s education, delays in the acquisition of literacy-related skills could substantially hinder his or her academic progress. Teachers,
parents, social workers, and others could potentially design early literacy interventions for children from low SES families. Talking more about literacy with these children through engaging activities such as storybook reading or letter blocks can provide them with a pathway to success.

FUTURE QUESTIONS

In the present study, coding was only done for three time-points because of time constraints. In the future, all twelve time-points (child ages 14 months to 50 months) could be analyzed to determine whether SES is related to certain types of literacy-related talk such as reading-related words, writing-related words, or alphabet-related words.

Due to time constraints, the relationship between the home literacy environment and kindergarten outcomes has not yet been explored. Future studies could investigate the relationship of early literacy conversations in the home and kindergarten measures of reading and writing skills.

Works Cited


Optical Astronomy and Photometry of Active Galactic Nuclei using the Antipodal Transient Observatory

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ABSTRACT
Astrophysics relies on precise and accurate instruments to observe high energy, large scale events that occur throughout the universe. These high energy events and objects such as galactic nuclei serve as laboratories to study the properties of high energy, relativistic particles and the conditions of the early universe. As such, accurate instruments are crucial for observing the full radiation spectrum. I describe the development and analysis of the Antipodal Transient Observatory (ATO) as a scientific apparatus as well as the initial observations made of highly active galactic sources. I determine the ATO’s limiting magnitude parameter to be between 20 and 21 and the Field of View to be ~40 arcminutes and comment on the validity of the Synchrotron Self Compton (SSC) radiation model for selected AGNs Mrk 421, Mrk 501, and W Comae.

KEY TERMS
- ATO (Antipodal Transient Observatory)
- AGN (Active Galactic Nuclei)
- GRB (Gamma Ray Burst)
- Markarian 421
- Markarian 501
- W Comae

FACULTY MENTOR: JAMES BUCKLEY, PH.D.
Professor of Physics
Professor Buckley’s research specialties include gamma-ray astrophysics and astroparticle physics, optical and multiwavelength astronomy, direct and indirect searches for dark matter, the physics of active galaxies and origin of cosmic-rays, and development of photodetectors and high-speed electronics.

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Peer Editor:
Marie Draper, a junior majoring in Physics and French
Observational Astronomy can provide clues about the physical processes taking place in environments which surpass anything that can be realized on Earth. In our work, we apply multiwavelength observations to the study of highly relativistic jets emitted by the supermassive black holes at the centers of active galaxies. These extreme environments can be characterized by examining the spectra and time-variability of emissions from these sources. From the known laws governing electromagnetic radiation and some assumptions about the interstellar media, we can draw conclusions about the environment which generated the radiation and thus the physical laws at work in these extreme environments. Few objects display more extreme environments than Active Galactic Nuclei (AGN) and Gamma Ray Bursts (GRBs). The study of these astrophysical objects motivated the development and analysis of the Antipodal Transient Observatory (ATO).

AGN, the unresolved centers or nuclei of some giant elliptical galaxies, outshine the rest of the galaxy by several orders of magnitude. AGN are thought to be powered by the accretion of matter into supermassive black holes (Khassen, 2010 and Osterbrock, 1991). Not only does the stellar density near the AGN create some of the most luminous objects in the galaxy, but many AGN also display relativistic sources of radiation. Accretion produces radiation as matter releases a large quantity of potential energy when being pulled into a black hole. Ultrarelativistic jets, while their exact physical cause is uncertain, eject material from near the central black holes of galaxies at nearly the speed of light with bulk Lorentz factors between 10 and 100. Through interactions within these jets, with the surrounding interstellar media, and with magnetic fields, these relativistic particles generate the broad-band spectra and rapid flux variability characteristic of AGN.

GRBs are some of the most mysterious events in the universe. These events appear to be isotropic and, in recent years, have been identified with distant, very high redshift galaxies. GRBs are, therefore, some of the oldest and most powerful events in the universe. Extremely fleeting on an astronomical timescale (many lasting only seconds or minutes) GRBs emit gamma broad-band, nonthermal emission with much of the spectral power in the \( \gamma \)-ray waveband. The power of these events may be orders of magnitude larger than conventional supernovae and briefly outshine entire clusters of galaxies (Stern and Poutanen, 2004) The current leading hypothesis predicts that these showers of \( \gamma \)-rays are caused by massive explosions caused either by the collapse of high mass stars called \( \text{hypernovae} \) or similarly energetic events such as mergers of compact objects. The short time scales and unpredictable distribution of these events means that little is yet known for certain about them.

Much information on astronomical objects such as AGN and GRBs can be gleaned from multiwavelength astronomical observation and analysis of the emitted radiation. Therefore, I have worked to develop the ATO as a specialized apparatus for recording information pertaining to AGN and GRBs in the visible spectrum. We attempted to

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1 Accretion is the process by which matter is pulled into a body with a high gravitational field such as a neutron star or black hole.
2 The bulk Lorentz factor describes the average speed of a system of matter with respect to the speed of light.
3 The red-shift of a galaxy is correlated with its distance from Earth.
verify the wide field of view (FOV) and high slew speeds\(^4\) of the telescope while adding polarimetry hardware. In addition, in consideration of the resources available for GRB observation, we attempted to adjust the telescope to respond automatically to GRB alerts in order to get the quickest observations of these energetic sources. This paper describes some of the work done to upgrade the telescope hardware and software to achieve these goals and the analysis of photometric data taken in the 2011-2012 observing season.

THE ANTIPODAL TRANSIENT OBSERVATORY

The Antipodal Transient Observatory (see Figure 1) is a fully automated optical telescope located at the VERITAS\(^5\) site in southern Arizona. The term “Antipodal” refers to the presence of an identical telescope located on Mt. Saraswati in the Indian Himalayas. With 170 degrees of separation, the two identical telescopes improve the temporal density for monitoring time-variable phenomena. The large daily observation time, combined with the rapid slew speed of the scope with 1 degree field of view (FOV) makes the ATO ideal for observing rare or unique astronomical events such as GRBs. While this research project concerns only the American telescope, the same modifications will ultimately be applied to the Indian telescope after they are fully tested.

![Figure 1](image)

The ATO telescope as it appears during the day with the storage shed rolled back.

ATO Optics

The ATO is a 0.5-meter modified Ritchey-Chretien telescope (RCT) with a refractive corrector.\(^6\) Cassegrain telescopes are characterized by their concave primary mirror, which acts as the entrance pupil, and their secondary convex mirror which focuses the light to form an inverted image at the focal plane. RCTs, also known as Aplanatic Cassegrain telescopes, are a specific subclass of Cassegrain Telescopes which have

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\(^4\) The slew speed is the speed at which a telescope can transition from observing one object to another.

\(^5\) Very Energetic Radiation Imaging Telescope Array System

\(^6\) A Ritchey-Chretien telescope is a specific type of Cassegrain Telescope.
hyperbolic primary and secondary mirrors. The term *Aplanatic* refers to an optical system in which coma and spherical aberrations are both zero to a third order approximation.

Therefore, the ATO is limited by second order astigmatic aberrations, meaning that the error increases by the square of the angle, resulting in at worst a .1% error in object resolution (Schroeder, 2000).

A tertiary optical system is located between the filter wheel and the secondary mirror of the ATO. This set of three lenses was introduced to further correct the optics for an even larger diffraction-limited FOV. This widens the ATO’s FOV from 7 arcminutes to almost 60 arcminutes.

**ATO Computer System**

The ATO employs a suite of observatory control software known as OCAAS/Talon. This set of programs contributes to telescope control, image reduction and formatting, and basic image analysis. The programs are all written in C, contributing to efficient runtime and usually straightforward compilation. Many of the telescope-specific configurations are contained in a set of ASCII text files with a .cfg extension which contributes to easy adjustment of parameters based on the changes in hardware. In addition to the programs of OCAAS/Talon, there are also a set of control programs specific to the ATO at VERITAS. These programs control the power to the CCD camera, remote access camera, and flatlamps. Two types of program compose the OCAAS/Talon software package. The first are the top-level GUIs and the second are the background daemons (Raiser, 2012).

The GUIs make up the basic means of interfacing with the telescope hardware. Each program converts a number of menu or button options into machine level commands which are passed, by way of the daemons, to the telescope hardware.

**XObserve**, or XObservatory, serves as the main means of communication between the astronomer and the telescope. The program contains a convenient GUI in which the astronomer can automatically home the scope at the beginning of a night of observations, manually move the telescope through the digital paddle window, and slew to selected astronomical objects. This program also conveys messages from the background controller programs to the user through the message system within XObserve. XObserve also includes the interface which launches the automated schedule of observations. XObserve, as the most basic of the telescope interfaces, is a required component for any observations.

**Telsched** is a second important user interface tool provided through Talon. This program allows for the scheduling of observations throughout the night. This includes the ability to read database files of sources directly to a schedule. These sources consist of those in the standard Guide Star Catalog as well as simply formatted customized entries such as those for AGNs Mrk 421 and 501. User input to the Telsched GUI is translated into a telescope schedule file. This schedule file is recognized by Telrun, the background daemon that executes batch observations.

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7 OCAAS stands for the Observatory Control and Astronomical Analysis System. Talon is the name of the program once it was released under the Gnu Public License as open source software.
8 A CCD or Charge Coupled Device uses applied voltages to convert photons to digital current pulses.
9 With a .sls extension
As its name suggests, **Camera** controls most interactions with the Telescope’s CCD camera. When XObs is not running in batch mode, the exact specifications of all scans can be set through the various menus in the Camera GUI. These specifications include exposure time and shutter position during exposures. These allow for a manual set of bias, thermal, and dark correctional images to be taken, as well as the exposure time to be adjusted to most effectively image astronomical objects. Included in this program is also a small analysis tool that plots the pixel brightness within a small aperture about a source, overlays a Gaussian curve, and calculates the FWHM which are used in data analysis. This tool is also extremely important when setting the default focus distance which is often done manually. During a batch run or when the telescope is offline, the Camera program also serves as a means of displaying the .fts, .fits, and .fit formatted images which are recorded by the CCD.

All of the higher level GUIs communicate with their respective pieces of hardware indirectly through the background process known as daemons. These daemons are initiated during the boot procedure and convey not only messages, but also status reports to and from their related hardware components. Such messages include the status and temperature of the camera and the pointing coordinates of the telescope.

**Telescoped** is the main daemon for the operation of the telescope itself. There are several versions of telescoped present in the Talon files, each related to a specific controller for the telescope. For the case of the ATO, which uses CSIMC boards, the version of telescoped used is telescoped.csimc. This program formats and communicates pointing instructions from XObs and XEphem to the telescope such that the CSIMC boards respond with the correct movements. Telsched also includes a conversion of the RA/DEC axes of the stellar objects into the pointing corrected and location/time dependent angular motions of the two telescope axes. In addition to communicating to the boards, telescoped also closes the loop on the motion control by comparing the pointing coordinates from the encoders and deciphers any error or status messages passed through from the telescope which are logged in the telescoped.log file.

**Camerad** is the daemon which controls the interaction with the CCD\(^{10}\) camera. Without the CSIMC boards present in the telescope, Camerad is a more basic means of communicating with the camera hardware directly. This includes conveying open and close shutter commands as well as CCD reading commands to the camera statuses such as filter location, temperature, and CCD processing status from the camera.

**Telrun** serves as a bridge between the scheduler, observer, camera and telescope. This daemon is initialized by the astronomer through XObs after the telescope is first homed. Telrun then reads the .sls schedule file as saved by telsched based on the priority codes set in the scheduler. The daemon then communicates the instructions from the schedule to both telescoped and camerad to synchronize the observation process. Finally, based on the results of the scan, the schedule is marked with the status of every observation to indicate whether or not it has been completed successfully. Upon termination of a given schedule, Telrun automatically returns the telescope to the established stowing location while remaining in the batch mode of operation. From this point, if a new schedule file is uploaded, the telescope can begin to execute the new schedule automatically.

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\(^{10}\) Charge Coupled Device
Development and observing on the ATO system is greatly aided by the presence of the phenom-2 machine located in the Physics Department at Washington University in St. Louis. Not only does this machine serve as a back-up drive for the data taken by the ATO, but also as an independent machine for compiling updated software. Both the phenom-2 in St. Louis and phenom at the VERITAS site are identical machines in terms of hardware, operating systems and Talon installations. The duplication of the systems allows for observers to test for proper compilation of programs and simulated running conditions\(^\text{11}\) in order to decrease risk and time spent when implementing new programs on the phenom machine. This enables a remote user in St. Louis to operate the ATO. This is aided by the infrared security camera installed in early 2012 which allows the remote observer to monitor the telescope behavior and to implement an emergency stop if the telescope behaves in an unexpected and dangerous way.

**Gamma Ray Burst Coordinate Network**

High slew speeds and wide FOV makes the ATO ideal for observations of events such as GRBs. In late 2012, the ATO was allocated a unique address for the distribution of GRB alerts from NASA’s Gamma Ray Burst Coordinate Network (GCN). We have integrated the packet communication software available through the GCN into the mechanisms of Telrun so that any alerts of GRBs will be responded to immediately and automatically, presenting observers with visible, UV, and polarization-sensitive images of GRBs mere moments (often seconds) after the alert is received.

In summary, much of the progress made on the ATO was through the development of its software. In cooperation with Ryan Dickherber\(^\text{12}\), the source code for the telescope control programs was rebuilt to run on a modern kernel. The telescope control software was modified to accommodate the custom filter wheel which functioned on different commands than the original filter protocol. Modifications made to Telrun allowed the ATO to stow automatically which streamlined the observing process. Finally, I began additional modifications to Telrun to automate the observation of $\gamma$-ray bursts upon the receipt of a signal from the GCN. Through these modifications, the ATO is not only functional, due to the rebuilt code, but also more accurate and autonomous.

**Starfinding and World Coordinate System**

In order to be scientifically useful, objects must be locatable and identifiable within an image. An object’s World Coordinate System (WCS) coordinates designate an astronomical object’s position independent of the earth’s position. A basic measure of these coordinates is written into the header of each image. These coordinates, however, are written based on the direction of the telescope and will only reflect the WCS coordinates if the object of interest is directly in the center of the image. Because only the center is labeled with coordinates, the exact scale of the image cannot be determined without a full set of coordinates. Talon provides the *WCSfits* program as a means of applying the correct coordinate system to the entire image, thus enabling identification of field stars for relative photometry and identification of pointing errors that could compromise measurements (Raisher, 2010).

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\(^\text{11}\) Phenom-2 can only run in “hardwareless” mode.

\(^\text{12}\) Washington University in St. Louis
When this project began, the WCSfits program was nonoperational due to poor memory allocation within the program when analyzing the images. After analyzing the source code, I rewrote it to be compatible with the updated GCC compiler. The WCSfits program, now operational, applies a set of WCS parameters based on the image itself. The program starts by analyzing the recorded brightness of each pixel and compares it to the surrounding pixels. These brightness comparisons are then used to create a plot of intensities against the pixel positions. The intensity behavior around each intensity maximum is analyzed to determine whether a given intensity maximum is a star or an anomaly. Once the maxima are classified as stars or anomalous pixels, the stellar layout of the image is compared to stellar coordinates supplied by the Guide Star Catalog. The program attempts to match the position and scale of a coordinate overlay to the image. It performs this function by repeatedly shifting the matching coordinate grid to get the closest match between the grid and the reference stars in the image.

Image Corrections

The images taken by the CCD camera are not a perfect reflection of the emissions of astronomical objects. They are recordings of the charge across the CCD and as such are susceptible to various effects which are unrelated to the observed object. These effects, which are characteristic of the CCD, must be addressed in order to render the images scientifically useful. Both Talon and IRAF (see next page) include programs that compensate for these effects. They require, however, taking a set of special calibration images that can be used to correct the observation images.

Bias: The primary error inherent in any CCD image is the error caused by the gradual processing of cells in the CCD. Between the recording of the first and last pixel is a time difference equal to the time taken to read the majority of the CCD. This effect, though small, may still produce errors in images that use abnormally short exposure times or compile a large number of images into a single composite image.

Bias errors are corrected by averaging a set of zero-time exposures with the shutter closed. These images record only the signal measured by pixels during the reading of the CCD. Since all images include any errors due to reading bias, the average signal of each pixel over all zero-length exposures is subtracted from the corresponding pixel of every image.

Darks: Some CCD cameras are also susceptible to what are called dark currents. These occur when a slight potential difference across the CCD allows for the movement of electrons across the CCD due to random thermal motion, resulting in a false photon count. These dark counts, which happen at a measurable rate, depend on the exposure time. Regions of the CCD that exhibit dark currents will appear brighter over longer exposure times.

Dark or thermal errors are corrected by taking a set of images with the shutter closed. The duration of exposure should approximately match the planned astronomical observation times to most nearly match the effects of dark currents. These images are averaged on a pixel-by-pixel basis. The average value is subtracted from images based on the exposure time. However, the dark images are first themselves corrected by subtracting the average bias. By applying the bias to the dark images, the effects of the dark current are isolated in the second set of correctional images.
**Flats:** Errors in the image also result from a combination of gain variations in the CCD pixels and differences in optical transference to different portions of the focal plane. This can be even more prevalent when observations are made using filters of various materials and ages. Small aberrations in the optics of a telescope can also lead to uneven exposure of the CCD.

To correct for these effects, several images are compiled while the telescope is pointed at a “flat” or uniformly illuminated screen. The unfocused image of the light reflected off of the flat screen is nearly uniform in brightness meaning that any imperfections in the image are due to errors in the optical system near the focal plane or due to gain variations across the CCD. These flat fielding corrections compensate for imperfections by normalizing the signal in each pixel. Flat fielded images tend to be quite short in duration in order to capture the variation in photon count without saturating any given pixel. Pixel counts in each image are then divided by the pixel count in the flat fielded image to normalize the photon counts. These correctional images also must be adjusted for bias before being applied to images in general. Much like the dependence of dark errors on exposure time, the dependence of flat corrections on optical elements requires a separate set of flat corrections for every filter.

To summarize, every image of an astronomical object is corrected in three steps: The average bias signal is subtracted from the corresponding pixels in the observation image. Next, the signal from the dark image corresponding to the observation’s exposure time is also subtracted from the corresponding pixels. After adjusting for the raw photon count errors, the image is normalized by dividing the signals in the observation by the signals in the flat image. The image is then fully corrected as much as can be through purely computational means. Although errors may remain, they are mitigated by taking multiple exposures with the object appearing in slightly differing camera coordinates.

**IRAF**

The algorithms for applying the image corrections are part of the Image Reduction and Analysis Facility (IRAF). IRAF is an open source, astronomical image analysis program created and maintained by the National Optical Astronomy Observatories (NOAO). IRAF is designed as a command line environment for the processing and analysis of raw astronomical images. The suite of image correction programs include the added benefit of performing various book-keeping tasks such as keeping track of analysis parameters and checking and marking the image header so that the same corrections are not made more than once on a given image (Tody, 1993).

Photometric analysis is the process by which an object’s brightness is determined within an image. This determination is essentially a measurement of signal to noise. The signal is recorded within a circular aperture surrounding the object. The noise is calculated by averaging the photon counts within a specified annulus about the aperture wherein no other sources are present. From these two measurements, the brightness or flux of the signal region can be determined. Performing the same procedure for a reference star to determine its flux allows us to determine the relative brightness.

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13 The IRAF photometry package allows the size of the signal region and radial coordinates of the annulus to be specified in a parameter file.
IRAF assists in this process by recording the signal and noise automatically. In addition, using a starfinding algorithm within the aperture, IRAF can place the aperture according to the specified parameters to optimally contain the object of interest, and thus reduces human error in calculating the brightness. After performing photometry on each object, the results are written to a text file that is ultimately compiled into a comprehensive table for analysis.

DATA
The data analyzed here is separated into observing periods. During the first period, in early summer of 2011, some manual images were taken in an attempt to record the optical afterglow of a GRB. These images, along with several pointing mesh images, allowed me to test the WCS fitting program as well as to determine the actual field of view for the telescope. The second period occurred after a site visit in winter 2011/2012 in which the telescope was repaired and calibrated, and monitoring cameras were installed to enable remote observations. During this period, over 1,300 images were recorded of a dozen different sources. These images helped to determine the performance and accuracy of the ATO as well as to observe the V-band behavior of several active sources.

2011 - WCS and GRB
The specific GRB of interest was reported in the GCN/FERMI NOTICE 328342663-67 and occurred on 29 May 2011 at 6:19 UTC. The coordinates of the burst were reported to be at 11:43:53 RA and 13:30:36 DEC. Several observations made of nearby galaxies on the same night were analyzed to determine whether or not the GRB afterglow was recorded. While this strategy was unlikely to reveal conclusive evidence of a GRB, the set of images provided an important test of a number of key aspects of the data reduction methods and established a novel GRB observing strategy.

The observations allowed for testing of the functionality of the WCS algorithm to find which pictures contained regions within the 3.8 degree statistical error. While several images did contain the anticipated location of the GRB, the GRB itself was not captured. The application of WCS coordinates, however, demonstrated the success of the repairs to the WCS program and established the ATO’s FOV at approximately half a degree. Second, the analysis of these images provided a means to establish a photometry procedure.

2012 - Mrk 421, Mrk 501, W Comae
During the spring of 2012, the first scientific data was obtained through the regular submissions of schedules for automatic operation of the ATO telescope. These schedules contained several dozen images in a single night over several objects throughout the sky. Of particular interest were the more than 250 images taken over five months of Markarian 421, Markarian 501, and W Comae. These three AGN were also regularly viewed by the VERITAS γ-ray observatory which provided a set of higher energy

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14 This event fortunately occurred during an observing shift at VERITAS.
15 NGC 3810, NGC 3853, NGC 3872, and NGC 3968 were all within the GRB’s instrumental position error.
observations to allow for multiwavelength studies in addition to the optical light curves.

One major success for the ATO was the production of an initial set of light curves for the sources observed in the spring of 2012. The production of light curves demonstrated the consistency and accuracy of the installed pointing mesh as well as established a longitudinal study of AGN optical activity. Although the observing time was only 2-4 months, the light curves demonstrate some variability in emission intensity that will provide a basis for future observations.

While the light curves demonstrate the time-variability of the three sources, the accuracy of the data is questionable due to the assumptions and practices exclusive to this observing period. First, because these images were taken before the filter was fully programmed, the observations were made without any filter. Second, the calculations of relative magnitude were made on an assumed limiting magnitude of 19.5 rather than a value calculated specifically for the ATO. Finally, these observations were made before the optics were cleaned in 2013. Because these errors were uniform throughout the observing period, the time-dependence of the magnitude is still comparatively accurate. See Figures 2, 3, and 4, for light curves obtained in 2012.

![Figure 2](image.png)

*Figure 2* The light curve corresponding to the activity of Markarian 421. The relative magnitude is plotted against the date of observation.
**Figure 3** The light curve corresponding to the activity of Markarian 501. The relative magnitude is plotted against the date of observation.

**Figure 4** The light curve corresponding to the activity of W Comae. The relative magnitude is plotted against the date of observation.
Based on the broad observing frequencies of the telescopes Swift UVOT and XRT, Fermi LAT\textsuperscript{16} and the ATO, the data from each telescope were compiled into a set of multi-wavelength spectra. This range of data allowed us to combine the ATO observations with several other wavebands. The total variation of the sources over the five month observing period was 0.148 photons/s/cm\textsuperscript{2} for Markarian 421, 0.037 photons/s/cm\textsuperscript{2} for Markarian 501, and .017 photons/s/cm\textsuperscript{2} for W Comae. These measurements were calculated by converting the relative magnitude measurements to an absolute photon count in order to compare with Fermi and Swift data. While very little variation was observed over the course of the observations, this closely matched the relative activity as observed by Fermi and Swift.

When plotted by average incident energy on the detector, a doubly peaked spread emerged for both Markarian objects (see Figure 5). The initial peaks for Markarian 421 and 501 were $10^{17}$ Hz and $10^{20}$ Hz respectively. The second peaks both occurred near $10^{25}$ Hz range in the Markarian objects as predicted by the models by Acciari\textit{ et al.} and Kranich \textit{et al.} These models were supported by the observations of the Markarian objects on which they were based.

The multi-wavelength data of W Comae are presented in Figure 6. Observations from the Swift XRT place the $10^{18}$ Hz X-ray observations between one and two orders of magnitude higher than either of the Markarian objects.

\begin{figure}[h!]
\centering
\includegraphics[width=\textwidth]{multi-wavelength.png}
\caption{The SSC theoretical model as predicted by Kranich \textit{et al.} for Markarian 501 along with concurrent multi-wavelength observations. Markarian 421 results in a similar spectrum.}
\end{figure}

\textsuperscript{16} The Ultraviolet Optical Telescope, the X-Ray Telescope, and the Large Area Telescope
**Figure 6** The multiwavelength comparison of Markarian 421, 501, and W Comae. Note the abnormally high X-ray flux for W Comae.

**Figure 7** The limiting magnitude of the ATO based on exposure times. The three plots relate to three different SNR.
Astronomical Optics and Limiting Magnitude
The calculations of magnitudes and apparent brightness in the 2012 observations were roughly consistent with the assumption of a 19.5 limiting magnitude for the ATO, consistent with limiting magnitude estimates of other telescopes of similar sizes and field stars present in images. Upon cleaning the mirrors and refractive corrector during the winter visit of 2012/2013, the limiting magnitude likely increased slightly. Using the calculations in Astronomical Optics (Schroeder, 2000) and a safe signal to noise ratio of 50, we calculated the theoretical limiting magnitude of the ATO for the visible spectrum to be between 21 and 22 for reasonable exposure lengths (see Figure 7).

FOV of Telescope
After updating the WCS fitting program, we were able to overlay the WCS coordinates on the recorded images. This overlay allowed us determine that the plate scale and field of view (approximately half a degree), does not achieve the 1 degree FOV capability of the optical design (although it is greater than the FOV of many large research telescopes such as the Hubble’s 10 arc-minutes). We anticipate the eventual upgrade of the system with a 2048 x 2048, ~20 □m pixel CCD covering ~40 arcminutes. A larger FOV is valuable given the pointing errors and in providing a larger number of reference stars for relative photometry.

RESULTS OF DATA ANALYSIS
The data recorded by the ATO serves a two-fold purpose. Not only do they provide useful information about the astronomical bodies we observe, but they also verify the adjustments and repairs made in updating the apparatus.

Observing recommenced in early 2012 and although the data were sparse, we were able to draw a general comparison between the observations of the ATO, Swift/UVOT, Swift/BAT, and Fermi/LAT, as well as the ground-based VERITAS gamma ray telescopes. The wide range of observable wavelengths for the various telescopes allowed for the construction of characteristic spectra for each source studied.

For the three main objects studied, Markarian 421, Markarian 501, and W Comae, the Synchrotron Self Compton (SSC ) model was used to form a predictive baseline magnitude with which to compare our measurements. This model combines the two most prevalent forms of radiation, Synchrotron Radiation and Inverse Compton Scattering, into one model with only a few free parameters.

Synchrotron radiation occurs when a charged particle is accelerated perpendicular to its motion, under the influence of a magnetic field. In the relativistic case, the particle is strongly beamed outward in the direction of motion. This type of radiation is predicted to occur within the highly energetic particle beams and strong magnetic fields in AGN jets. Energetic plasma is ejected in the jets. By some mechanism, be it large scale electric fields or shock acceleration, charged particles are accelerated, creating high energy radiation within the angle subtended by the jet.

Inverse Compton Scattering is a process unique to highly energetic particles and radiation. In normal Compton scattering, a photon transmits a certain amount of energy to an electron. During this interaction, the electron gains some energy from the photon resulting in a lower energy photon and a higher energy electron. However in
highly relativistic jets, particles with kinetic energies far exceeding the energy of the photons with which they interact can exist (Rybicki and Lightman, 2004). These high energy electrons can up-scatter ambient photons up to very high energies.

The SSC Model incorporates both of these phenomena into a single explanation of nonthermal radiation seen in active galaxies and other astrophysical settings where particles can reach very high energies. Particles accelerated in the relativistic jets emit synchrotron radiation with a range of frequencies peaked around the average electron energy. Some fraction of these photons will then be Compton up-scattered by the same electrons which can further boost the energies of these photons up to X-ray or γ-ray energies. This creates a bimodal distribution of photons. The first group of photons, which occurs at a lower frequency, represents synchrotron emission from the accelerated electrons. The second distribution of photons, at a higher frequency, comes from Compton up-scattering of these synchrotron photons. Several parameters in the model affect the spectral shape including the density of electrons, magnetic field, size of emission region, etc.

By examining the emissions of Markarian 421 and Markarian 501, I found that during the early 2012 season, the two sources matched the predicted SSC model closely. Both Markarian objects had unusually intense high energy emissions which is to be expected as many of the observations were made specifically because they were exhibiting high levels of activity.

Aside from the Markarian objects, W Comae was also highly active and regularly observed during the early 2012 season. Unlike the two Markarian objects, however, an anomalously high level of X-ray level radiation recorded by Swift/XRT is not easily explained by a simple SSC model, but may require a more complicated emission model. However, little more can be concluded from the observations without a more detailed examination of the emission spectra.

CONCLUSIONS AND FUTURE WORK

The work I completed over the past two years has yielded a wide range of varying results. Through the analysis of the ATO optical data, we are beginning to provide an important, high-temporal density data set for multiwavelength studies of γ-ray blazars. However, another large project has been, on the whole, an engineering effort aimed at the development of the ATO as a stable optical instrument.

Therefore, the majority of conclusions we can draw are on the present and future utility of the ATO for the field of observational astronomy.

The data recorded in the spring of 2012 serve to confirm the general agreement of the multiwavelength spectra with SSC models. The deviations of emissions of Markarian 421 and 501 do not differ significantly enough or with enough confidence to refute the previous multiwavelength campaigns. This result is partially because of the uncertain experimental nature of the ATO’s data which were taken to validate the apparatus, but also because of the limited data size when compared to other astronomical surveys.

In the case of W Comae, we might conclude that the spectrum differs from the SSC model anticipated, but this conclusion requires a more detailed modeling effort beyond the scope of this work. Our observations suggest one of two results: Either the
SSC model does not accurately describe the emission processes at work in W Comae, or the parameters of the SSC model vary significantly between the cases of Mrk 421/501 and W Comae.

As stated above, the most significant progress of this work is the development of the ATO as a scientific apparatus. The star finding program was repaired and the WCS fitting program, which relied on the star finding program, was also repaired, allowing the objects imaged by the ATO to be verified based on galactic coordinates.

We developed an observing procedure and set of protocols for remote observing, including documentation for both remote and on-site observers to make the observing process more efficient. This efficiency will reduce the time spent solving some common problems that occur as part of regular observing. We also created a file structure to assist with remote data analysis and photometry as well as documentation on the data analysis procedure for future observations.

The observations made during 2012 provided a means of comparing the photometric values of the ATO against other established optical telescopes. These observations not only allowed for a basic analysis of the optical activity over several months, but they also provided a first estimate of the limiting magnitude. This estimate was calculated after cleaning the optics to bring the realistic limiting magnitude closer to the theoretical limit.

Much of the work in developing the ATO has been geared toward future campaigns in assisting VERITAS with complementary source observations. The inclusion of the polarized filters allows the optical data taken to establish constraints on the magnetic behavior of sources, giving greater depth to the VERITAS observations.

Over the years, we have explored a number of different focal plane detectors that can provide high sensitivity measurements of both the angle and degree of polarization (Roskar, 2003). Since these devices present technical challenges, we have recently added two fixed linear polarizers to the filter wheel to provide a simple method to determine the polarization from optical sources. These filters, oriented perpendicular to one another, allow us to measure the linear polarization of the emitted radiation.

Upon completion of the ATO updates, the same changes can be made to its sister telescope in India providing for nearly constant sky access. These three factors: the wide FOV, the high slew speed, and the antipodal viewing fields, could ultimately establish the ATO as the premier optical GRB apparatus in the world.

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Children’s Intuitions about Physical Ailments and Diseases

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ABSTRACT
The authors conducted one study to examine children’s intuitions of different health ailments. We presented four- through seven-year-olds with three vignettes describing a character with either a cold, broken arm or allergies. Our data suggests that children have an initial belief that any sick individual will recover from their ailment. However, our participants choose randomly when asked about the contagion factor of an un-described illness. This suggests that children understand that different ailments have different contagion properties. Additionally, all ages understood basic information regarding a broken arm. Only older children fully grasped information regarding a cold. Finally, four- through seven-year-olds did not correctly answer questions about allergies.

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Professor Markson studies conceptual development and social cognitive development in infancy and early childhood. Her research focuses on how children learn words and concepts, including the role of intentional understanding in this process. Current research projects explore children’s notions of conventions in language and culture, children’s reasoning about their own and others’ preferences, and social influences on the development of preferences in infancy.

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KEY TERMS
- Cognitive Development
- Health Knowledge
- Preschool Age
- Health Intuitions
- Chronic Illness
- Contagion
INTRODUCTION

Current research in cognitive development attributes reasoning in young children to a set of domain-specific systems of knowledge. Children’s scientific understanding of the world is currently broken down into three main domains: physical, psychological and biological. The domain of biology, which occurs the latest in development, is the least investigated. Research is divided between arguing that this system of knowledge starts to manifest itself between the ages of four and six, versus later in childhood. However, both views explain children’s understanding of biology using the Naïve Theory of Biology, which is broken down into three main components: first, the knowledge to make a distinction between living organisms and non-living objects; second, a mode of inferences for behaviors of biological nature, which entails a basic understanding of why an animal would do a certain action; and third, knowledge of causal explanatory framework for behaviors, such as understanding that a plant requires water for roughly the same reason that an animal requires food (Hatano and Inagaki, 1994).

Children’s understanding of health problems is classified within the domain of biology. Children frequently experience physical injuries and illnesses, but it is not clear how much young children understand about specific ailments, or sickness more generally. Previous studies show that children attribute diseases more to biological reasons than to justice explanations (Miller and Bartsch, 1997). That is, children understand there is an organic aspect of illness, and do not view it as a product of karma or retribution for a previous action. In addition, prior research has shown that preschoolers use causation reasoning to form a basic theory of germ contamination and that children actively avoid germs (Solomon and Cassimatis, 1999). For example, three-year-olds can predict that drinking contaminated beverages will make one ill (Siegal and Share, 1990). However, few studies have combined multiple factors of ailments and illnesses to look at them as a whole. Studies examining sickness have followed an interview-like procedure (Bares and Gelman, 2008). This method, while providing some useful information, has its flaws. These studies capture only what a child can express verbally, not their gut choices.

In addition, no current research investigates children’s first thoughts when they hear somebody is ill or injured. Do children automatically apply their basic theory of germ contamination to any ailment, or only to specific types of sicknesses? Do children intuitively think everything is curable? This information is crucial in real world applications where one needs to explain an ailment to a young child and does not want the child to assume anything incorrectly. Imagine the ill consequences of explaining to a young child that his parent has cancer, and having him think it is contagious.

The current study hopes to better understand children’s intuitions and basic understanding of a few common ailments. We employed a forced choice measure in order to get an answer for each question from our participants. We asked questions about characters without specifying a particular illness to get an initial assessment of children’s beliefs. This study looks at children’s assessment of ailments through two factors. The first is contagion, which is fairly heavily researched. The second is whether the ailment is chronic or not. This is much less studied and will give us a novel perspective of children’s intuitions.
METHOD

Participants
Participants in the study were 12 four-year-olds (8 boys and 4 girls, $M = 4$ years 6 months, range = 4 years 1 month to 4 years 11 months), 10 five-year-olds (9 boys and 1 girl, $M = 5$ years 7 months, range = 5 years 3 months to 5 years 11 months), 11 six-year-olds (6 boys and 5 girls, $M = 6$ years 5 months, range = 6 years 0 months to 6 years 11 months) and 8 seven-year-olds (5 boys and 3 girls, $M = 7$ years 5 months, range = 7 years 0 months to 7 years 11 months). Children were primarily from middle-income homes in the Greater St. Louis area and were predominately European American. One additional five-year-old was not included in this sample due to failure to understand the task instructions.

Materials
The study presented children with three vignettes about three different ailments: a cold, a broken arm and allergies. All three stories were in a single binder and presented sequentially. On each page, a question was asked and the participant answered the question by placing one of two available buttons on the page. Two warm-up questions were asked to familiarize the participant with the answering procedures. Two buttons were given to the child in a random order and the child was taught to place the correct button on a Velcro swatch on each page. The participant was not allowed to continue until he or she properly completed both questions. Each vignette started with a boy who was described as “something might be wrong with him. His mom says he has to go to the doctor later.” The participant was then asked about whether the character will always feel sick (chronic) and whether his brother will feel sick too after playing with the protagonist (contagion). These questions, presented without any other information, were meant to investigate basic intuitions and order effects. Afterwards, in each vignette, the specific ailment was described in two sentences. Two consecutive questions asked about whether the participant thought the ailment was chronic, and two asked about whether the participant thought it was contagious. This led to a total of six questions about each vignette, and 18 questions for each child in the study. The presentation of the two buttons to answer each question was random with respect to the order they were shown to the participant. See Appendix A for a complete list of stories and questions.

Procedures
Children completed the study individually in a private room in the Cognition and Development Laboratory at Washington University in St. Louis. After a brief warm session in a greeting room, the participant was lead into the testing room and asked to sit in a designated seat at a table. The binder containing the vignettes was placed before them, horizontal so the pages flipped away from the child. The experimenter opened the binder, handed the child the first two buttons and read the first warm up story and question. The buttons were presented in a random order. Once the participant put a button on the Velcro swatch, the experimenter put the other button in his pocket and turned the page. Two new buttons were located on the back of the previous page for
each question. After the child answered, the leftover button was returned to the back of the previous page to ensure the participant only had access to two buttons at a time. During the two warm up questions, the child was highly praised for placing the correct button in the correct location. During the study questions, only neutral feedback was given. In between each vignette, the experimenter said to the child “You are doing a great job reading my story! Let’s read the next one!” The three vignettes were read in a counterbalanced order between participants. All answers and all exclamations by the child were coded live during the study.

RESULTS
We assigned a score of 1 if the participant answered the question in what we considered the most instinctive fashion for an adult, and a score of 0 if they answered oppositely. For the intuitive questions (questions before any information was provided), a score of 1 was given if they thought the child would get better and spread his sickness to his brother; a score of 0 was given if the participant thought the character was always going to be sick and the brother was not going to get sick. In the broken arm vignette, a score of 1 was given for each question to which the child responded that broken arms are not chronic and not contagious. In the allergies vignette, a score of 1 was given for each question to which the child responded that allergies are chronic and not contagious. Finally, in the cold vignette, a score of 1 was given for each question to which the child responded that colds are contagious and not chronic.

We first looked at how well the participants understood each specific ailment. We conducted one-sample t tests to do so, looking at each age group separately. Because we asked four questions, we assumed random guessing would give a score of 2. Our results show four-year-olds’ responses were significantly different from chance, in both the broken arm vignette and the cold vignette, $t(11) = 2.000$, $p = 0.071$ and $t(11) = 3.447$, $p = .005$, respectively. Five-year-olds’ responses were significantly different from chance in only the broken arm vignette, $t(8) = 4.243$, $p = 0.003$. Six-year-olds’ responses were significantly different from chance in both the broken arm vignette and the cold vignette, $t(10) = 12.264$, $p < 0.000$ and $t(10) = 5.882$, $p < 0.000$, respectively. Finally, seven-year-olds’ responses were also significantly different from chance for the broken arm and cold vignettes, $t(7) = 15.000$, $p < 0.000$ and $t(7) = 2.497$, $p = 0.041$, respectively. These results are depicted in Graph 1.

We conducted several independent-samples t tests to examine whether there was an age difference in children’s understanding of the different types of ailments. Our results indicate that there was a difference between four-year-olds and six-year-olds, and also between four-year-olds and seven-year-olds, for the broken arm vignette, $t(21) = -2.837$, $p = 0.010$ and $t(18) = -2.849$, $p = 0.011$, respectively. Our results also indicate a difference between six-year-olds and four- and five-year-olds for the cold vignette, $t(21) = -2.147$, $p = 0.044$ and $t(18) = -2.466$, $p = 0.024$.

Next, we were interested in children’s differences in understanding contagion and chronic factors. In order to investigate this, we first conducted one-sample t tests. Since a total of six questions were asked about each factor across all three vignettes, we set chance at 3. For the chronic questions, only six- and seven-year-olds’ responses were significantly different from chance, $t(10) = 10.757$, $p < 0.000$ and $t(7) = 3.240$, $p = 0.005$. For the contagious questions, only four- and five-year-olds’ responses were significantly different from chance, $t(8) = 4.243$, $p = 0.003$. These results are depicted in Graph 1.
Graph 1 - Total Questions Based on Ailment

Graph 2 - Total Chronic and Contagion Questions across Ailments
p = 0.014, respectively. For the contagion question, responses from all age groups were significantly different from chance, t(11) = 2.548, p = 0.027, t(8) = 2.294, p = 0.051, t(10) = 3.750, p = 0.004 and t(7) = 5.292, p = 0.001, in ascending age. Using independent-samples t test, we also examined differences to chronic verse contagious answers based on age. The only significant result found was that six year olds differed from four- and five-year-olds in their answers to the chronic questions, t(21) = -3.390, p = 0.003 and t(18) = -3.429, p = 0.003, respectively. This is depicted in Graph 2.

We were interested in children’s initial thoughts about ailments, specifically if children thought another child who was described briefly as “does not feel well” would get better and could spread their ailment. Four-year-olds significantly (non-randomly) chose that the character would get better on the first two vignettes, t(11) = 2.966, p = 0.013 and t(11) = 5.000, p < 0.000. For all three vignettes, no matter the order, five-year-olds always chose that the character would get better (M = 1, SD = 0). Six-year-olds also significantly chose the non-chronic answer for all three stories, M = 1, SD = 0, t(12) = 5.500, p < 0.000 and t(12) = 5.5000, p < 0.000, in order, and so did seven-year-olds, with the exact same statistics, t(7) = 3.000, p = 0.020. No age groups significantly chose an answer for any of the contagion intuition questions. Data about chronic answers is depicted in Graph 3, and data about contagion answers is depicted in Graph 4.

We also investigated how answers to these intuition questions changed based on the order of the stories. To do this, we looked at the absolute value of differences of scores for these questions between vignettes. We then used one-sample t tests to see if it differed from no change (0). Our results indicate that four-year-olds significantly change their answers between the second and third vignette about the contagion question, t(11) = 2.345, p = .039. Six-year-olds significantly changed their answers on the contagion question between the first and third vignette, t(12) = 2.739, p = 0.018. Five- and seven-year-olds never significantly changed their answers. Data about chronic answers is depicted in Graph 3, while data about contagion answers is depicted in Graph 4.

DISCUSSION

In this study, we examined children’s intuitions of health problems and their understanding of three specific ailments. Several interesting results came from the data in this study. To begin, the study showed that four-, five-, six- and seven-year-olds all have mostly correct thoughts on broken arms. All but five-year-olds also held accurate beliefs about colds. The data for the five-year-olds was close to being significantly different from random guessing, and we believe, with a proper sample size, will improve past significance. This data shows that children understand basic features of common ailments.

Children as young as four years old can properly use previous knowledge to make predications on contagious factors and whether a common illness is chronic or not. For more complex ailments, however, children become confused. All ages answered seemingly randomly for the questions about allergies. This could be caused by several different reasons. First, allergies are on a spectrum of severity. Many who suffer from allergies are not inhibited from doing normal activities in everyday life, including
Graph 3 – Chronic Intuition Questions

Graph 4 – Contagion Intuition Questions

Graph 3

Graph 4
many participants who partook in this study. In addition, allergies may occur only at certain points during the year, instead of yearlong, as one would assume for a chronic disease. These variations could cause children to misunderstand basic concepts of allergies. Second, we described the character with allergies by his sneezing and an itchy throat, symptoms associated with germs. Without thinking about allergies specifically, children could have connected a sneeze with spreading a disease and chosen accordingly. Either way, our results clearly show children can understand common ailments, but struggle with more complex ones such as allergies.

As expected, older children performed differently from younger children. Specifically four-year-olds performed worse than six- and seven-year-olds on questions regarding the broken arm. Six-year-olds answered, on average, more correctly on the cold questions than four- and five-year-olds. The lack of significant differences between seven-year-olds and other age groups may be due to improper sample sizes. It will be interesting to see if these differences still exist after we run a complete sample. The findings do make sense, however, as older children have more exposure and experience with physical injuries and illnesses, giving them an increased knowledge about different aspects of ailments.

Interestingly, all children significantly answered contagion questions correctly, while only the two older age groups correctly answered the chronic questions. Children were able to properly answer contagion questions by applying a basic theory of germ contamination, which other research has shown is present in young children. However, children do not have an intuitive way of knowing whether a disease is chronic or not to adults or children. Any information regarding this must therefore be learned. As such, it makes sense that older children, who have learned more, can answer such questions better.

One of the most interesting results provided from this study is the data collected regarding basic intuitions. In almost every story order, for every age group, children believed that the character would get better, but there was no consensus on whether the ailment was contagious or not. Children automatically assume that, when someone gets sick, they will eventually get better. This may be explained by the fact that almost every sickness and injury that a young child experiences is curable, or at least asymptomatic, with medication. In addition, if a child did experience a chronic illness such as cancer, they would not be included in this study. It would be interesting in the future to replicate this study with chronically hospitalized children and see if they answer differently due to their experience with a chronic illness.

In addition, the results for the contagion intuition questions are interesting because they show that children understand that different ailments exist and a person may be sick with any one of them. If the children were assuming that the character was sick with a cold, the most common ailment, they should have answered that the character’s brother would get sick too. However, our data shows all ages answered this question randomly. Because children did not know what the character was afflicted with, they guessed. This thought process shows a solid understanding that different types of sickness exist.

Because the stories provided information regarding a variety of illness, we wanted to see how the basic intuition answers changed as the study progressed. Only four- and six-year-olds changed their answers. In addition, further statistics show that the
children did not change their answers in a specific direction. This may be caused by a recency effect: participants may have used information about the ailment in the previous vignette to answer the next basic intuition questions. To avoid this problem, we looked only at the responses to questions about the first vignette. However, the data for the first vignette was similar to the data for the second and third vignette, which leads to the same conclusions as discussed above.

From this study, we have learned that children as young as four years old understand that different types of physical injuries and illnesses exist. Children have a strong grasp on common ailments, but struggle with more complex ones such as allergies. From the basic intuition questions, we have learned that it is important to explain that a specific illness is not curable, because children initially believe that all illnesses are curable. As illnesses are common transient events during childhood, it is important to distinguish common ailments, like colds, from more severe ones, and to make sure that children understand the differences. In addition, it is unclear whether children can differentiate between curing an illness and alleviating the symptoms, so further research is necessary. This difference between curing an ailment and treating the symptoms applies to other common ailments, such as chicken pox, where the virus lives on in the body but symptoms can be treated. It would be interesting to see at which age children start to make this distinction. Although much more research can be done on this topic, this study makes a solid start into comprehending children’s understanding of different ailments, and their intuitions surrounding them.

Works Cited


APPENDIX A

BROKEN ARM VIGNETTE

<table>
<thead>
<tr>
<th>Page</th>
<th>Story Read Aloud:</th>
<th>Intuitive Button Choice</th>
<th>Other Button Choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>This is Kyle. Something might be wrong with him. His mother says he has to go to the doctor later. Do you think Kyle will ever feel better?</td>
<td>Smiley Face (feel better)</td>
<td>Sick Face (not ever feel better)</td>
</tr>
<tr>
<td>2</td>
<td>In the morning, Kyle plays with his brother Dustin. Do you think Dustin will feel sick too? Do you think Dustin will have to go to the doctor like his brother or will he be able to go to the park to play?</td>
<td>Doctor</td>
<td>Park</td>
</tr>
<tr>
<td>3</td>
<td>Kyle still doesn’t feel well. So his mom takes him to the doctor. The doctor says, “Oh no Kyle, you got a broken arm!” Kyle’s arm really hurts and he has to wear a cast now. Do you think Kyle will always have a broken arm?</td>
<td>No Broken Arm</td>
<td>Broken Arm</td>
</tr>
<tr>
<td>4</td>
<td>Kyle has a broken arm! Kyle’s arm really hurts and he has to wear a cast now. Do you think in a few months, in a long time, Kyle will be able to play sports?</td>
<td>Sports</td>
<td>No Sports</td>
</tr>
<tr>
<td>5</td>
<td>Kyle’s friend Alec comes over to see if Kyle is okay and play. If Alec shares Kyle’s toys, will Alec get a broken arm too?</td>
<td>No Broken Arm</td>
<td>Broken Arm</td>
</tr>
<tr>
<td>6</td>
<td>Oh no! Kyle just sneezed on Alec! Will Alec now get a broken arm too?</td>
<td>No Broken Arm</td>
<td>Broken Arm</td>
</tr>
<tr>
<td>Check Questions</td>
<td>Do remember what was wrong with Kyle? Do you know what that is?</td>
<td>N/A</td>
<td>N/A</td>
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</table>
### APPENDIX A

#### ALLERGIES VIGNETTE

<table>
<thead>
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<th>Story Read Aloud</th>
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<th>Other Button Choice</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>This is Brian. Something might be wrong with him. His mother says he has to go to the doctor later. Do you think Brian will ever feel better?</td>
<td>Smiley Face (feel better)</td>
<td>Sick Face (not ever feel better)</td>
</tr>
<tr>
<td>2</td>
<td>In the morning, Brian plays with his brother Bradley. Do you think Bradley will feel sick too? Do you think Bradley will have to go to the doctor like his brother or will he be able to go to the park to play?</td>
<td>Doctor</td>
<td>Park</td>
</tr>
<tr>
<td>3</td>
<td>Brian still doesn’t feel well. So his mom takes him to the doctor. The doctor says, “Oh no Brian, you have allergies! You are allergic to the trees and plants outside.” Brian’s throat is really itchy and his nose is runny. He sneezes a lot. Do you think Brian will always have allergies?</td>
<td>Allergies</td>
<td>NoAllergies</td>
</tr>
<tr>
<td>4</td>
<td>Brian has allergies! Brian’s throat is really itchy and his nose is runny. He sneezes a lot. Do you think in a few months, in a long time, Brian will be able to go outside?</td>
<td>No Outside</td>
<td>Outside</td>
</tr>
<tr>
<td>5</td>
<td>Brian’s friend Oliver comes over to see if Brian is okay and play. If Oliver shares Brian’s toys, will Oliver get allergies too?</td>
<td>No Allergies</td>
<td>Allergies</td>
</tr>
<tr>
<td>6</td>
<td>Oh no! Brian just sneezed on Oliver! Will Oliver now get allergies too?</td>
<td>No Allergies</td>
<td>Allergies</td>
</tr>
</tbody>
</table>

Check Questions
1. Do remember what was wrong with Brian?
2. Do you know what that is?
### APPENDIX A

### COLD VIGNETTE

<table>
<thead>
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<th>Page</th>
<th>Story Read Aloud:</th>
<th>Intuitive Button Choice</th>
<th>Other Button Choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>This is Sam. Something might be wrong with him. His mother says he has to go to the doctor later. Do you think Sam will ever feel better?</td>
<td>Smiley Face (feel better)</td>
<td>Sick Face (not ever feel better)</td>
</tr>
<tr>
<td>2</td>
<td>In the morning, Sam plays with his brother Miles. Do you think Miles will feel sick too? Do you think Miles will have to go to the doctor like his brother or will he be able to go to the park to play?</td>
<td>Doctor</td>
<td>Park</td>
</tr>
<tr>
<td>3</td>
<td>Sam still doesn’t feel well. So his mom takes him to the doctor. The doctor says, “Oh no Sam, you have a cold!” Sam’s head is really hot and his mom takes his temperature and he has a fever. His head hurts and he is very sleepy. Do you think Sam will always have a cold?</td>
<td>Cold</td>
<td>No Cold</td>
</tr>
<tr>
<td>4</td>
<td>Sam has a cold! Sam’s head is really hot and his mom takes his temperature and he has a fever. His head hurts and he is very sleepy. Do you think in a few months, in a long time, Sam will be able to go to the park?</td>
<td>Park</td>
<td>No Park</td>
</tr>
<tr>
<td>5</td>
<td>Sam’s friend Doug comes over to see if Sam is okay and play. If Doug shares Sam’s toys, will Doug get a cold too?</td>
<td>Cold</td>
<td>No Cold</td>
</tr>
<tr>
<td>6</td>
<td>Oh no! Sam just sneezed on Doug! Will Doug now get a cold too?</td>
<td>Cold</td>
<td>No Cold</td>
</tr>
<tr>
<td></td>
<td><strong>Check Questions</strong></td>
<td><strong>Do remember what was wrong with Sam?</strong></td>
<td><strong>Do you know what that is?</strong></td>
</tr>
</tbody>
</table>
Summaries of Student Work

Toward a Better Understanding of...

Anatomy of an Epidemic:
Critically Understanding and Evaluating the Nature and Construction of a Food-Allergy Epidemic

Margaret A. Abbey

Mentor: Glenn D. Stone

There is something perverse and terrifying about a body that rejects one of its basest needs for survival: food. Not only can the body reject certain foods, but it can mount a physiological, immunological attack against the ingested food—to a fatal point.

This is what an Immunoglobulin Class-E food allergy is: it is an individual’s body inaccurately recognizing a certain food, specifically its food protein, as an invader that must be destroyed. In many cases, food allergies are severe and life-threatening, and end in death for approximately 150 Americans every year. The scientific “how” and the “why” of food allergy have been studied extensively in the biomedical sciences, but little to no work on food allergy has been done from a truly humanistic angle—an angle that may uncover a means of whittling down these questions to critical considerations of why are rates of food allergy increasing worldwide, but particularly, in the United States. This lack of humanities-centric, academic inquiry has not only plagued common understanding and public perception of food allergies and their sufferers, but also may be inadvertently influencing the landscape of the increases in food allergy.

The term used to label the seemingly “exponential” rise in food allergy, the food-allergy epidemic, must first be analyzed thoroughly. This project seeks to survey the very nature of this epidemic through a collection of ethnographic vignettes self-reported by those in the context of a food-allergy online forum, in order to uncover the manner in which food “allergics” and people caring for food-allergic individuals construct the “epidemic” through language and memory within a collective, shared, and medically-driven identity, and how this construction may be one wielder of the influence shaping the “epidemic.”
Currently, fracture risk is determined by dual energy X-ray absorptiometry (DeXA), which ascertains a relative risk score based on tissue mineral density (TMD) and age. However, this metric provides limited utility in individuals with moderate bone quality. A proposed modality to bridge this gap is reference point indentation (RPI), wherein micro-scale mechanical testing recapitulates the organ-level fracture resistance. We demonstrate that combining RPI and DeXA provides a better assessment of fracture risk than either metric alone.

Fifteen RPI measurements were performed at 5mm increments on tibia mid-diaphysis of cadavers. The tibias were removed and scanned using micro-tomography (μCT) to determine TMD and porosity at the indent sites. The proximal femur was removed, analyzed, and loaded compressively at the femoral head until failure.

It has been shown that RPI produces microfractures and is correlated with bone toughness. Here, TMD was marginally correlated with RPI and porosity was weakly correlated with RPI, indicating that both parameters play a minor role, if any, in RPI evaluation. Systemically, univariate correlations of IDI and total hip TMD with fracture load at the femoral neck had a strong relationship. More importantly, the significant multivariate relationship between these three parameters reveal that bone quality changes may be systemic—indicating that RPI can detect systemic bone quality changes at clinically relevant sites. This evidence shows that RPI evaluates bone quality independently of mineral density, a metric of bone quantity. RPI demonstrated robustness as the effect of bone porosity was negligible. Moreover, our study demonstrates the utility of providing the relative assessment of femoral neck strength via RPI. Therefore, the combination of RPI and DeXA provides the highest level of predictive fidelity and may aid in better determination of fracture risk in patients with atypical bone metabolism.
Toward a Better Understanding of…

Examine the Impact of Race Identity, Social Anxiety and Paranoia on the Jumping to Conclusions Bias

Jennifer R. Alexander

Mentor: Thomas L. Rodebaugh

The jumping to conclusions (JTC) bias is a reasoning bias defined as making decisions based on minimal evidence. Although the JTC bias is associated with the severity of abnormal beliefs, there is also evidence that suggests that the JTC bias may be exacerbated by anxiety. Bensi & Giusberti found that high-trait anxiety individuals JTC significantly more than low-trait anxiety individuals.

The Social Probabilistic Inference Task (SPIT) was used to measure the JTC bias. Participants were informed that they were being introduced to a person at a party. Participants then determined if that person liked or disliked them based on a series of positive and negative facial expressions shown to them. The main index of the task is the number of facial expressions requested before reaching a decision of whether he or she was liked or disliked by the person. The more facial expressions requested, the lower the tendency to JTC.

The aim of the study was to examine how race identity affects JTC response style; specifically, whether participants would show a higher tendency to JTC if introduced to a person within their same racial group (in-group) or outside their own racial group (out-group). First, we hypothesized that individuals higher in social anxiety and paranoia will demonstrate significantly higher JTC bias when compared with individuals that are lower in social anxiety and paranoia. Second, we anticipated that participants would demonstrate significantly more JTC bias for out-group members than for in-group members.

Participants (N = 49) who self-identified as Black completed 2 SPIT tasks (one in-group and one out-group) across 2 time points. SPIT tasks, social anxiety and paranoid measures were administered online. Results are forthcoming.
Genetic and behavioral research that aims to understand complex, heterogeneous clinical disorders, like Major Depressive Disorder (MDD), has begun to focus on potential endophenotypes, or intermediate phenotypes or markers between underlying genetic causes and MDD. Specifically, studies of MDD suggest that reduced response to reward and heightened stress response are potential endophenotypes of depression. This study intends to investigate the psychological, emotional and biological mechanisms involved in reward and punishment processing.

Anhedonia, the lack of experienced pleasure, is a particular variable of interest in this study. In the past, depression and more specifically anhedonia have been related with reduced response bias on reward tasks, altered function in the dopaminergic system, reduced response to positive stimuli and a reduced willingness to expend effort to obtain reward. However, it is unclear whether these behaviors are all related within an individual and how strongly behavior on each task type will be related to anhedonic/depressive symptoms. A final and important question is whether a “reward responsiveness” metric that combines performance on all trials (and possibly genetic profile scores and resilience of the reward response to stress) better explains anhedonic symptoms than behavior on a single task type.

To investigate this, we will recruit healthy young adults who will complete a variety of behavioral tasks designed to assess reward and emotion processing, complete individual difference questionnaires (measuring anhedonic and depressive symptoms), and complete saliva samples for gene and cortisol analysis. We will use the data collected to gain information about how healthy young adults process monetary gains/losses and whether these processes differ as a function of individual differences. Furthermore, we will use the information to assess how the different tasks relate to one another and how behaviors across these tasks are impacted by certain genes and reward processing systems.
Toward a Better Understanding of…

Case Control Study of Epithelial Exfoliation in Bacterial Vaginosis

Courtney Amegashie

Mentor: Amanda Lewis

The human vagina is host to many bacterial communities through a finely-equilibrated, mutualistic relationship. The vagina provides nutrients to the bacteria, which in turn help rid the vaginal ecosystem of harmful, non-indigenous species. When the microbiome is disturbed, bacterial vaginosis (BV) often results. Affecting 1 in 3 women in the U.S., bacterial vaginosis is prevalent, but vaguely characterized. In the clinical setting, women who exhibit vaginal inflammation, fishy malodor upon application of potassium hydroxide, vaginal epithelial cells surrounded by bacteria in wet mount microscopy, or abnormal discharge are diagnosed with bacterial vaginosis. Due to the broad diagnostic features of BV, it has proven difficult to characterize the etiology of the disease. The focus of this research is to identify cellular phenotypes of the vagina that correlate with the presence of BV in order to facilitate the clinical identification of the disease.

Increased epithelial cell exfoliation has long been associated with BV, but this relationship has not been quantified. Our lab has previously studied the epithelial shedding of a clinical sample of women with and without BV and found significantly more exfoliated vaginal epithelial cells in affected individuals. Through a blind study of 222 women with either BV (Nugent score 7-10), intermediate BV (Nugent score 4-6) or no BV (Nugent score 0-3), we seek to correlate the number of exfoliated epithelial cells to the presence and severity of BV in these women. By characterizing the BV phenotype at the cellular level, our lab hopes to shed light on the disease’s complex etiology and to improve our ability to diagnose and ultimately treat BV.
Cancer is a disease of the genome that causes sporadic cell division. Cancer may arise due to point mutations, gene deletions, gene duplication, and other modifications in the sequence of the genome. The completion of the human genome has changed the course of biomedical research. Exploration of the human genome led to discovery of a special group of RNAs called long intergenic non-coding RNAs (lncRNAs). In recent studies, lncRNAs have been found to be up-regulated in prostate cancer. Prostate Cancer has been treated through hormonal therapy, but tumors in prostate cancer eventually become immune towards the hormones administered, becoming Castration Resistant Prostate Cancer (CRPC). The goal of this research project is to find lncRNAs causing the resistance to androgen treatment for prostate cancer expression. Bioinformatics used frequently in RNA sequencing, was used to analyze the whole genomes of individuals by assembling RNA transcripts into a genome with only the exons and looking for regions of high differential expression. RNA transcripts were then put through Cufflinks and CuffDiff to find 208 differentially expressed genes in tumor tissues and 18 were confirmed to be lncRNAs. The RNA transcripts from both untreated and CRPC populations were sent through GSEA to determine the correlation of the functions of the Polycomb Repressive Complexes to the untreated and CRPC. Further research will be done to see if any of the 18 lncRNAs are involved in the tumorigenesis in other cancers and which lncRNAs guided the PRC1 and PRC2 in CRPC.
Toward a Better Understanding of...

**Protein Biomarkers and Their Relation to Executive Functioning following Pediatric Traumatic Brain Injury**

*Sydney Ariagno*

*Mentor: Desiree White*

Traumatic brain injury (TBI) poses a significant public health threat to our population, especially when these injuries occur in children. However, despite the overwhelming numbers of TBI every year, the current hospital methods for assessing traumatic brain injury are not specific or technical enough to be able to provide an accurate prediction of what patient outcome and recovery is to be expected. Protein blood serum biomarkers present a promising avenue towards developing a novel method of assessing, diagnosing, and quantifying TBI. Specifically, this study will focus on the biomarkers UCH-L1 and GFAP and their ability to predict psychological deficits (particularly concerning executive processing) longitudinally following injury. Biomarker levels acquired during patients’ initial seven days following injury will be compared to those patients’ executive abilities at three, six, and twelve months following injury, as measured by the Behavioral Rating Inventory of Executive Functioning, the Conners’ Rating Scale of Behavior, and the Child Behavior Checklist. Correlations detected between biomarker amounts and performance on these questionnaires would indicate that biomarkers can be used as a precise and specific diagnostic tool to yield accurate predictions of what deficits and levels of recovery patients can expect following TBI.
Investigating the Role of DTI Directional Diffusivity as a MR Biomarker for Axonal and Myelin Damage in Multiple Sclerosis and Acute Disseminated Encephalomyelitis

Wint Yan Aung

Mentor: Tammie L. S. Benzinger

Diffusion Tensor Imaging (DTI) is a non-invasive, quantitative magnetic resonance (MR) imaging technique that measures the rate and direction of movement of water molecules within tissues. In this study, we investigate the role of directional diffusivity as a MR biomarker for axonal and myelin damage in white matter demyelinating diseases, Multiple Sclerosis (MS) and Acute Disseminated Encephalomyelitis (ADEM). MS is a progressive disorder in which demyelination, axonal degeneration, and inflammation contribute to disease pathogenesis. ADEM is classically an acute, monophasic disease in which axonal damage is present but minimal. However, relapses and conversion to MS in some ADEM patients pose a diagnostic dilemma. Based upon in vivo animal studies with acute axonal and myelin injury, and histopathologic correlation, we hypothesized that DTI directional diffusivity can discriminate between axonal and myelin pathologies in humans. Nine pediatric patients with baseline MR and DTI scans obtained within 20 months from date on presentation were selected from MSADEM longitudinal MR imaging study. This included 7 MS patients (ages at baseline scan 14-18) and 2 ADEM patients (ages at baseline scan 6-9) with no further change in disease status to this date. Twenty-five controls (age range 6-24) were also included. ROI analysis demonstrated significantly higher mean normalized axial (AD) and radial diffusivity (RD) in MS patients compared to ADEM patients. AD and RD characterize diffusion parallel and perpendicular to axonal tracts respectively. High baseline values suggest extensive axonal and myelin damage in MS patients. These initial results indicate that AD and RD could be used as a biomarker for axonal and myelin damage. Additional subjects are needed to confirm our findings. A longitudinal study will further our understanding of the natural history and potentially resolve the challenging diagnostic difficulties.
It has been well established that opioid receptor signaling plays a major role in the regulation of stress, pain, depression, and the rewarding properties of drugs of abuse such as morphine, nicotine, and cocaine. Although the Kappa opioid receptor (KOR) and Mu Opioid receptor (MOR) have been a key focus of narcotic research, knowledge is still limited on how the G-protein coupled receptors signal and yield behavioral responses. Study of specific brain regions and neural circuits can be difficult as the synthetic drug compounds diffuse throughout the brain with little spatial or temporal control. Thus, opto-genetic receptor constructs, activated by site specific laser activation, will provide a useful tool in the study of opiate cellular signaling mechanisms. We created a novel opto-genetic tool and molecularly characterized this chimeric receptor which utilizes rhodopsin light-sensitive activation machinery and results in opioid receptor signaling. Characterization of these chimeric receptors will result in a better understanding of their activation and signaling as well as a determination of their signaling similarity to endogenous opioid receptors, which will prove useful for *vivo* behavioral studies. In addition, our studies will work to better define native opioid receptor signal transduction, effects on cell biology, and neural systems. Optimization of OMOR and OKOR activation protocol will elucidate the G-protein and arrestin-mediated signaling time points at which protein kinase and adenylate cyclase activity is turned on, and how arrestin-dependent MAPK is initiated. We also characterized the length and intensity of light (efficacy) stimulation necessary to elicit a peak response, and calculated the power (dose-response) curve for each construct. This pharmacological characterization of a novel tool side-by-side with native opioid receptors for will provide valuable information as we implement these tools *in vivo* neural circuit dissection studies in drug addiction, depression, pain and stress behaviors.
Human Achilles tendons are located in the lower leg behind the calf muscles. They are responsible for connecting calf muscles to calcaneus bones and are crucial to many everyday activities such as walking and jumping. However, Achilles tendon injuries are extremely common among athletes due to sudden stretches and contraction of the tendon, and recoveries after surgeries are not ideal. In order to prevent such injuries and improve recoveries, a more comprehensive understanding of the Achilles tendon’s structure and mechanical properties are required.

Previous research on Achilles tendon has mainly focused on its tensile and material properties. However, the results cannot fully explain the commonality of Achilles tendon injuries. Consequently, an exploration of other properties of Achilles tendon is suggested. Our research focuses on the torsional properties of Achilles tendon; the behavior of the tendon when it is twisted and under torsional force. We hypothesize that natural torsion in human Achilles tendon provides additional mechanical benefits such as elasticity and energy storage, which facilitates Achilles tendon to sustain high \emph{vivo} stress.

To explore the torsional properties of Achilles tendons, specific clamps must be built to fix the tendons onto the test machine. Our work has mainly been focused on the design and manufacture of the clamp. After the clamps were produced, pig’s extensor tendons were dissected and used as a pilot test for human Achilles tendons. Stress, strain and torque were measured under different angles of torsion. Future work will focus on getting more data from pig’s extensor tendon, testing on human Achilles tendon and establishing a computational model to explain the behavior of human Achilles tendon under torsional force.
Exploring Subcellular Localization of MSL2 N-terminal Splice Variants, MSL2.1 and MSL2.2

Meera Basu

Our lab works with a family of ten mechanosensitive (MS) ion channels in *Arabidopsis thaliana* that are homologs of the *Escherichia coli* MS channel MscS. In my project this summer, I worked with plastid-localized MscS-Like (MSL)2, which is required to maintain osmotic homeostasis of plastids. My project was aimed at investigating the localization of MSL2 splice variants to subcellular organelles, because understanding their localization increases our comprehension of the molecular mechanisms used by plants to respond to osmotic stress. We analyzed the subcellular localization of two naturally occurring MSL2 N-terminal splice variants, MSL2.1 and MSL2.2. MSL2.1 has a predicted chloroplast targeting sequence, while MSL2.2 has a predicted mitochondria targeting sequence. In order to determine if these splice variants were indeed differentially localized, we fused Yellow Fluorescent Protein (YFP) to each splice variant and transiently expressed them in tobacco leaves via *Agrobacterium* infiltration. We used confocal microscopy to determine organelle localization of the fusion proteins. Chloroplast localization was visualized through chlorophyll auto-fluorescence. Mitochondria, however, do not auto-fluoresce, so we stained our MSL2.2-YFP construct with Mitotracker, a mitochondrial stain. Our confocal images of tobacco cells expressing the MSL2.1-YFP construct provided further confirmation for chloroplast localization. Our confocal images of MSL2.2-YFP indicated that MSL2.2 also localizes to chloroplasts. Using Mitotracker stain, we did not observe localization of MSL2.2 to mitochondria in addition to chloroplasts. The results from this project showing localization of both MSL2.1 and MSL2.2 splice variants to chloroplasts provide insight into how plants maintain osmotic homeostasis at a molecular level in chloroplasts, organelles that are vital for plant cell metabolism.
The Hawaiian Islands are a biodiversity hotspot, containing a significant number of endemic species and the greatest number of endangered species of any state in the country. This research focused on evaluating which management strategies can be used to successfully increase the population size of the critically endangered plant species, *Hesperomannia oahuensis*. Currently, the *Hesperomannia oahuensis* population size is only six to ten individuals, known from two field sites on O‘ahu, Hawai‘i. Specifically, I focused on three strategies: (1) reducing rat population sizes in the field, (2) hand pollination in the field, and (3) interviewing individuals about the known obstacles and threats to this species. I, along with staff from the Lyon Arboretum and the Oahu Plant Extinction Prevention Program, hiked to Pahole Natural Area Reserve to monitor rat traps around the plants, hand-pollinated the blooming flowers with pollen from the other population located in a nearby valley, and installed a camera to take a once daily picture of a bud to inform botanists when to return and pollinate this flower. We were able to successfully hand-pollinate three individual plants and install the camera. Through interviews, we learned that this plant has low pollen viability, has low germination rates on account of unknown insects eating portions of the seeds, and often has its flowers removed for lei-making if found in unprotected areas. In addition, while working in the micropropagation lab at the Lyon Arboretum, we learned that this particular species is unresponsive to attempts of seed storage and cloning using aseptic technique. If more plant material becomes available, we could try alternative methods of micropropagation. These actions will help the species survive for at least another year under normal conditions.
If you have ever visited the Caribbean region, whether the British, Dutch, Spanish or French-speaking islands, you are likely to have come across the term “Liming.” Perhaps you heard it in a song blasting from a passing car, visited a bar by the name or noticed that the cellular network is called Lime. Nonetheless, it is a term that has travelled the region and even found its way to Caribbean diasporas in Toronto and London.

Liming is the unofficial national past-time of Trinidad and Tobago. Liming is purposefully doing nothing. According to anthropologist Thomas Erikson, it is the art of doing nothing well. Liming is an informal, flexible social engagement that frees the mind and allows one to temporarily forget their responsibilities and obligations so as to be completely engaged in the moment.

This research looks at the social development of liming in Trinidad, focusing on how the practice arose out of a history of colonial oppression and how it changes with the coming of new pressures associated with neo-colonialism and a newly attained “developed” status. Through participant observation and interviews, I aim to explain the purpose liming serves to people and garner inter-generational perspectives. I anticipate that liming may act as a declaration of freedom and independence, as an act of resistance in the face of certain societal structures and pressures such as capitalist ideas of work ethic and productivity, class distinctions, scheduled time and Western models of development.

This work will contribute to scholarly conversations on leisure and work. It will build on works that discuss resistance while challenging the polarized approach of leisure and work as put forth by scholars. It will also add to the literature specifically focused on the Caribbean and contribute to the documentation of the national culture and identity of Trinidad.
DNA double-strand breaks (DSBs) are frequent events in eukaryotic cells. Usually inflicted by pathological damage, unrepaired broken ends can cause dangerous chromosomal rearrangements and cell death. The ciliated protozoan *Tetrahymena thermophila* generates thousands of developmentally programmed DSBs during sexual conjugation and repairs them via non-homologous end joining (NHEJ). Because *Tetrahymena* NHEJ has a significant role in developmental as well as pathological contexts, the organism offers a unique look at how NHEJ achieves a high degree of mechanistic flexibility under a range of biological circumstances. We identify key *Tetrahymena* NHEJ components DNA ligase IV, Ku80, and XLF. XLF and Ku localize to the germline micronucleus while ligase IV occurs in the somatic macronucleus. Upon induction of DNA damage by radiation, ligase IV organizes to subnuclear foci which are gradually repositioned to the nuclear periphery. Our results reveal a temporal and special dimension to ligase IV recruitment after pathological damage. Importantly, we begin to highlight how the recruitment pathways, partner interactions, and compartmentalization of NHEJ enzymes differ between the two types of DSB response.
Enterotoxigenic *E. coli* (ETEC) are the most common cause of traveler’s diarrhea and a major cause of severe diarrheal illness among young children in developing countries where these organisms are responsible for an estimated 800,000 deaths annually. ETEC are a diverse group of pathogens that share the ability to colonize the human small intestine, where they produce and deliver heat-labile and/or heat-stable enterotoxins. Recent studies have shown that during intestinal colonization, ETEC bind and degrade the major mucin in the intestinal lumen, Muc2. Confocal microscopy studies of ETEC infected tissues show co-localization of Muc2 and lipopolysaccharide (LPS) on the cell surface of the bacteria. Similarly, flow cytometry studies suggest that purified Muc2 binds to the surface of ETEC. Theoretically, ETEC might employ mucin binding as a way to disguise themselves from recognition by the innate immune system. To examine this hypothesis, we set out to construct a LPS-negative (rough) mutant of ETEC by disrupting *rfal*, the gene encoding O-antigen ligase, a critical LPS biosynthetic enzyme. The rough mutant generated in the present studies will be used to examine Muc2 binding relative to the wild type parent strain, and whether binding to mucin(s) prevents or diminishes pathogen recognition by the host.
Toward a Better Understanding of…

THE HUB SINGAPORE CASE:
CREATING AN EFFECTIVE SPACE FOR SOCIAL ENTERPRISE

George Boyar and Micajah Dudley

Mentor: Konstantina Kiousis

The historic idea of what constitutes a workplace or working environment has been reinvented with the 21st century. Numerous alternatives have rushed into to fill the gaps, such as coworking spaces. However, they are woefully understudied and poorly understood in terms of growth and development. Exploration of contemporary coworking spaces in a qualitative, and where possible, quantitative nature is essential to understanding the development of new sectors such as social entrepreneurship. The HUB Singapore offers an interesting case study to help us understand what needs to be researched. We looked closely at three main avenues of inquiry; 1. what has been effective in creating coworking spaces that support and develop social entrepreneurship ecosystems?; 2. challenges faced and overcome by coworking spaces themselves and coworking member companies, and 3. challenges the community will face in the future.

We approached these questions through extensive interviews with the HUB Singapore staff and over twenty individual coworkers. In the interviews we asked a series of questions to coworkers about their experience in the space, their own challenges, and the challenges of the HUB itself. Due to time restrictions our investigation of the HUB is meant purely as a case study of a relatively successful coworking space. The hope is that from this study we can identify which areas are in most dire need of exploration and create a blueprint of sorts for further research. Specifically, the HUB Singapore has been successful in providing affordable office space in a central location and surrounding that with a deeply involved community. Current challenges include a culture gap and provision of basic logistical needs. This work explores the essentials of a supportive ecosystem and the role a coworking space plays through the lens of the HUB Singapore.
Films serve many important functions in society, from their potential to alter perceptions through their portrayals of various groups/ideologies to their ability to serve as barometers of social understanding. Film portrayals are particularly powerful when they present a minority group or groups who are only partially understood. Images of people with disabilities, for example, may be some viewers’ only exposure to these individuals, and thus may encapsulate their understanding. For this reason, films are important areas of study since they can indicate the current social understanding of what they are portraying; in turn, the implications of these portrayals can drastically impact individual perceptions. Approximately one in seven Americans have disabilities and many of them receive assistance and care from family members. According to the National Alliance for Caregiving (2009), approximately 65 million people were caregivers in the past year and the majority was female. Family members who provide assistance or support are often included in film portrayals of people with disabilities. Though the caregivers may not be the central characters in the films, their portrayal still indicates the socially contrived role of these individuals, and, more broadly, influences how others perceive the responsibilities and expectations of these caregivers. In this research, I analyzed fifteen films and found that the films often focused on the motivations behind offering care. The depictions of these motivations elucidate the fact that film portrayals of caregivers often perpetuate the illusion that all caregivers are altruistic and patient rather than the reality, which is that there is no universal definition of the ideal caregiver.
In New York City, a number of organizations exist to serve various LGBTQ (lesbian, gay, bisexual, transgender, queer/questioning, etc. identities, which I will refer to as “queer”) populations. SALGA-NYC, formerly known as the South Asian Lesbian and Gay Association in New York City (now simply known as a South Asian queer organization), is one such organization. Aiming to serve the “desi queer” population of New York City, the organization provides monthly support group meetings, collaborates with other organizations to throw parties, organizes as South Asian queer presence at many political and activist events in the City, and more. I use ethnography (participant observation and thirteen in-depth interviews) to explore the experiences of individuals involved with SALGA-NYC to understand queer diasporic space, and the ways in which individuals may use culturally specific queer spaces to further understand their intersectional identities. Further, I analyze SALGA-NYC’s place in the South Asian queer community, its potential to radically challenge the intersecting forces of oppression that influence the lives of South Asian queers, and the ways in which its financial and organizational capacity prevents it from meeting this potential and meeting the needs of more marginalized areas of the community, particularly in terms of class, country of origin, and gender identity. Ultimately, I hope to speak to the political economy of community-based queer organizing, and the ways in which these organizations and this economy can influence individual experiences.
Comparing Fiber Orientations from Diffusion MRI and Histology in the Macaque Brain

Charles Chen

Mentor: David Van Essen

Diffusion MRI uses anisotropic diffusion of water in neural tissue to reveal underlying orientations of fibers in each imaging voxel. Tractography algorithms reconstruct fiber trajectories from these orientations. However, these algorithms exhibit much stronger connections to cortical gyri than cortical sulci, which is not observed in connectivity patterns measured with invasive tracer injections in macaque monkeys. Diffusion fiber orientations tend to point towards the cortical surface on gyral crowns, but are tangential to the cortical surface in sulci. We attempt to validate fiber orientations near the grey-white boundary of the cerebral cortex, comparing orientations from diffusion MRI to those in histology. Coronal sections from an adult macaque brain were immunostained with antibody to myelin basic protein, scanned on a NanoZoomer microscope, and downscaled to a 0.007 mm/px resolution. Structure tensor analysis was performed in MATLAB to obtain fiber orientations. A diffusion-weighted MRI dataset of a perfusion-fixed adult macaque brain was acquired with a 4.7 T Bruker scanner at a 0.430 mm/voxel resolution. The bedpostX fiber orientation modeling algorithm (FSL software) allows reconstruction of up to three fiber orientations per voxel. Histology and diffusion MRI show good agreement in white matter and near the gyral crowns. Discrepancies occur where structure tensor analysis correctly determines the sharper angle that terminating fibers take with respect to the surface normal at the grey-white boundary compared to angle measures from diffusion MRI that show fibers running near tangential to the surface normal. It is likely these fibers are instead traveling along the bank to terminate at the crown, illustrating the gyral bias in tractography. The general similarity between histology and diffusion MRI from these two animals validates the orientation estimates of diffusion MRI. Characterizing their discrepancies may provide a better understanding of the anatomical basis of gyral biases and possible approaches for reducing these biases.
Selective β1 Adrenergic Blockade Limits Cardiac Arrhythmias Due to Severe Hypoglycemia

Y. Stefanie Chen

Mentor: Simon Fisher

In one out of two people with insulin-treated diabetes, administered insulin lowers blood sugar to severely low levels (severe hypoglycemia). It has been found that deaths associated with severe hypoglycemia may be mediated by cardiac arrhythmias. These fatal cardiac arrhythmias are possibly triggered by the marked sympathoadrenal response that occurs during severe hypoglycemia. In order to explore the role of increased catecholamines in and limit the occurrence of these lethal arrhythmias, it is necessary to explore novel therapeutic interventions that may be translatable to the clinical spectrum. The current study was undertaken to test the hypothesis that an adrenoreceptor blockade, specifically of the β-1 receptor, will help prevent lethal cardiac arrhythmias and deaths due to severe hypoglycemia. To investigate the effects of the blockade, hyperinsulinemic, severe hypoglycemia (10-15mg/dL) clamps with simultaneous electrocardiogram monitoring were performed in 9-week old Sprague-Dawley rats injected with atenolol (β-1 blocker; n=7) or saline (control (CON); n=6). During the severe hypoglycemia clamp, there was a not a significant difference in glucose infusion rate between the β-1 blocker and CON groups (6.3±0.8 vs. 7.3±0.3 mg kg \(^{-1}\) min \(^{-1}\)) which suggests that the beneficial counterregulatory (glucagon) response was not impaired in the treated rats, as hoped. Of the rats that experienced arrhythmias, the β-1 blocker rats had 300-fold less frequent episodes of threatening 2nd degree heart block during severe hypoglycemia than CON (0.006±0.002 vs. 2.024±1.600; n=5, n=2; not significant). While the β-1 blockade significantly reduced heart rate following injection in the treated group (-15.9±1.7% vs. -9.7±2.2%; p<0.02), this significant difference was not maintained throughout severe hypoglycemia (264±7 vs. 268±7bpm). No mortality was observed. While these current values are insignificant, further studies should be conducted with more rats in each group or a study with STZ-diabetic rats that better model the proarrhythmic condition of diabetes.
Toward a Better Understanding of...  

Danger of Pre-pump Clamping and Negative Pressure-Associated Gaseous Microemboli during ECLS – In Vitro Study  
Brian Chin

Mentor: Akif Undar, Penn State University

The objective of this experiment was to test two different rotary pumps to find the relationship between revolution speed and negative pressure, and to test whether negative pressure led to emboli production during simulated ECLS.

Negative pressure was created in the tubing between a clamp and either of two rotary pumps by clamping the tubing upstream of the pump for 10 seconds, and then releasing the clamp. We hypothesized that this negative pressure would allow internal blood gases to come out of solution and form emboli. The Maquet Rotaflow centrifugal pump (MAQUET Cardiopulmonary AG, Hirrlingen, Germany) using only non-pulsatile flow and the Medos Deltastream DP3 diagonal pump (MEDOS Medizintehnick AG, Stolberg, Germany) in nonpulsatile and pulsatile modes were evaluated for emboli production. Each pump was tested at various rpm in order to see the association between rpm, negative pressure and emboli produced. The EDAC Quantifier was used to measure emboli count and size and a customized Labview 7.1 (NI USB-6521, National Instruments, Austin, TX, USA) program was used to measure and record pressures and flow rates in real-time.

We found a larger negative pressure is associated with a larger number of and volume of emboli. Of the two pumps, the Rotaflow pump displayed a larger negative pressure at identical rpm as the DP3 pump. It also provided a faster flow rate with larger and more emboli.

We conclude that there was a distinct association between higher rpm and larger negative pressures in each pump. Higher emboli production from internal blood gases coming out of solution was also connected to larger negative pressures. These results show a significant danger to pre-pump clamping when using a rotary pump in the event of ECLS component failure.
INVESTIGATING THE ROLE OF AvrRpt2 CYSTEINE PROTEASE IN INCREASING VIRULENCE OF THE PLANT PATHOGEN Pseudomonas syringae ON Arabidopsis thaliana PLANTS

Allen Choi

Arabidopsis thaliana is an important model for performing plant research, and has been used to investigate the mechanisms by which the plant pathogen Pseudomonas syringae infects and causes disease symptoms. P. syringae is known to suppress plant defenses by injecting effector proteins into plant cells. One of these proteins is AvrRpt2, which increases bacterial virulence in susceptible plants. The mechanism by which AvrRpt2 helps P. syringae infect plants is not well understood, but previous research has shown that AvrRpt2 has cysteine protease activity. To determine whether the cysteine protease is required for these functions of AvrRpt2, transgenic plants expressing wild type AvrRpt2 and mutant AvrRpt2 genes were made. The mutant AvrRpt2 genes contain mutations in the cysteine protease catalytic triad, specifically cysteine 122 and histidine 208 to alanine mutations. These transgenic lines were infected with P. syringae DC3000 by dipping plants into a solution of bacteria. Initially, bacterial growth within the plant was scored on days 0, 2, and 4 of infection. However, no difference was found between bacterial growth transgenic wild type plants and non-transgenic control plants, or between transgenic mutant plants and non-transgenic control plants. This is likely due to the A. thaliana line being already very susceptible to P. syringae. However, when disease symptoms were quantified, there was a clear difference in the virulence of DC3000 on the different plant lines. These infection experiments showed that AvrRpt2 WT transgenic lines develop more severe symptoms than a non-transgenic control line, while the mutant transgenic lines had similar or less severe symptoms than the non-transgenic control. These results indicate that the AvrRpt2 cysteine protease is required for increasing DC3000 virulence in susceptible A. thaliana plants.
Toward a Better Understanding of...

**Cornstarch to Stem an Oil Well**

*Clarence Chu*

*Mentor: Jonathan Katz*

The 2010 oil spill in the Gulf of Mexico wasted millions of barrels of oil and greatly harmed marine wildlife. Cornstarch-stiffened drilling “muds” were theorized to have the potential to “kill” such an oil spill due to their ability to shear stiffen. This would allow the “muds” to reach the bottom of the well as a coherent column and avoid being spit out of the well as droplets like other “muds” previously tried. To investigate the mechanism of shear stiffening we used a rheometer to impose various shear rates on cornstarch suspensions and to determine the threshold shear rate where they suddenly stiffen. As the shear rate increases, starch grains push against each other, which cause the grains to jam against the surfaces of the rheometer and thereby stiffen the suspension. We determined that even when the shear rate is reduced the grains remain jammed and the suspension remains stiff.
Heart rate variability (HRV) is the variation in the time interval between consecutive beats of the heart and is a predictor of cardiac events: the larger the variability, the healthier the heart. In patients with coronary heart disease (CHD), low HRV predicts mortality. Low HRV also correlates with depression, a risk factor for CHD. Thus treatments that increase HRV have the potential to profoundly impact patient health. Recently, low-levels of omega-3 fatty acids in patients have been found to be associated with low HRV and depression. Thus, the goal of this study is to test the hypothesis that diets rich in omega-3 fatty acids will increase HRV in patients with CHD and correlate with improved health of these patients.

To test whether diets rich in omega-3 fatty acids increase HRV in patients with CHD, 72 patients with CHD and depression were split into two groups of 36. One group of the patients received 50 mg of sertraline and a placebo; the other half received 50 mg of sertraline and 2 grams of omega-3/day for 10 weeks. Before and after the 10-week treatment, we measured HRV and heart rate patterns of each patient over a 24-hour period. These measurements included sleep time when it is easier to study HRV and heart rate because a person’s activities are relatively predictable. We are presently comparing HRV between the two groups, stratified by gender, age, and smoking status, to see if increased dietary omega-3 fatty acids increase HRV and decrease depression in the patients. Positive results would call for diets high in omega-3 fatty acid to increase the health of patients with CHD and/or depression.
The protein alpha-synuclein (SNCA) is associated with both sporadic and familial Parkinson’s disease. A mutation at amino acid position 53 from an alanine to a threonine causes familial Parkinson’s in humans; however mice naturally have a threonine instead of an alanine. Mice may tolerate this threonine because one or more of the six other amino acid differences between human and mouse SNCA ameliorates the cytotoxic effects of the threonine. I looked at the effects of substituting mouse amino acid residues into human A53T SNCA at positions 87, 103, 107, and 122 and substituting the human amino acid residue at position 53 into mouse wild type synuclein using site directed mutagenesis. The goal is to determine if any mouse amino acid substitution into the human protein reverses the cytotoxicity of human A53T SNCA. I successfully generated these five new SNCA variants. All five variants have been introduced into the p413 GAL1 yeast expression vector and are in the process of being tested for cytotoxicity in yeast. Interesting variants from the yeast assay will be studied further; for example, their propensity to form amyloids will be determined. Studies of these alpha-synuclein variants will identify amino acid residues important in determining the pathogenicity of alpha-synuclein, and may provide targets for drug development.

I also examined spinal cord tissue from A53T SNCA transgenic mice injected with fibrillized synuclein variants. Misfolded injected SNCA propagates through the nervous system in a prion-like fashion, and causes accelerated onset disease in these transgenic mice. Nitrosylated SNCA is found only in affected animals, and we wished to determine its relationship with unnitrosylated SNCA in motor neuron inclusions seen in these mice. I used immunofluorescence and confocal microscopy to show that nitrosylated SNCA is found not only in inclusions but also in cytoplasm.
In the callitrichid project, a long-term behavioral study is being conducted which focuses on the reproductive strategies of two species of tamarins, the saddleback tamarin (*Saguines fuscicollis*) and the emperor tamarin (*Saguinus imperator*) that live in the Amazon jungle of Peru. The research season for the project is May-September. Our main methods in conducting the research were stakeouts and follows. On stakeouts, one of the assistants stays at a particular site and, when a group of tamarins come, takes note of group composition as well as behavior. This was done so that we could get a sense of the number and composition of a group before starting follows. For follows, a group of 2-3 researchers or assistants set out to follow a specific group of emperor or saddleback tamarins and takes various behavioral research samples throughout the day on the individuals. The number of individuals in a group of tamarins ranged from 3 to 8 and, since they all look exactly alike, we used a collaring system to tell the individuals apart from one another. We were interested in the behavior of the individuals in general, as well as the behavior in relation to other members of the group and the home ranges for each group.
Toward a Better Understanding of...

Synthesis of Triazocyclicnonane

Damari Croswell

Mentor: Liviu M. Mirica

One of the most prominent factors thought to be involved in the development of Alzheimer’s Disease (AD) is the amyloid β peptide (Aβ), found in plaques often located in the cerebral space of deceased AD patients. This peptide comes in two forms—a 42 amino acid chain (Aβ_{42}) and a 40 amino acid chain (Aβ_{40}). Aβ_{42} is neurotoxic and metal ions are thought to have some significant, likely stabilizing relationship with it. The ability to negate this relationship has many therapeutic implications. In order to determine this, a variety of metal chelating compounds must be synthesized from various precursors. The synthesis of these precursors is the current focus of this project. I synthesized a “Tri-tosyl-TACN” precursor compounds from basic amine molecules. A series of reactions were completed using reflux techniques and purified using filtration techniques. After being analyzed for purity by Nuclear Magnetic Resonance Imaging, the product of each step was isolated. The final tri-tosyl-TACN product was collected and stored in preparation for later reactions.
Mood and Motor Changes Associated with Deep Brain Stimulation of the Subthalamic Nucleus in Parkinson’s Disease

William Dewispelaere

Mentor: Tamara Hershey

While deep brain stimulation of the subthalamic nucleus (STN DBS) has been shown to reduce the motor symptoms associated with Parkinson disease, its effect on mood remains a subject of debate. While some studies report mood improvement, others offer case reports of severe depression or anxiety following STN DBS therapy. Furthermore, the influence of current and historical psychiatric disorders on these acute outcomes has not been rigorously investigated. Because 25-40% of patients with PD have clinically significant psychiatric disorders, understanding these effects has broad implications for managing patient outcomes and expectations. Based on studies of similar design, we predicted that on DBS would improve mood and motor function compared to off DBS. Psychiatric state was assessed for 36 subjects with PD and STN DBS at an initial interview time. During the contact manipulation day, subjects were off of their anti-parkinsonian medication and stimulated at their clinically optimal contact location using pre-determined stimulation settings. Mood and motor data were collected for two settings: DBS on and DBS off. It was found that DBS on significantly improves valence, anxiety, apathy and motor function compared to DBS off (p≤0.006). Those with higher levels of depression at the initial interview derived less motor benefit from DBS compared to those with lower levels of depression (p=0.05). Subjects with current DSM-IV mood or anxiety disorders improved more in terms of apathy, anxiety and arousal than those without (p≤0.03). These results suggest that DBS has a positive effect on mood, and that there may be underlying neural changes that make those with psychiatric disorders more sensitive to DBS therapy. Future studies should focus on psychiatric influences on long-term outcomes, as well as the relationship between contact location, mood changes and psychiatric history.
TOWARD A BETTER UNDERSTANDING OF...  

INAPPROPRIATE COMPENSATORY BEHAVIORS AMONG AFRICAN- AND EUROPEAN-AMERICAN MALE ADOLESCENTS AND YOUNG ADULTS  

Elizabeth Diemer  

Mentor: Alexis Duncan  

The objective of this study was to characterize inappropriate compensatory behaviors (ICB) in a population-based sample of male adolescents and young adults. Data from 318 European American (EA) and 400 African American (AA) male offspring from 532 families at high risk for substance use problems due to paternal alcohol problems and 235 low risk families were analyzed (median age 17.65). Lifetime eating disorder symptoms, other DSM-IV psychiatric disorders, substance use, and suicidality were assessed using an adaptation of the Semi-Structured Assessment for the Genetics of Alcoholism. Individuals who endorsed purging behaviors (with and without non-purging behaviors); (n=26; 3.63%) and non-purging behaviors only (n=158; 22.07%) were compared to those with no history of ICB using chi-squared tests with p-values adjusted for familial clustering. Among purgers, vomiting was the most frequently endorsed purging behavior (57.69%), followed by laxative (26.92%) and diuretic use (23.08%); however, excessive exercise was the most commonly endorsed ICB among both purgers (65.38%) and non-purgers (84.81%). Purgers were more likely to have histories of alcohol use disorder and nicotine dependence compared to nonpurgers and those who did not report ICB (p<.001). Men who had engaged in any form of ICB were significantly more likely to be AA (p<.0001) and to express weight concern (p<.0001) compared to those who had not. There were no significant between-group differences in the prevalence of binge eating (34.62% for purgers, 37.34% for non-purgers and 29.78% for no compensatory behaviors), or any other variables assessed. These findings suggest that in male adolescents and young adults the prevalence of ICB may vary between EAs and AAs, and that these behaviors are associated with substance use disorders. Future studies in larger, ethnically diverse male samples are needed to further explore associations between ICB and substance use disorders in men.
*Toward a Better Understanding of…*

**Carotenoid Variation in *Roseiflexus castenholzii* under Native-Like Growth Conditions**

*Abigail C. Dommer*

*Mentor: Robert E. Blankenship*

*Roseiflexus castenholzii* (RFX) is an early evolving thermophilic phototroph naturally found in hot springs. RFX contains a unique photosystem deriving its components from purple and green sulfur bacteria and the novel Alternative Complex III instead of a cytochrome *bc* type complex. In nature, RFX grows in microbial mats in matrix with cyanobacteria such as *Arthrospira platensis* (Spirulina). In the laboratory, RFX is grown on standard O2YE media which contains yeast extract as the carbon source. In this project, RFX was grown in Spirulina powder instead of yeast in order to mimic the native-like growth conditions. The cells and pigment expression were monitored approximately every twelve hours for seven days to see how the change of carbon source affects the overall growth of the cells. The resulting experimental cell yield was comparable to the yield of the control culture grown on standard media. However, the experimental cells showed significant variation in color from the control cells. To understand this result, the pigments were extracted from the cells and high pressure liquid chromatography (HPLC) was used to identify and compare the pigment content. The cells were found to contain the same bacteriochlorophyll a, but a different composition of carotenoid pigments. The chromatographic data suggests that the carotenoid derivatives vary in the extent of their chain conjugation when the organism is grown under an alternative carbon source. Therefore, growth media ingredients that more closely mimic the natural system should be chosen to produce cells with more native-like light harvesting systems.
Meta-ethics is the field in academic philosophy that investigates the status of our moral discourse, such as the meaning of moral terms and the metaphysics of moral properties. A moral error theory claims (roughly) that moral judgments are systematically false. Richard Joyce has put forward an influential argument in favor of such a theory, based on the claim that morality purports to have a special type of normative authority over agents, regardless of the content of their attitudes or interests. In this paper I offer a critique and rehabilitation of Joyce’s argument. I contend that his argument fails because it relies on an inadequate account of normative authority. Then I go on to propose and defend my own account of normative authority, and argue that my account furnishes us with a revised and improved argument for a moral error theory.
The average age for total hip replacement is 66. Provided average life expectancy of 76-81 years, the quality and longevity of hip replacement is vital. Aseptic loosening is the main complication of total hip arthroplasty. Ten-year follow-up studies indicate symptomatic loosening severe enough to require femoral component replace in 3-20% of patients. Inducing bone growth around the implant provides the stabilization necessary to prevent loosening and reduce stress-shielding. Electrical stimulation of proximal bone to induce growth provides a unique non-pharmaceutical method of inducing osteointegration and thereby improving clinical outcomes. The present study investigates the optimal design of an electroactive femoral implant capable of inducing osteogenic stimulation of local bone. We postulate that there is an ideal design capable of inducing an optimal electric field for maximizing bone formation around the implant, thereby minimizing excessive bone growth and possible damage in the surrounding soft tissue. This study aims to distinguish that design through analysis of impacts of variable change on several bone layers.
Toward a Better Understanding of...

X-Ray Source 3D Reconstruction using Compton Imaging with X-Calibur

Marie Draper

Mentor: Matthias Beilicke

By retracing the path of X-rays from astrophysical sources such as black holes, rotating neutron stars, and active galactic nuclei, we can paint a more complex and detailed image of the sky. While most X-rays do not penetrate the lower layers of Earth’s atmosphere, we can study the X-rays emitted by radioactive decay here on Earth’s surface. To research the polarization of X-rays, one of the high-energy astrophysics groups at Washington University in St. Louis has developed a hard X-ray polarimeter, X-Calibur, which relies on Cadmium-Zinc-Telluride detectors with which the X-rays interact. This study proves that the polarimeter can also be an effective Compton imager, taking advantage of the process by which photons change the energy of free electrons. By measuring the energy deposits of two interactions from the same X-ray in the CZT detectors of X-Calibur, we can reconstruct the direction and position of the source from which the X-ray came. This study utilizes a C++/ROOT computer program to analyze these Compton events and perform the following two procedures. We can reconstruct the 3D position of a single X-ray source and determine the angular resolution of the separation between two simultaneously emitting X-ray sources. As we improve the accuracy and resolution of these results, X-Calibur will become an increasingly effective Compton imager. With these techniques, we will ultimately be able to reconstruct X-ray source position from the entire sky all at once.
In the absence of a core equilibrium point in two-dimensional voter landscapes, formal theorists have identified the uncovered set as a potential constraint on instability, and cited a number of institutional arrangements in which politicians would enter into this set. Prior research has offered empirical evidence for this finding in committee negotiations; this paper examines another hypothesized scenario: two-candidate competition in a large electorate. This paper uses a computational model to incorporate the latest insights from the behavior literature into a model of party competition. In the model, voters vary in their level of sophistication. Highly sophisticated voters have strong attitudes, and punish politicians who adopt discordant views. Unsophisticated voters have weak attitudes, and adopt the positions of their preferred party. This model simultaneously allows for the existence of opinion leadership, and lets public opinion drive party platforms. In the model, I show that, even for very high levels of opinion leadership, parties with bounded rationality still approach the uncovered set. I use a computer algorithm to demonstrate a property of the uncovered set that helps explain this result.
Mammalian sperm acquire fertilization capacity only after residing in the female genital tract for a finite period of time. This maturation process is called capacitation and results in two major changes in sperm physiology, induction of a distinctive motility pattern known as hyperactivation and competence to undergo the acrosome reaction, an exocytotic event that allows the sperm to fertilize the egg. One distinct physiological change that occurs during capacitation is hyperpolarization and our research focuses on the factors that hyperpolarize the sperm plasma membrane.

Using the SLO3 knock-out mouse strain, it has been shown that activation of a sperm-specific K+ channel, the SLO3 channel, triggers hyperpolarization in sperm. SLO3 channels are only present in mammalian sperm and are activated by membrane depolarization and alkaline pH. SLO3 channels are required for hyperpolarization as conditions that trigger hyperpolarization in wild-type fail to do so in SLO3 mutant sperm.

Further recent results suggest that SLO3 might identify as a potential conserved mechanism that controls membrane potential in most if not all mammalian sperm. To test this model we seek to determine if hSLO3 promotes membrane hyperpolarization in human sperm. Specifically we will characterize the e-physio properties of hSLO3 to determine if pharmacological agents that block hSLO3 channels will prevent the hyperpolarization produced by capacitating conditions.

We hypothesize that hSLO3 channels in human sperm might play a similar role to mSLO3 channels in mouse. Hence, these channels will activate causing membrane hyperpolarization when sperm is exposed to high external pH.

We have characterized the voltage range of activation of hSlo3 channels in Xenopus oocytes and confirmed that they are activated by intracellular alkalization, high pH. Through our analysis of hSLO3 we expect to determine if these channels drive a key physiological event of sperm capacitation in humans.
Effect of Trehalose on the Thermal Stability of the Potential Therapeutic Protein, Gelsolin

Ashley Earley

Mentor: Joanna Krueger, University of North Carolina Charlotte

Gelsolin is a six subunit actin binding protein that severs f-actin released upon cell death. Exogenous administration of gelsolin has shown promise in improving trauma patient survival by reducing blood viscosity. However, proteins are unstable and easily denature and lose all functionality, particularly with an increase in temperature. Trehalose, a stable disaccharide, has shown great potential as a protein stabilizer. As a result, the effect of adding trehalose on the thermal stability of gelsolin is being explored using Circular Dichroism (CD). CD measures the ellipticity of absorbance to estimate the secondary structure of proteins. Using CD, the experimental melting temperature (T_m) where 50% of the protein is denatured can be calculated. For 0.2 mg/mL gelsolin without trehalose the T_m was found to be about 67.5°C. The T_m of 0.2 mg/mL gelsolin in 0.3 M Trehalose was found to have greatly increased to 77.3°C. These results indicate that the melting temperature increases with increasing trehalose concentration suggesting that trehalose can act to increase the thermal stability of gelsolin in solution. This would be beneficial for developing a more stable protein therapeutic using gelsolin.
Lung disease is the fourth leading cause of death and disability in the United States. To better understand diseases that affect the adult lung, it is necessary to study the signaling pathways that are activated in response to tissue injury. Fibroblast Growth Factors (FGFs) are a family of growth factors and receptors that are key signaling molecules for growth, development, and repair. Fibroblast Growth Factor 2 (FGF2) has been shown to be important in wound healing, myocardial infarction recovery, and implicated in the pathogenesis of pulmonary fibrosis. In previous studies, mice lacking Fgf2 (Fgf2⁻/⁻ mice) showed an increased mortality after bleomycin-induced lung injury, which models pulmonary fibrosis. We hypothesized that the main underlying phenotype of Fgf2⁻/⁻ mice is a deficiency in epithelial repair. To test this, we implemented a model in which we gave Naphthalene to Fgf2⁻/⁻ mice and compared their recovery to wild type mice. Naphthalene is a drug that causes damage to Clara cells, a specialized lung epithelial cell that expresses a secretory protein (CCSP) that can be readily detected by immunostaining. The mice were observed during a recovery period of 10-14 days. After looking at lung histology and immunostaining, we anticipate observing a delayed recovery of CCSP expressing cells and a decreased number of proliferating cells at peak injury in Fgf2⁻/⁻ mice. Based on initial examination, Fgf2⁻/⁻ mice appear to exhibit a delay in lung epithelial recovery. However, further examination and larger sample size is required for statistical significance and fully conclusive results.
X-ray polarimetry has great potential to reveal new physical information about the astrophysics of high energy sources. I present the results and conclusions of systematic and performance tests of the 20-60 keV hard X-ray polarimeter X-Calibur. The data used in these tests were taken using the CHESS hard X-ray synchrotron source. The results presented are very important for understanding the data taken from observations of hard X-ray sources such as binary black hole systems and accretion powered neutron stars while using X-Calibur when it is flown with the InFOCuS hard X-ray telescope in late-September 2013. Also presented is a brief summary of Hercules X-1, a source that produces hard X-rays in the range of X-Calibur’s energy detection. The research into Hercules X-1 was motivated by the possibility of the system being observed by X-Calibur at some point in the future.
Toward a Better Understanding of...

**CCR7 Chemokine GPCR Acts as a Negative Regulator of the Wnt/β-Catenin Pathway and Cell Proliferation in SW480 Colon Carcinoma Cells**

*Lubov Ezerskiy*

Mentor: Lilianna Solnica-Krezel

G-protein coupled receptors (GPCRs) are the largest receptor family that signal via small G proteins. Whereas, GPCRs have multiple roles in immune and nervous systems, they have not been considered as major regulators of development or cancer cell proliferation. Our group has shown that chemokine GPCR signaling negatively regulates β-catenin to limit embryonic axis formation at the onset of zebrafish development. Previous studies suggested that an activated Gαq pathway inhibited β-catenin stimulated cell proliferation in human colon carcinoma SW480 cell line via triggering a Ca²⁺-dependent nuclear export and degradation of β-catenin. This implies that an unknown endogenous GPCR signaling axis exists in intestinal epithelium that can inhibit β-catenin. We hypothesized that if SW480 cancer cells are treated with GPCR CCR7 ligands CCL19 and CCL21, they will inhibit cell proliferation and decrease β-catenin levels in these cells. We determined that both the receptor (CCR7) and the ligands are expressed in the cells. Studies of SW480 cell proliferation revealed that the ligands induced a significant reduction in the number of proliferating cells. Further, both agonists, CCL19 and CCL21 down regulated levels of total β-Catenin and its unphosphorylated and more stable form in a time dependent fashion. pNurr77 protein was previously implicated in regulation of β-Catenin. We observed that the CCR7 agonists induced a decrease in levels of pNurr77 in the nucleus and an increase the cytosol, suggesting that pNurr77 is involved in the export of β-catenin from the nucleus. Additional experiments showed that CCR7 may be utilizing G proteins different from Gαi for the nuclear export and proteasomal degradation of β-catenin in SW480 cells. Based on these results we propose that the CCR7 ligands CCL19/21 may be used in slowing the growth of the SW480 cells and therefore could possibly be used to limit tumor growth.
Through this research, I seek to gain an understanding of the experiences of immigrants to the United States as they navigate the healthcare system. By utilizing participant observation and interviews, I explore obstacles to acquiring quality healthcare, and the reasons that they exist, as well as the ways in which individuals are approaching and overcoming these obstacles. I argue that narratives about immigrant populations act as a means of creating and reinforcing barriers to healthcare, yet narratives can also function as a means for immigrants to access resources and services that the system has made unavailable to them.

Various tensions exist in immigrants’ navigation of the healthcare system. The medical system is presented as individualized, yet certain structural factors impede the progress of immigrant populations interacting with health providers. Further, there exist distinct categories of the Other: a hierarchy of non-citizens seems to be in place and reinforced in the medical system. The narrative of “the immigrant” is established before an individual arrives at a doctor’s office or the Department of Family Services. Non-citizen populations are navigating the healthcare system in “the land of the free” but are facing stringent restrictions. Immigrants construct their narratives in order to navigate the system, and are indicted for doing this, despite the fact that structural factors are the cause of these shifting narratives.
Obesity rates are continuously climbing in America. The detrimental health effects of obesity are well documented, but research on how maternal obesity affects the health of offspring is very limited. In this study, the effect of maternal diet on prostate health in male offspring was investigated by exposing two groups of female mice to different diets for four weeks. The control group was fed a chow diet (13% fat energy) and the experimental group was fed a high fat diet (58% fat energy). The male offsprings' prostates were harvested at 16, 26, and 63 weeks. The cell proliferation in the prostates of adult non-obese male mice born from high fat diet mothers was investigated, and the cell signaling pathway of cell proliferation was studied. The results revealed the maternal obesity impacted prostate health in male offspring and there was a significant, positive correlation between a maternal high fat diet and hyperplasia of the prostate. This finding implies that maternal obesity predisposes offspring to a greater risk of prostate cancer. From histological analysis of the prostates, proteins, phospho-PTEN and phospho-Akt expression, which are markers for cell division, increases in the experimental mice. This seems to imply that the hyperplasia seen in the experimental mice seems to be caused through the PTEN/Akt pathway. Diet is a modifiable risk factor for prostate cancer. Thus this underlines the need to increase education about the risks of parental obesity to mitigate the risk of prostate cancer of the offspring and improve health in the United States.
A nickel, chromium, aluminum material known as the Russian alloy (Ni:Cr:Al) is a non-superconducting alloy with a weak temperature-dependent magnetic response. The Russian alloy’s weak magnetic properties combined with its hardness after heat treatment make it a candidate for use in high pressure, low temperature experiments. The goal of this research was to adapt the alloy for use in a diamond anvil cell high-pressure system as a gasket material. Such a gasket would allow measurements at lower temperatures than other common gasket materials. In order to be used in high-pressure experiments, gaskets must be both hard and ductile. In order to study the mechanical properties of Ni:Cr:Al gaskets, I subjected samples of the material to various heat treatments and measured the hardness. After hardening I studied how the material deforms under pressure by placing the gaskets between two diamond anvils and applying pressure. Gaskets that show signs of cracking during this indentation process are likely too brittle and may crack through if used in a measurement. I found that many of the hardest Ni:Cr:Al gaskets cracked when subjected to pressure. Unfortunately, the gaskets that showed no signs of cracking were somewhat softer than other materials typically used for gaskets. Due to its favorable magnetic properties, however, the Russian alloy will likely still prove useful as a material either for gaskets or diamond anvil supports in a diamond anvil cell.
Human brains fold during development, giving them their familiar wrinkled appearance. The folded brain, with its higher surface area-to-volume ratio, gives the owner a mental advantage. Despite decades of research, we still do not fully understand the mechanisms that drive brain folding. Problems with the development of brain folds (called gyri) lead to problems with other aspects of development, as disordered brain folding patterns have been linked to mental and emotional disorders, such as schizophrenia and autism. A new theory seeks to explain the mechanical and biological phenomena that drive this advantageous folding process by suggesting that brain folds are caused by circumferential expansion in the cortex, with growth in the subcortex driven by the stress from growth in the cortex. We hypothesize that this model has the potential to produce the characteristic gyri and accurately replicate their stress patterns.

To test this hypothesis, we used specific mechanics theory to describe brain growth, where natural growth occurs in the cortex causing growth in the subcortex as a result of changes in stress. Using computer software simulations, we tested the growth models by systematically varying parameters, such as cortical thickness and growth rates, in order to see how such changes alter brain folding and to compare the computer generated folding patterns to those obtained from MRI data. If in the end we can accurately model how brain folds develop, we should then be better able to understand and treat the causes of abnormal development more effectively.
The kappa-opioid system plays a critical role in the encoding of stress and the rewarding properties of alcohol, reflecting its abundant expression in the paraventricular nucleus and striatum, respectively; as such, it is well situated to mediate alcohol consumption in the context of stressful life circumstances and psychopathology. A functional haplotype in the gene that codes for the kappa-opioid ligand precursor prodynorphin (PDYN) (rs2235749, rs910079, rs910080) has previously been associated with altered prodynorphin mRNA levels in the ventral striatum and substance use disorders. Furthermore, genetic variation across PDYN has been linked to differential propensities to drink in negative emotional states.

Genetic and neuroimaging data were available from 334 participants who completed the Duke Neurogenetics Study. We tested a moderated mediation pathway model in which an interaction between this PDYN Haplotype and early life adversity predicted reward-related ventral striatal reactivity, which predicted substance-related coping strategies and alcohol use. PDYN haplotype indirectly predicted alcohol use via early life stress moderational effects on reward-related ventral striatal reactivity and alcohol-related coping strategies (95% Boot-strapped CI for effect size: [0.005, 0.118]).

The results of this study suggest that this PDYN haplotype indirectly effects alcohol use through its effects on ventral striatal reactivity to reward and alcohol-related coping strategies in the context of stress exposure. Importantly, this study is limited by its medium-small sample size, which may inflate coefficients in our path model. It will be important for future research to replicate the described model and experimentally manipulate prodynorphin levels in non-human animals. Additionally, the sample consisted of a relatively healthy sample of young college students; it will be important for further research to examine whether this model predicts clinically significant levels of use and is generalizable to other populations.
Effect of Small Organic Acids on the Fate of Trace Metals in Aquatic Systems

Hayley Gadol

Mentor: Jeff Catalano

Microbes and plants in nature produce chemicals that aid the dissolution of iron oxide minerals to Fe (II) in solution. This does not occur readily without other chemicals present in the solution. It has already been shown that Fe(II), as well as other chemicals, catalyzes this dissolution. The purpose of this experiment was to see how the presence of small organic acids, citric, oxalic, and acetic, affect the dissolution and recrystallization of iron oxide minerals in water at pH 4 and pH 7. The results of these reactions will be analyzed using ICP-OES and IC and the experiments will eventually be repeated at pH 3, 5, 6, and 8 as well as with dissolved Fe(II) already present in the system.
Toward a Better Understanding of...

Spirituality and the HIV Illness Experience

Sarah Gallo

Mentor: Shanti Parikh

Although advanced antiretroviral treatment has successfully helped HIV-positive individuals thwart the progression of their disease since the mid-1990s, physical symptoms constitute only part of the HIV illness experience. In this study, I investigated the ways in which spirituality manifests in the daily lived experience of being HIV positive in St. Louis. The research seeks to better understand how spirituality can benefit as well as serve as an obstacle to current pharmaceutical treatment and how it shapes the relationships of a patient to his or her body, self, and loved ones. For this study, I conducted an extensive literature review on spirituality in chronic illness and HIV specifically as well as embodiment and psychological surrender in addition to semi-structured interviews with 11 HIV-positive individuals.

Based on my findings, I argue that in the space created between the pharmaceutical technology of antiretrovirals and the reality of being an HIV-positive person in treatment, spirituality facilitates an ultimately empowering process of surrender that allows people living with HIV to reclaim their autonomy. Spirituality provides a context for their struggles by helping them to reconcile the reality of being diagnosed with a stigmatized disease, and emerges as a tool for HIV-positive people in St. Louis to navigate the uncertainty of living with a chronic disease and mitigate feelings of alienation from their own bodies.

While many HIV-positive people feel they are forced to surrender to the policies that dictate how they get treatment and the physical realities of their illness, the process of spiritual surrender can ironically be proven to help individuals regain their sense of self. These findings could have implications for how psychosocial support is provided to people living with HIV as well as on future policy regarding antiretroviral distribution.
A general problem in the field of restoration ecology is that small restorations have fewer species than would be expected based on their area alone, when compared with large restorations. There are many possible mechanisms, but one possibility is that plant-animal interactions might be considerably different on the edge of habitats, changing the overall strengths of these interactions in small habitats with a higher edge to area ratio than large habitats. Missouri Ozark glades are an ideal system to study this pattern: they have a defined edge where the desert-like clearing ends and the forest begins; they have many endemic species; and they are often the target of restorations. This experiment utilizes the large-scale experimental glade restoration at Washington University’s Tyson Research Center to test the hypothesis that rodent seed predation increases at the edge of the glades due to the cover that trees offer from aerial predators, leaving an island in the middle of large glades where seeds would not be subject to heavy predation. The area of this low-predation zone would decrease with decreasing glade area, so in smaller restorations, species introduced through seed might not be able to take hold in the habitat. This preference for edge habitat in rodent foraging behavior has been well-documented in natural systems, however, our results show that while the small glades showed no difference in predation based on tray location within the glade, the large glades showed more predation on the interior of the glade than the exterior, suggesting that the rodents could prefer to live in the large glades over the forest. This could be due to the flush of weedy species often present in early restorations: we suggest that management of these weedy species with fire or manual pulling is critical to reducing rodent predation and allowing plant establishment.
Since the 1950s, oil shale has been studied as a possible source of domestic petroleum. Oil shale, found in large quantities in the Green River Formation, includes an organic material called kerogen. This material can be extracted from the mineral content of the shale by “retorting,” a process in which the shale is heated to around 370°C. The goal of this project was to investigate the physical and structural changes in oil shale as it is heated using $^1$H and $^{19}$F nuclear magnetic resonance (NMR). Upon heating, the $^1$H NMR signal from the organic material of the shale changed: the $T_2$ decay times increased with increasing temperature, becoming more liquid-like. By allowing the samples to return to room temperature between heatings, we determined the temperature which created irreversible changes in the shale. Temperatures below this “sweet spot” temperature of 400°C primarily resulted in reversible changes (i.e. melting of the kerogen). Oil shale samples were also heated ex situ and imbibed with heptane, Fluorinert (FC-77), or fluorine gases under a variety of pressures to explore porosity. Though more work needs to be done, we gained some insights into the process of pyrolysis and developed practical methods for heating and studying oil shale in a laboratory setting.
Assessing Exotic Plant Naturalizations Caused by Botanical Garden Introductions in Hawai‘i

Rebecca Gilbert

Mentor: Anukriti Hittle

The negative environmental and economic effects of invasive plant species are now widely appreciated. However, just 100 years ago, exotic plant introductions were widely celebrated and were part of the mission of botanical gardens around the world. As a result, an important area of research in conservation biology is to evaluate the invasive potential of plants that occur in botanical gardens. Like most botanical gardens, The Honolulu Botanical Gardens (HBJ) historically had unregulated plant introductions. The main goals of this research were to examine the flora of the HBJ and to ask: 1) What proportion of botanical garden plant introductions have been naturalized in Hawai‘i and 2) What best management practices and policies can we institute to control existing naturalized species? To answer the first question, I examined reports from the O‘ahu Early Detection Program (OED) which outlined the newly naturalized plant species in the gardens as well as island-wide. I found that 5% of the total species in Wahiawa Garden and 4.45% in Koko Crater had become naturalized. To answer the second question, I worked to assess the best management plan for each of the identified naturalized species in the gardens. We did site visits to determine the current state of each naturalized species and checked each species’ Hawai‘i Pacific Weed Risk Assessment (HPWRA), which gauged plant species’ risk of becoming invasive. Considering this information and potential removal obstacles such as species’ large seed banks, herbicide resistance, and inaccessible locations, we determined whether each species should be removed through tree contract, killed with herbicide, or monitored in order to achieve the greatest impact within the constraints of the gardens’ limited budget. Along with the HBJ director, we drafted an invasive species policy for the gardens that will help guide their future plant acquisitions.
Erythropoiesis is the maturation of hematopoietic stem cells into red blood cells, and involves two phases (1) proliferative burst phase and (2) terminal erythroid differentiation. Erythropoietin (EPO) is a glycoprotein hormone that plays a major role during terminal erythroid differentiation, thereby making it the target of much clinical attention in the treatment of anemia. It is well established that EPO regulates the rate of erythroid differentiation when it binds to EPO receptor (EPOR) which activates the signal transducer and activator of transcription 5 (STAT5). While elucidating the mechanism by which STAT5 is activated in erythroid progenitors, we identified the neuropeptide neuromedin U (NmU) to be a novel cofactor that functions with EPO to expand early erythroid progenitor cells. Preliminary data from our lab demonstrates that NmU alone activates STAT5 in primary human early erythroid progenitor cells. This result was unexpected, because NmU is known to mediate signal transduction cascades through its cognate receptor neuromedin U receptor type-1 (NMUR1), a G-protein coupled receptor that is not known for activating STAT proteins. We hypothesize that NmU activates STAT5 in erythroid progenitor cells by binding to a NMUR1-EPOR heterodimer. To detect this hypothesized complex, we conducted co-immunoprecipitation assays followed by detection and identification of precipitate proteins via Western blot analyses. The detection of the NMUR/EPOR complex will further our understanding of early stages of erythropoiesis and the role of cell surface receptors during this process.
The low production of a neurotransmitter called dopamine causes symptoms of a number of neurologic diseases such as Parkinson’s Disease (PD) and Tourette Syndrome. Apomorphine is a dopamine-mimicking drug commonly administered for treating PD, given its strong dopaminergic action. Its pharmacology and effects on the regional blood flow are also widely studied. Traditionally, brain sensitivity to dopaminergic challenges has been effectively measured by using PET scan, to measure cerebral blood flow or glucose metabolism. However, it is not applicable for longitudinal studies or research in children.

Another effective way of measuring the effects of a drug in the brain is using pharmacological fMRI (phMRI) to measure the blood oxygen level dependent (BOLD) response in different parts of the brain. The drug concentration in the blood a certain amount of time after a dose translates to a certain amount of effects in the brain. Different parts of the brain respond to different extents, thus exhibiting variable levels of BOLD. We aim to test the hypothesis that phMRI can detect and quantify regional BOLD responses to a series of 4 small apomorphine doses in living humans, and that these responses are relevant to neurologic disease. Our goals will be to map brain regions that display a significant BOLD response to apomorphine in normal volunteers; determine whether PD patients, who often lack subsets of dopaminergic neurons, exhibit altered regional BOLD responses to apomorphine: and estimate the population variability in these regional BOLD responses to allow effective design of future human studies using power analyses.

Hopefully the new method of quantifying regional BOLD responses by using fMRI will be applicable to related important problems, including but not limited to: studies of treatment complications in PD, studies of dopaminergic sensitivity in children with Tourette Syndrome, and serial quantification of dopamine function during pre-symptomatic treatment trials of neurodegenerative diseases.
This project explores the classroom experiences of middle school Black boys in St. Louis with a specific focus on how their racial, gender, and class identities may be shaped by their experiences in English and Social Studies classroom settings. Through ethnographic interviews with and observations of two 6th grade teachers, this work provides a unique lens through which the educational experiences of these boys can be explored, compared, and re-imagined.
Development of various types of neurons in the retina requires precisely regulated gene expression, mediated by the coordinated actions of retinal-specific transcription factors and general epigenetic regulators. This research focuses on the epigenetic mechanisms that regulate retinal development in order to better understand how misregulation of gene expression leads to retinal disease. One type of general epigenetic regulator, histone methyltransferases, catalyzes the methylation of specific lysine residues on histone tails. MLL1 is one such methyltransferase, and catalyzes Histone H3 Lysine 4 methylation, which is associated with gene activation. MLL1 has been implicated in adult brain stem cell-mediated neurogenesis, tumorigenesis, and cell cycle regulation, but its function in the retina remains unknown. To determine whether MLL1 is necessary for retinal development and function, we conditionally knocked out Mll1 (CKO) function in retinal progenitor cells, and characterized the retinal phenotype using morphological and electrophysiological assays. Histological analysis showed that the normal three neuronal cell layers formed in the retinas of CKO mice, but that the thickness of each layer was reduced, particularly the inner nuclear layer, which drives visual signal processing. Consistent with this, electroretinograms of Mll1 CKO mice revealed defects in the ability of the retina to convert light stimuli into neuronal signals, resulting in a loss of vision. Gene expression studies of Mll1 CKO retinas revealed a significant loss of horizontal cells, which are an inner nuclear cell type critical for modulating photoreceptor signals, as well as a modest loss of amacrine, bipolar and ganglion cells. Thus, MLL1 appears essential for the development of retinal neuronal cell types that allow for proper visual processing, particularly in specifying horizontal cells, amacrine cells, bipolar cells and ganglion cells.
Film education is the collection of practices that aim to teach children to critically evaluate a film and analyze its content with knowledge of how the techniques and language of cinema are manipulated in its conveyance. It has gained increasing attention in recent years as the ever ampler use of media makes not only having access to, but being capable of discerning and analyzing media content indispensable to effectively participate in society. The goal of this study was to determine under which circumstances film education can best be used to improve the overall education (considering both formal and informal practices) received by children and/or the way children experience education. The study consisted of a survey of film education programs, which constituted the basis for an analysis of the forms and purposes of such programs. From this, the optimal form and procedure for an original film education project in Argentina’s Cordoba province was subsequently determined. The survey distinguished the programs by several criteria (including the context of education, the method of screening the movies, and the attention given to teachers’ training) and discerned three principal categories: programs offered directly to teachers or schools, programs intended as an extracurricular addition to formal education, and those focused on filmmaking. The study concludes that the innovative film education project proposed should be a combination of informal education practices implemented in a formal education setting, consisting of screening events facilitated by specialized staff and held in the school itself. The teachers would participate in the activities and be provided teaching materials, encouraging them to introduce film education in their classrooms following this experience. The proposed project would thus focus entirely on the formal education context and give administrators and teachers an example of a different and enriching activity that they can sustain independently.
Different types of cancers respond to various stimuli, making it difficult for doctors to construct all-inclusive strategies of treatment. Personalized medicine using targeted molecular therapy is thus becoming an effective treatment strategy. Human epidermal growth factor receptor 2 (HER2) is a transmembrane oncoprotein important for the pathogenesis of various types of cancer, including pancreatic cancer. HER2 overexpression has been linked to worse prognoses for patients with pancreatic cancer, making it a suitable molecular target to improve their survival. The goal of this project is to develop positron emission tomography (PET) agents for visualizing HER2 expression in vivo. In this study, we compare subcutaneous and orthotopic pancreatic cancer models in tumor-bearing mice. Subcutaneously implanted tumors are common models for investigating radiotracers; however, orthotopically implanted tumor models may be more relevant, since predictable growth kinetics may be obtained. This model also comes the closest to mimicking human pancreatic cancer. Zirconium-89 ($^{89}$Zr) was used as the PET radionuclide for this study, because it matches the pharmacokinetics of intact antibodies. We investigate $^{89}$Zr-labeled anti-HER2 Pertuzumab antibody, because Pertuzumab is included in the treatment regimen for pancreatic cancer. Pertuzumab was conjugated to the chelator desferoxamine (DFO) and radiolabeled with $^{89}$Zr. In vitro cell studies were performed to confirm specificity and immunoreactivity of $^{89}$Zr-DFO-Pertuzumab. Athymic nu/nu mice were implanted with PANC-1 cells subcutaneously and orthotopically. In vivo studies were performed by injecting the tumor-bearing mice with $^{89}$Zr-DFO-Pertuzumab. PET imaging occurred at 2 and 6 days post injection. In vitro cell studies determined $^{89}$Zr-DFO-Pertuzumab was specific and retained immunoreactivity for HER2. Tumor uptakes in the subcutaneous and orthotopic models were 12.5% ID/g and 2.5% ID/g, respectively. Preliminary results indicate that subcutaneous tumor models overestimate $^{89}$Zr-DFO-Pertuzumab uptake relative to the orthotopic tumor model. $^{89}$Zr-DFO-Pertuzumab is a promising radiotracer for noninvasive and sensitive detection of HER2 expression to monitor disease progression in pancreatic cancer.
Aneurysmal subarachnoid hemorrhage (SAH) affects 30,000 people annually. One of the most common and potentially treatable sources of neurological injury in SAH patients is delayed cerebral ischemia (DCI). Several processes underlie DCI, one of which is the severe narrowing of the intracranial arteries, a condition known as arterial vasospasm. Recent studies have linked matrix metalloproteinase 9 (MMP-9) activity with the pathophysiology of brain injury following aneurysmal SAH. Other studies have linked serum and cerebrospinal fluid (CSF) MMP-9 levels with the development of vasospasm and worsening neurological outcomes. As preliminary data for a single-institution, open label, randomized controlled Phase I trial, we looked to optimize the logistics required in serially measuring serum and CSF levels of MMP-9 expression and activity. To do so, daily CSF and serum samples were taken from 20 SAH patients and nine controls. Samples were analyzed via enzyme-linked immunosorbent assay (ELISA) to determine expression. Preliminary results suggest that MMP-9 levels continue to rise in patients with vasospasm versus those without. In addition, in patients who received an endovascular coiling, those with vasospasm were observed to have a significant elevation in serum MMP-9 expression, both in the serum profile and in mean serum expression. MMP-9 serum expression was also found to rise significantly in the second half of our study window as compared to the first half, which correlated with DCI and the onset of vasospasm. These results show that MMP-9 serum and CSF levels can effectively be measured with ELISA, and provide further evidence that MMP-9 may represent both a biomarker to monitor for vasospasm, as well as a potential therapeutic target for pharmacological agents in the treatment of DCI.
During the Spanish colonization of Peru in the 16th century, the colonial government forcibly resettled as many as 1.5 million native persons into planned towns called reducciones. The reducción movement was implemented to reorganize extended households into nuclear units to “civilize” and evangelize the indigenous population. Additionally, it facilitated the enforcement of the Spanish labor tax, which required communities to supply workers for the silver mines and other government projects.

Despite the movement’s enormous scale, little is known about the details of its implementation and effects on the indigenous population. Historic documents discuss the reducción movement only in broad terms. The Proyecto Arqueológico Zaña Colonial (Zaña Colonial Archaeology Project) was created to investigate the details of the reducción movement that historical documents are unable to address. The project has excavated several reducciones and late pre-Hispanic settlements in the Zaña Valley on the north coast of Peru. The research presented here focuses on the plant remains recovered from these sites in the effort to reconstruct the diet of the native population both before and after the reducción movement.

Soil samples were collected during excavation from several contexts within each site. These samples were examined using a microscope, and the different plant species were identified. This data was used to infer the plant-based portion of the diet at the sites being studied.

Currently, there has not been enough data analyzed from pre-Hispanic sites to determine how diets changed during the reducción movement. When all the data has been collected, the diets of the pre-Hispanic and colonial communities will be compared. It is expected that the increased labor demands from the Spanish colonial government decreased the time people could spend producing food and led to a diet that favored high-calorie crops that require little labor, but this has yet to be determined.
In clinical and imaging applications, novel near infrared (NIR) fluorescent dyes have shown promise in opening new avenues for highly efficient molecular probes with specific biomolecules. Because of their low background autofluorescence and high tissue penetration, NIR fluorescent dyes and dye-conjugates can serve as powerful imaging agents to track defined tissues, cells, or molecules in living organisms.

Our goal is to develop novel molecular probes that target specific cell types for molecular imaging of disease—particularly, for diagnostics of peripheral nerve damage and image-guided surgery of kidney tumors. Specifically, we will use antibodies specific to AQP1 and PLIN2 to outline the boundaries of tumors in kidneys. AQP1 and PLIN2 are recently identified markers specific for renal cell carcinoma, which can be tracked using monoclonal antibodies developed by our collaborators.

A secondary goal of our research is to optimize and standardize conjugation of NIR dyes to antibodies. At present, dye-conjugation to antibodies often destroys the specificity of the antibodies to their targets. Using the library of NIR dyes in our lab, we will optimize a labeling technique that retains antibody specificity. Once a functional dye-antibody conjugate is available, we will use cell based and animal models to assess the imaging quality of the new probes relative to the current gold standards in the field. The generation of new higher quality bioimaging probes will facilitate both live in vivo imaging of basic cellular processes, such as the nerve damage response, and image-guided surgical procedures—enhancing our knowledge of the biological world and patient health. Successful hallmarks at this juncture include low cell toxicity, low background, and high contrast. Moving forward, the probes could be further optimized by reducing their molecular size to achieve faster imaging while retaining excellent specificity of the probes.
At the turn of the twentieth century, racialized and gendered industrial schools were established throughout the country, though particularly in the South, to rehabilitate black female juvenile delinquents through the use of Progressivist and racial uplift ideologies. Through exploration of two sisters sentenced to the Missouri State Industrial School for Negro Girls in Tipton during the 1930s, this project reveals how the social construction of “delinquency” manifested tangible realities for these young women. Thus, I argue that the rhetoric used to institutionalize these bodies reinforced social understandings of respectability, femininity, blackness, sexuality, and criminality. By examining the case histories of Mabel and Addie, it is evident that the control of the young black female body was implicit (and oftentimes explicit) in the reformatory’s educational and behavioral models. The “delinquency” that these young women experienced was not reflective of their actions, but rather, intricately connected to a particular social discourse surrounding the regulation of young female sexuality and the policing of “vulnerable” bodies. Being sentenced to Tipton, then, served as a mechanism for the state of Missouri to contain a particular population which was already marginalized in a variety of ways. Although an analysis of the case histories of Mabel and Addie reveal the lived experiences of only two young women at the reformatory, the similarities that exist in their records and the thousands of other “girls” who passed through Tipton’s doors are too important to ignore. It is thus possible to use these examples as a lens through which to examine not only the target population of the institution, but the daily realities and surveillances these young women experienced.
This research broadly looks at the implementation of urbanistic projects in contemporary Latin American cities. Specifically, the project examines transformations of urban public transportation in Bogotá, Colombia and how the emergence of a new integrated transit system has not only shaped the social and spatial fabric of the city but also upholds a vision of globalized urban modernity. The ethnographic approach to urban mobility prioritizes cultures of use and knowledge surrounding these different forms of transit and highlights the ways in which these understandings of metropolitan travel are different across Bogotá’s highly polarized socioeconomic landscape.
The issue of climate change is considered by many to be one of the most pressing global challenges of the 21st century. Although there appears to be little debate among environmentalists about the urgency of climate change, environmental organizations vary widely in their approaches toward tackling the climate crisis. In particular, the strategy of green consumerism, which encourages businesses and individuals to “go green” and “vote with their dollars,” has both gained increasing support and sparked harsh critique within the environmental movement. The purpose of this research is to connect the ongoing academic debate over green consumerism to the Sierra Club, America’s largest and oldest environmental organization, and to examine the broader historical trends which facilitated the recent popularity of green consumerist messaging. Specifically, this article is interested in connecting linguistic and rhetorical strategies found in Sierra Club literature to a critical analysis of green consumerism as a whole. Based on public information made available through the Sierra Club website, I identified several components among different campaigns, including variations in pronoun use, visual presentation, consumerism, environmental justice, environmental preservation, and collective political action. Although these differences may be interpreted as support for further polarization within the environmental movement, I argue that full awareness of these contradictions is necessary for crafting comprehensive, integrated campaigns which are equipped to address the climate crisis.
As a female artist in Weimar, Germany, Expressionist Käthe Kollwitz worked and excelled within a highly gendered society characterized by stark nationalism and expectations of sacrifice and duty. Kollwitz lived from 1867 to 1945, one of the richest periods in European history, and both defied and followed social and career expectations of women during this time. By comparing Kollwitz’s art to that of such male contemporaries as Max Liebermann and Georg Kolbe, one can explore the difference in depiction of themes and motifs such as the relationship between a mother and her child, the sacrifice of a parent during wartime, and the notion of duty and obligation in the Weimar Republic during the First World War. By tracking the development of Kollwitz’s art throughout her career—in addition to literary contributions such as her diaries, letters, and published articles—one can analyze her changing attitude towards the sacrifice demanded by the German government of its citizens during World War I, and her use of motherhood in art as a political agent. Kollwitz was unique in the community of female artists at this time in that she was able to maintain a family and a career, thereby both defying and following gender roles. I present a theory of how the “motherhood” (in the traditional sense of the word) portion of her life ended after her youngest son died at the beginning of World War I, and her art became her child, just as it had been before she had children. Käthe Kollwitz is an example of a successful woman who confronted and changed the role of women in art and politics in Weimar, Germany.
During the blood stage of human malaria, *Plasmodium falciparum* (Pf) parasites generate vast amounts of free heme via digestion of host hemoglobin. Although most of this heme is sequestered into crystalline hemozoin, it has remained unknown if parasites also express heme oxygenases (HO) to enzymatically degrade a portion of this heme for metabolic utilization or disposal. To approach this question, I analyzed the parasite genome and identified four HO-like proteins that show low-level sequence homology to known heme-degrading enzymes from other organisms. I cloned and expressed these recombinant parasite proteins in *E. coli* but found no evidence for HO activity, suggesting that the functions of these proteins have diverged from known HO enzymes to fulfill alternative biological roles within parasites.

To interrogate the functional properties and cellular roles of these HO-like proteins within parasites, I tagged each protein at its genomic locus with green fluorescent protein. By fluorescence microscopy, two of these proteins were found to be localized to the cytosol, and no differences in protein expression throughout the parasite’s life cycle were observed. To further clarify the involvement of these proteins in heme metabolism and broader parasite biology, future studies will include identifying *in vivo* binding partners of each protein by immunoprecipitation experiments and assessing the effect of truncating each HO-like protein on parasite fitness and development. If any of these proteins are found to be essential for parasite viability, these proteins could serve as targets for the development of novel drug therapies to combat this devastating disease.
During action potentials, sodium channels open to cause membrane depolarization and inactivate to allow the membrane potential to return to rest. Inactivation occurs when the linker between two domains of the sodium channel, which carries hydrophobic triplet of residues, IFM, interacts with the intracellular face of the channel. Multiple molecular mechanisms for inactivation are indicated in neuronal channels, and it has been assumed that the same putative sites cause inactivation the human cardiac sodium channel (hNav1.5). However, this hypothesis has not been tested. The goal of this study was to determine whether the same sites are involved in hNav1.5, and whether new insight on this specific channel could be gained.

In order to study inactivation in hNav1.5, we performed mutations on the DIII and DIV S4-S5 linkers, which are known to affect inactivation in other sodium channels, on the pSP64T-hH1 SCN5A plasmid. We hypothesized that these residues directly and cooperatively interact with the IFM motif, as in the neuronal isoform. Using RNA injection and cut-open voltage clamp protocols, we analyzed the responses Xenopus Laevis oocytes to different voltage pulse protocols. For the first mutation tested, N1659A (DIV S4-S5), a comparison of the activation and inactivation I-V curves to WT shows that N1659A shifts activation by 10 mV to depolarized potentials and significantly blocks inactivation.

To assess whether N1659 is actually involved in the hydrophobic interaction, we will use cut-open voltage clamp fluorometry to assess the movement of the DIV S4-S5 linker. If our hypothesis is correct, we expect to see F-V data match up with I-V data during inactivation. Future work will include also performing both regular and fluorometry cut-open experiments on additional mutations in different locales, such as A1326, which has been implicated in inactivation and resides on the DIII S4-S5 linker.
The concept of preclinical Alzheimer’s disease implies that amyloid-beta deposits may accumulate in the brain years prior to clinical manifestations. Cognitively normal individuals with preclinical Alzheimer’s disease pathology as detected by elevated uptake of PET tracer 11C Pittsburgh Compound B (PIB) have elevated risk of progression to symptomatic Alzheimer’s disease. We sought to analyze whether cortical thickness and white matter integrity changes can be identified in participants who have longitudinal increases in PIB. 91 asymptomatic adults (clinical dementia rating 0, mean age 63 years) had PIB PET scans ~2.6 years apart. All participants remained asymptomatic (Clinical Dementia Rating = 0) throughout the duration of the study. Mean cortical binding potential (MCPB) was calculated for each scan, and PIB-positivity (PIB+) was defined as an MCPB greater than 0.18. Volumetric MRI and diffusion tensor imaging (DTI) were obtained at the time of the second PIB scan. Mixed models were utilized to test whether cross-sectional volumetric and DTI measurements are related to PIB accumulation. All participants were PIB-negative (PIB-, MCPB < 0.18) at baseline. Increases in MCPB were associated with multiple regions of elevated cortical thickness, predominantly in the temporal lobe, but also involving the posterior frontal lobe and occipital lobe. Additionally, longitudinal increases in MCPB were associated with lower apparent diffusion coefficient and no change in fractional anisotropy. Our findings suggest that increasing levels of amyloid deposition, even when below established thresholds for “PIB positivity,” are not benign. The finding of paradoxically elevated cortical thickness and lower apparent diffusion coefficient in brain regions previously identified as associated with Alzheimer’s disease suggests a clue to early Alzheimer’s disease pathophysiology. Longitudinal data is needed to determine the changes in cortical thickness and mean diffusivity over time, as well as whether these participants convert to Alzheimer’s dementia.
Diacylglycerol (DAG), a lipid-signaling molecule downstream of PLCγ2, has previously been implicated for its critical role in the development of inflammation in the joints. In macrophages, DAG levels are closely regulated by DGKζ, an isozyme of the diacylglycerol kinase family that facilitates the conversion of DAG into phosphatidic acid. Genetic manipulation to knockout the function of DGKζ functionally blocks this degradation of DAG, leading to its accumulation and activation of phosphokinase C. Here we demonstrate that DGKζ-/- bone marrow-derived macrophages exhibit increased mRNA expression of the anti-inflammatory cytokine IL-10 upon stimulation with unmethylated CpG, a pathogen-associated molecular pattern that activates TLR-9. While it remains unknown how DGKζ and DAG levels fit in to the events upstream of IL-10 gene expression, our Western Blot analysis has indicated that differential phosphorylation of certain major players in the NF-κB-pathway and MAPK-pathway are not responsible for this enhanced gene expression. Other research has demonstrated that a decreased level of IL-10 results in a more robust phenotype of the autoimmune condition Macrophage Activation Syndrome (MAS). Therefore IL-10 may serve in a protective capacity against this condition. MAS is a severe complication of systemic juvenile idiopathic arthritis, characterized by an influx of pro-inflammatory cytokines and accompanied by hepatosplenomegaly and deficiencies in leukocytes and erythrocytes. Consequently, we hypothesized that the induction of IL-10 upon blocking DGKζ may provide the basis for a novel therapy for MAS. In vivo experiments involving repeated, intraperitoneal CpG injection of BL6 mice allowed for optimization of the procedure before investing in completing the experiment with DGKζ knockout mice. Our data show that WT mice injected with a modified CpG exhibit several hallmarks of MAS, including splenomegaly, disruption of splenic architecture, and evidence of a cytokine storm.
This experiment explored how mnemonic strategies, in this case the link system mnemonic, could affect free recall accuracy as well as subject confidence in their recalled responses. Many experiments have assessed and proven the effectiveness of mnemonics over simpler and more common strategies for memorization. Our experiment differed from most in that we also looked at the effects of the mnemonic on confidence ratings. Subjects learned one of two memorization strategies, repetition or the link system method, in a brief instructional phase that preceded a study phase. In the study phase, subjects were presented with 8 word lists of 20 words each, with odds and evens counterbalanced between subjects. Following this phase they participated in a distraction task, recalled what words they remembered, and then rated their confidence of the presence or absence of certain words (actual studied items or lures) during the study phase. So far data hasn’t shown any significant difference in measures of accuracy or amount of critical intrusions. However, the confidence ratings of those using the standard repetition method did differ significantly from the mnemonic group, potentially indicating that the mnemonic is more effective in terms of assuring the user of the validity of their memory.
Colonial systems of extractive, cash crop based economics were widespread throughout the British holdings within the New World. The only major bastion of resistance to this trend was New England, a place incapable of supporting itself on any one good, and therefore forced to enter into the trade of many. I hope to examine the rise of mercantile efforts in New England and the tensions these new economic forces created in a society built on notions of Puritan ethics. To this end, I plan to use economic data accumulated through the use of merchants’ books to determine economic growth, and first person accounts like The Apologia of Robert Keayne, edited by Bernard Bailyn to determine philosophical thought. Taken together, I hope this research will provide insight into the conflicting incentives at play in the lives of mid 17th century Massachusetts merchants, and give some indication as to why Massachusetts eventually developed in the directions it did.
Toward a Better Understanding of…

Diabetes Mellitus Is Uncommon among Patients with Amyotrophic Lateral Sclerosis

Theodore Hyman

Mentor: Timothy Miller

Recent clinical observations suggest a scarcity of Type 2 Diabetes Mellitus (DM) among patients with amyotrophic lateral sclerosis (ALS), a fatal, paralytic neurodegenerative disease. Previous studies have reported later ALS onset in subjects with comorbid DM. BMI and high LDL/HDL ratio—risk factors for DM—appear to correlate with lower incidence and slower progression of ALS. Here, we measure the prevalence of Type 2 Diabetes and other comorbidities in ALS and examine their effects on ALS progression.

We measured the prevalence of DM in three patient populations: ALS patients seen at Massachusetts General Hospital (n=320) or Johns Hopkins Hospital (n=357), and subjects from seven ALS clinical trials (NEALS, n=1410). Prevalence of DM and other comorbidities in the NEALS sample were compared to those reported for Americans at large. Rates of ALS progression and survival were measured with respect to diabetes status and BMI.

The prevalence of DM in the NEALS (5.3%, $p<0.0001$) and MGH (6.5%, $p<0.05$) cohorts was significantly lower than expected for Americans (11.3%), while the JHH cohort had a non-significantly reduced prevalence (7.8%, $p<0.16$). Rates of obesity (24.7% observed, 35.7 expected, $p=0.0001$) and hypertension (28.5% observed, 33.2% expected, $p=0.004$) were significantly reduced. Rate of ALS progression was not significantly affected by DM status or BMI. Survival risk was not significantly affected by DM status, but was negatively correlated with BMI ($p=0.002$).

The low prevalence of obesity observed in our samples suggests that low BMI may curb the risk of DM among ALS patients. Alternatively, the low rate of hypertension suggests a possible underreporting of non-neurological conditions for patients with ALS. Despite these possibilities, if ALS independently serves a protective role against DM, further research into this effect could lend new insights into the etiology and treatment of both diseases.
The CLOCK protein network of the hypothalamus plays a critical role in the establishment and maintenance of circadian rhythms, as well as regulating numerous homeostatic processes including weight, appetite, and body temperature. PER1 is an integral protein of the central loop of the CLOCK system. Emerging research suggests that PER1 is critical for reward and stress responsiveness and may contribute to substance use disorders. In humans, the C allele at rs3027172 reduces glucocorticoid-driven (stress-related) expression of PER1 and predicts increased adolescent alcohol abuse in the context of high early-life adversity. The ventral striatum is part of a neural network that supports reward-driven and appetitive behaviors, and has been implicated in risk for substance dependence; moreover, a recent study has shown that clock-pathway genes moderate its activity. This study examined if ventral striatum response to reward might mediate the relationship between rs3027172 genotype and alcohol use problems.

Participants (n=338), completed the Duke Neurogenetics Study, an ongoing protocol assessing a wide range of behavioral and biological phenotypes. Participants provided a saliva sample for genotyping, completed a self-report questionnaire assessing childhood adversity, and completed a reward task while fMRI data were acquired. We tested a moderated mediation model in which an interaction between rs3027172 and early life adversity predicted reward-related ventral striatal reactivity, which predicted substance-related coping strategies and, in turn, alcohol use.

Rs3027172 indirectly and directly predicted alcohol use via early life stress moderational effects on reward-related ventral striatal reactivity and alcohol-related coping strategies. These findings are consistent with previous reports and provide a plausible neural mechanism, i.e., ventral striatal response to reward, that may contribute to alcohol use in rs3027172 C alleles who are exposed to early-life adversity.
The boundary between belief and unbelief is significant in the public sphere now more than ever in America. In a society founded on Christian ideals that have shaped public discourse, the rise of unbelief has produced major disagreement and debate over the potential of unbelievers to achieve moral maturity to the same degree as their believing neighbors. At the same time, the societal push for universalism has brought about an ideal of inclusivity across beliefs. This project examines the tension between universalist inclusivity and normative understandings of moral maturity by examining James Fowler’s “Faith Development Theory.” This structural developmental theory posits that every human being, regardless of religion or lack thereof, has “faith” and that every human being follows the same developmental model through stages of faith. “Faith,” according to Fowler, is one’s orientation to the cosmos, one’s Ultimate Concern, or one’s center of value and power. Through a close reading informed by a variety of renowned scholars, I argue that Fowler’s theory excludes nonbelievers from the higher stages of development, despite his claim to universalist inclusivity, based on his use of Christian imagery and language. Throughout his work, the gap between the definitions Fowler offers for terms like “faith,” “transcendence,” and “secularism,” and their assigned meanings grows, and his work becomes increasingly exclusive and distrustful of unbelief. Thus, Fowler’s theory represents a field of thought (Christian Universalism) that heralds two contradicting ideals: 1) universalist inclusivity and 2) a normative notion of ideal moral maturity. I conclude that this tension results in an ironic and implicit exclusion and distrust of the nonbeliever.
This project examines the role of feminism in informing the experiences of both sex workers and individuals who provide services to sex workers and studies the ways in which state and international policies rely on gender stereotypes and reproduce gender inequalities in an effort to manage trafficking and sex work. The research takes on a two-prong approach. First, I read and analyze major national and international policies addressing migration and sex work. The Trafficking Victims Protection Act relies on an image of a victimized, sexually passive woman—reinforcing sexist stereotypes and reproducing the oppressive systems that make women vulnerable to exploitation in the first place. If a woman does not fit this image of a victim, she may not have access to support services. This is dangerous and problematic—women who work in the sex trade are uniquely vulnerable to exploitation. Secondly, I conduct ethnographic research with two populations in Copenhagen, Denmark. I interview current and former sex workers, as well as the caseworkers and professionals who provide them with legal and personal services. If we are to develop more effective, targeted policies to address the needs of the victims of trafficking and sex workers, it is critical that we continue to develop a nuanced understanding of their lives and experiences. There is a growing field of feminist scholarship that focuses on the intersections of feminism and prostitution, and many have made compelling arguments that advocating for the rights of sex workers is an inherently feminist act. The assertion that prostitution is always degrading and oppressive—a position that is heavily implied in the TVPA—denies women agency and ignores women who choose to do sex work.
**The role of miRNA 221/222 in Prostate Cancer**

*Kathryn Jacobs*

*Mentor: Li Jia*

Prostate cancer is the most frequently diagnosed cancer as well as the second deadliest cancer in men in the United States. Once the cancer reaches a late androgen-independent state, current anti-androgen treatments can no longer control the prostate cancer growth. Androgen action is mediated through an intracellular receptor called androgen receptor (AR). Through past research it is known that prostate cancer is dependent on AR for growth even after androgen depletion and that AR plays a critical role in all stages of the disease. One challenge in prostate cancer research is to understand the mechanisms involved in the AR-mediated development of androgen-independent prostate cancer. For this project, we studied the roles of certain AR-regulated micro RNAs 221/222 on the survival and growth of androgen dependant (LnCaP) and androgen-independent cells (C42B). miRNA 221 and 222 are highly expressed in castration-resistant prostate cancer. In this study we looked at the relative expression levels of both miR221 and mir222; expression was upregulated for both miRNAs in C42B cells in the presence and absence of DHT (male hormone), which was consistent with the literature. In ChIP-Seq analysis it was found that there is an AR binding site close to these miRNAs. We then did a luciferase assay (to look at the transcriptional activity of the promoter) for the native promoter of these miRNAs there was a noted decrease in luciferase for C42B cells in the presence of DHT, when compared with LnCaP cells. When the miRNAs were put into a construct with a minimal promoter, the luciferase activity was high. Most AR binding effects on prostate cancer cause upregulation and overexpression of genes, however these results signify that AR binding has an inhibitory effect on expression of mir221/222 in androgen-independent prostate cancer.
Invasive species are a global threat, causing environmental and economic damages ranging from biodiversity loss to decline in fisheries. *Kappaphycus*, a non-native algae, was intentionally introduced in Kaneʻohe Bay, O‘ahu for aquaculture 30 years ago; now *Kappaphycus* is smothering coral where it can no longer house and feed marine organisms. To tackle this invasive algae, The Nature Conservancy partnered with the State of Hawai‘i and the University of Hawai‘i to develop a method of removal. Starting in January 2013, the SuperSucker—a marine vacuum cleaner—entered Marker 12, the largest reef in Kaneʻohe Bay. The current management plan to prevent the spread of *Kappaphycus* is to first remove algae with the SuperSucker and then place native sea urchins *Tripneustes gratilla* that eat left-over pieces of *Kappaphycus* as a bio-control. The goal of this research was to measure *Kappaphycus’* regrowth rate and determine the optimal time to place sea urchins. To determine regrowth patterns, I selected 10 random GPS points where algae were “vacuumed” in January (representing five months after removal), February, March, April, May, and June for a total of 60 GPS points. I measured the percent coverage of *Kappaphycus* after removal at these 60 points using a 16-point quadrat. Although June did not act as a control with a high percent cover even when algae was just removed and May had a higher percent than expected, if June and May data points are ignored, there is a trend for *Kappaphycus* to grow exponentially two months after removal, making the second month the optimal time to prevent a growth spurt starting on the third month. *Kappaphycus* is considered the biggest threat to marine life in Kaneʻohe Bay; thus, defining methods that limit further growth of invasive species is critical research in conservation biology.
Astrocyte Type-I IFN Regulation of the Blood Brain Barrier during WNV Encephalitis

Harsha Jujjavarapu

Mentor: Robyn Klein

West Nile Virus (WNV) is a mosquito-borne flavivirus responsible for a growing epidemic of lethal viral encephalitis in the United States. The virus is somehow able to pass through the blood brain barrier (BBB), a complex arrangement of vascular endothelial cells and astrocytes, which normally protects the central nervous system (CNS) from pathogens. This bypass by virus forces BBB dysregulation so leukocytes can enter the BBB and clear WNV. However, leukocytes, themselves, cause much damage to the CNS and dysregulation may also allow more WNV to enter the CNS. Thus, BBB permeability must be tightly regulated during CNS infection. Type-I Interferon (IFN) is an antiviral cytokine that enhances BBB integrity and reduces leukocyte entry. Here, we show that type I IFN signaling in astrocytes regulates endothelial barrier permeability in vitro following WNV infection. In vivo, we compared control mice with intact IFN signaling (IFNAR fl/fl) to mice lacking type-I IFN receptors in the astrocytes of the central nervous system (IFNAR fl/fl glial fibrillary acidic protein (GFAP) Cre). After peripheral WNV infection, IFNAR fl/fl GFAP Cre mice exhibited enhanced and accelerated mortality and clinical disease scores compared to IFNAR fl/fl controls. However, when these mice were infected intercranially, no differences in survival rate and time were apparent. This data leads us to believe that astrocyte IFN signaling delays viral entry and burden in the CNS after WNV infection. In the future the specific actions of IFN at the BBB will be scrutinized.
Toward a Better Understanding of...  

Photoluminescent Spectroscopy of CdTe Quantum Wires  
Ethan Kahn

Mentor: Richard Loomis

Solution synthesized CdTe quantum wires have been thermal and photoenhanced, resulting in high quantum yield CdTe/CdS, core/shell quantum wire heterostructures. Attempts were made to capture photoluminescence spectra of single wires at room temperature, to be followed by further low temperature experiments. While weak emission was observed, from the lack of absorption features it was concluded that the sample had degraded due to excessive exposure to oxygen. Before research continues, a new quantum wire solution must be synthesized.
Both esters and amides are important functional groups in organic chemistry, and are found in numerous natural and synthesized compounds. This study focuses on a novel method of converting N-alkoxyamides into methyl esters using electrochemical oxidation. In order to optimize and show the utility of this synthetic method, multiple electrolysis reactions were performed in order to find the conditions that produce high yields. Methyl 4-oxo-4-(phenylmethoxyamino) butanoate was synthesized to serve as a testing reagent and oxidized to form dimethyl succinate and benzyl alcohol. All products were examined using nuclear magnetic resonance spectroscopy. Through systematically varying conditions, it was found that doubling the current of electrolysis produces no noticeable effect on yield and that there is a small positive correlation between charge passed through a reaction and yield. Furthermore, it was determined that although it is integral for the reaction, much less electrolyte can be used to perform the conversion than previously observed, and the reaction can occur in good yields with a much higher concentration of the N-alkoxyamide. Through this study, insight into how to improve this electrochemical oxidative conversion of N-alkoxyamides into esters was gained and thoughts for future studies have been proposed. In addition to optimizing the reaction, it is also important to test the technique's utility by determining whether it is still able to convert N-alkoxyamides into esters when additional functional groups are present in the compound. Research into testing such compounds is ongoing.
FGF14 is in the Fibroblast Growth Factors (FGF) family of proteins that are found in a range of organisms, including humans. Unlike classical FGF’s, FGF14 is not secreted and does not bind to any known FGF receptors. FGF14’s significance in neuronal communication has been confirmed by the fact that FGF14 null mice suffer from cognitive impairment, seizure-like episodes that are representative of paroxysmal dyskinesia, and symptoms of ataxia, characterized by hindlimb tremors and an abnormal gait. Because these mice are germ line knockouts, they do not give us a temporal sense of when FGF14 is important. It could be that FGF14 is important during development and not in the fully developed mouse. To determine whether FGF14 is functionally significant in the adult mouse, sensorimotor tests were conducted on adult wild-type mice with FGF14 expression knocked down and adult FGF14 null mice with FGF14 expression restored. FGF14 expression was knocked down or restored via cerebellar Lentivirus injections, and a balance-beam apparatus was used to test the mice’s motor skills. Mice were trained to walk across a suspended balance beam for 3 days and then tested for 5 days; each trial was recorded on video and the mice were blindly scored on how long they took to cross the beam and how many times they slipped. When compared to wild-type mice injected with a control non-targeting virus, the FGF14-knockdown mice took longer to cross the balance beam and slipped more times, i.e. they performed worse. When compared to FGF14 null mice injected with a control virus, the FGF14-restored mice took less time to cross the balance beam and slipped less times, i.e. they performed better. These results suggest that FGF14 is involved in adult mice’s motor coordination and that FGF14 is thus functionally significant in adult mice.
Dental appliances are recommended for patients with mild to moderate obstructive sleep apnea (OSA) that are intolerant to continuous positive airway pressure (CPAP) therapy. The Sleep Wake Center has a dental appliance program that custom-fits appliances for referred patients. This study measured the efficacy of the TAP III dental appliance given to patients for OSA or upper airway resistance syndrome (UARS) in the last 2 years. Of 46 patients who were given the TAP III appliance, 21 patients had a follow-up visit, with an average follow-up duration of 3.6 ± 2.1 months. Fifteen of 46 patients had follow-up objective testing to assess the efficacy of the TAP III appliance. A significant difference in TAP III efficacy was noted between obese and non-obese patients, however a significant change in BMI before and after dental appliance treatment was not seen. This study highlighted deficiencies in follow-up care of patients receiving dental appliances that may be resolved by standardizing post-appliance follow-up and objective efficacy testing.
Coupling metal nanoparticles (NPs) with semiconducting thin films offers exciting opportunities to tune many of the optical, optoelectronic and electronic properties of semiconductors. Gold nanorods (AuNRs) are particularly attractive candidates for coupling to many semiconductors owing to their localized surface plasmon resonance (LSPR) frequencies, which fall in the visible spectrum. Besides coupling to the incoming electromagnetic radiation, plasmons create intense electric fields at the interface of the metal and semiconductor and can impact a variety of electronic properties as well. Cuprous oxide (Cu$_2$O) semiconducting films are of particular interest due to their direct band gap of 2.2 eV, which is in the visible range of the electromagnetic spectrum as well. However, in order for Cu$_2$O to be useful in applications and devices such as solar cells, its light absorption and photoresponse must be improved.

In this project, we embedded AuNRs inside Cu$_2$O thin films to improve the light response of these composite films. Initially, 100, 200 and 500 nm thick Cu$_2$O films were deposited onto AuNRs on conducting Indium Tin Oxide substrates. The Cu$_2$O films were deposited using a standard electrochemical deposition process. The light induced current for pure Cu$_2$O films strongly depended on the thickness of the film, with thicker films having higher photoresponses. However, the trend is inverted for films deposited onto AuNRs, with thinner films having a higher photoresponse. These results show the strong potential in improving the viability of Cu$_2$O-based photoelectric devices such as solar cells and optical sensors.
This research focuses on the Guatemalan operations of a U.S.-based child sponsorship organization, specifically examining the racialization of sponsorship narratives by non-indigenous Guatemalan employees. The child sponsorship industry generates millions of dollars every year to maintain development initiatives throughout the world. Largely based in Europe and North America, these organizations depend on the selling of “sponsorships,” a process in which a donor makes a monthly payment to become the “sponsor” of an individual child. These “sponsorships” are marketed and sold through the generation of individual personal narratives that appear in online catalogs. In this project I explore the way in which Guatemalan sponsorship workers insert their own ideas of race and poverty into these individual narratives.
Toward a Better Understanding of…

On using Network Theory to Identify Significant Elements in Protein-Protein Interaction Networks

Rohan Khazanchi

Mentor: Hesham Ali, University of Nebraska at Omaha

Network theory has been used by researchers for multiple purposes in the past to model biological data as well as social, transportation, business, and many other types of data in various domains. When analyzing a network that represents protein-protein interactions (PPIs), identifying elements of significant importance and biological-relevance is critical. Such networks are normally very large and it is essential to narrow down the search space to allow researchers to focus on a manageable set of targets for further analysis. In this work, we hypothesize that there is a high correlation between structural properties associated with elements in a PPI network and their biological significance. We identify special elements, such as hubs and driver nodes, as well as special sub-networks, such as dense clusters in the obtained biological networks. We then investigate the hypothesis that relationships between topological and biological importance can be seen in/between hub nodes and driver nodes within a network and within clusters. Our proposed approach includes how to identify these types of nodes and examine their relationships within human, yeast, rat, and mouse PPI networks. In addition, we examined their relationships with other types of significant elements, with their neighbors, and with the rest of the network. We performed numerous tests to explore potential relationships between network properties and their associated biological significance. Obtained results showed that identifying and cross-referencing different types of topologically significant elements (nodes in the PPI networks) can exemplify properties such as transcription factor enrichment, lethality, clustering, and gene ontology enrichment. Further, we discovered a key relationship between network properties and how sparse/dense a network is—a property we described as “sparseness.” Overall, we verify our original hypothesis that structurally important nodes do have significant biological relevance.
Mapping Temperature with Multispectral Imaging in the Extended NIR (exNIR)

David Kim

Mentor: Mikhail Berezin

To explore the feasibility of employing an optical approach to biological thermometry, the extended near infrared or exNIR (900-1400nm) spectra range was investigated. We identified that as temperature increases the spectrum of the characteristic peaks of water undergoes changes both in intensity and peaks positions. A linear relationship between absorbance and temperature within physiologically and therapeutically relevant temperature range was demonstrated. Identified temperature-sensitive ratio-metric parameters were further used in conjunction with a multispectral exNIR imager to illustrate distinct temperature gradients in the phantoms.
In the U.S. alone, demand for organ transplants outweighs the donor organ supply, which leads to thousands of deaths each year. Engineered tissues and organs have been explored as an alternative to donor organs. However, one of the most significant barriers along the path to implantation of engineered tissues and organs in patients is the challenge of recapitulating microvascular networks within these tissue constructs. Without a blood supply, cells occupying inner regions of the scaffold are oxygen- and nutrient-deprived and likely to undergo necrosis. The development of novel modular scaffolds where poly(ethylene glycol) (PEG) microspheres are synthesized and cross-linked by bio-orthogonal copper-free click chemistry reactions aims to address this issue. Through a series of steps, the formation of stable, biocompatible scaffolds can be done without the use of organic solvents or cytotoxic reagents. In addition, functionalizing the PEG with various moieties provides the scaffolds that are formed with modularity that allows them to present a range of microenvironments. An ideal microenvironment to encourage development of blood vessels should include an angiogenic biomolecule, such as vascular endothelial growth factor (VEGF), accessible porous regions for vessel infiltration, and an adhesion peptide, such as RGD to promote endothelial cell attachment. We demonstrate that tethering of heparin onto PEG microspheres allows for controlled release of VEGF to promote the recruitment of blood vessels into the scaffold. We also demonstrate the use of porogenic PEG microspheres to increase the porosity of the scaffolds for better microvessel infiltration. Our results suggest that our scaffolds have the intended capacity for growth factor release as well as the porosity necessary for vessel infiltration. Future work includes implanting the scaffolds into an animal model and evaluating the extent of vascularization.
Phosphorylation-Dependent Cell Death and the N-terminus of Mechanosensitive Channel MSL10

Sarah Kloepper

Mentor: Elizabeth Haswell

The bacterial mechanosensitive channel MscS, which functions primarily as an osmotic safety valve to release dangerously high levels of membrane tension, has been found to have ten homologs in the plant species Arabidopsis thaliana. The function of these channels, dubbed mechanosensitive-like (MSL) channels, is under current study. One channel in particular, MSL10, has no phenotype in the knockout mutant, but displays stunted growth and cell death signaling when overexpressed, possibly due to increased levels of unphosphorylated serine residues in the N-terminal domain of the MSL10 proteins. To explore the effect of N-terminus phosphorylation on cell death, mutants mimicking phosphorylation and mutants preventing phosphorylation were transiently overexpressed in tobacco, and tissue was assayed for cell death. N-terminal truncations of each mutant protein were also overexpressed to differentiate channel function from N-terminus phosphorylation state. Both full-length and N-terminal MSL10 caused significantly more cell death in their phosphorylation-preventing form than in their phosphorylation-mimicking form, suggesting that cell death signaling is indeed regulated by the phosphorylation state of the N-terminus, and that cell death signaling is distinct from channel function.
Chromatin packaging is important in regulating gene expression. Classically, chromatin has been demarcated into two types based on staining patterns in interphase nuclei: euchromatin and heterochromatin. Previous studies showed that the *Drosophila melanogaster* Muller F element exhibits an unusual amalgamation of euchromatic and heterochromatic properties. Using comparative analysis of *D. ananassae* and *D. melanogaster*, we seek to analyze the genomic characteristics of the Muller F element and the evolution of this domain.

As part of the Genomics Education Partnership project, students across the nation improved the assembly and manually curated gene models for portions of the *D. ananassae* Muller F element and euchromatic reference region derived from the Muller D element. Using these resources, I reconciled the gene models in these regions and checked for other elements of interest, including pseudo-genes and repetitious elements. The high-quality *D. melanogaster* assembly, RNA-seq data, and gene annotations are used as reference. Gene density, repeat density, codon bias and gene size on *D. melanogaster* and *D. ananassae* Muller F elements are compared with their euchromatic reference regions.

Analysis confirms significant differences between *D. ananassae* and *D. melanogaster*, especially in the Muller F element. The *D. ananassae* Muller F element is reported to be significantly larger than that of *D. melanogaster*. We find that the majority of this expansion can be attributed to increases in transposon density and from Wolbachia (an endosymbiont of *Drosophila*) DNA incorporated through lateral transfer. These changes affect how genes inside this region are organized, producing larger genes affecting gene function.

The similarities and differences found in this comparative analysis should elucidate some of the factors leading to the expansion of the Muller F element of *D. ananassae* and the evolution of genes in highly repetitive regions of the genome. As similar expansions of genome size have occurred repeatedly in the evolution of eukaryotic genomes, the results will be of general interest.
As an advocate at the St. Louis County Domestic Violence Court, I help petitioners seeking orders of protection by providing emotional support, translations of the court process, and information about resources outside the legal system. While advocating I have encountered petitioners frustrated by the process and by what they perceive as the court’s refusal to listen to their story. I have noticed a tension between what she deems a priority and what the court believes to be most relevant. I am interested in how petitioners tell their story as they struggle to understand the workings of the court. I would like to track how this narrative evolves from when she first makes contact with the court to when she leaves with or without an order of protection. How does she piece her story together and what aspect of her story does she highlight or repeat? I observed the four Domestic Violence Court divisions for four weeks, conducted anonymous interviews with judges and advocates, and will conduct in-depth interviews with the petitioners I observed. From this ethnographic work, I hope to answer the following questions: How does the petitioner organize her story to align with what she believes the court wants to hear and in contrast, what does the court expect to hear from her in order to make its judgment? My analysis of this relationship will help me understand if a cultural, or more specifically linguistic, barrier exists between the two and will hopefully lead me to identify what it means to be literate in court culture. I hope to employ my research to compile a proposal that can improve the Domestic Violence Court’s advocacy program.
Over the last several decades, the fields of performance studies, dance studies, queer theory, and critical theory have gained increasing prominence in both academic and artistic circles. The connections between these fields have become increasingly relevant for artists and theorists interested in interrogating the limits of contemporary cultural and political discourse. My interest in these fields lands at the intersection of two equality elusive realms of practice: improvisational dance and queer subjectivity. Dance improvisation, within Western theatrical dance, emerged in the 1960s through the work of various postmodern performance groups—at same time, movements of second-wave feminism and gay liberation were paving the way for an articulation of queer subjectivity to later emerge. Today, much of queer politics can be characterized by its intersectional critique of the links that bind race, class and capitalism to the subjugation of non-normative embodiments of sexuality and gender. This study focuses on the relationship between improvisational dance and the formation of a queer subjectivity that now serves as a political identity as much a sexual one. I conducted my Practice-as-Research inquiry at Ponderosa e.V., an artist-run dance and performance space in Stolzenhagen, Germany. As an ongoing site of research into art-making and collective living, Ponderosa offered me the opportunity to investigate the ways in which improvisational practices subvert regimes that constrain our embodiment to normalized realms of experience and expression. By applying the theoretical frameworks offered by queer theory to a number of practices and performances I participated in while at Ponderosa, this analysis reveals improvisation’s ability to perform critique and thus create space for an expanded queer subjectivity to emerge.
Many studies have shown that non-coding RNAs (ncRNAs) play an integral role in many physiological processes and can be altered in disease states like acute myeloid leukemia (AML). One of the best understood classes of ncRNAs are microRNAs (miRNAs), which regulate gene expression by targeting complementary messenger RNA (mRNA) transcripts and preventing their translation into protein. Recently, whole genome sequencing has revealed recurrent point mutations of miRNA-142 in a subgroup of AML patients (~2%), representing the first recurrently altered miRNA associated with malignancy to date. Interestingly, all mutations occurred in the “seed sequence” of miRNA-142-3p. The “seed sequence,” located at nucleotides 2-7 of the 18-25 bp miRNA, is the most critical region guiding miRNA-mRNA complementarity interactions. Thus, these AML associated mutations are anticipated to cause loss of normal miRNA-142-3p function. To assess this hypothesis, ex vivo methylcellulose assays were performed to evaluate hematopoietic progenitor proliferation and differentiation in the setting of wild type or mutant miRNA-142 over-expression. Progenitor enriched c-kit+ mouse bone marrow was harvested from wild type mice and infected with a GFP marked lentivirus containing wild type or mutant miRNA-142 mini-genies. No overall differences in colony number or type were seen between the various groups in this model. To further investigate how these AML associated mutations affect normal miRNA-142 function, an in vitro luciferase reporter system was used to measure the ability of these mutants to target the known oncogene and miRNA-142 target, Rac1. Preliminary results show that one miRNA-142 mutant, T33C, showed complete loss of Rac1 targeting ability compared to wild type miRNA-142. Efforts to further validate the role of these mutations in destabilizing miRNA-142 target interactions are currently underway. As one miRNA can regulate hundreds of genes, understanding how these mutations disrupt miRNA-142’s normal role may further shed light on key pathways disrupted in AML pathogenesis.
Shared decision making (SDM) is a collaborative process between clinicians and patients to make health decisions based on both patient preferences and clinical evidence. Despite its many advantages, SDM is not widely implemented in practice. While many clinicians recognize that patient preferences play an important role in treatment planning, they do not always elicit these preferences during clinical encounters. One of the primary barriers to the implementation of SDM is the assumption by some clinicians that some patients are unable or unwilling to make complex medical decisions under uncertainty because of age, health literacy, or other patient characteristics. We conducted a study exploring physicians’ attitudes, beliefs, and perceived social norms about practicing SDM through semi-structured, qualitative interviews with physicians in four practice areas: obstetrics and gynecology, internal medicine, medical oncology, and surgery. We structured our interviews according to key SDM behaviors: (1) acknowledging a decision to the patient, (2) describing the potential benefits, potential risks and cost of options, (3) eliciting values and preferences, (4) allowing the patient to review information about the decision and return to the clinic to make a final decision, and (5) disagreeing with a patient’s choice. Results suggest that many clinicians believe some patients prefer a physician-led model of care. When a patient questions this belief and asserts preferences that are inconsistent with a treatment recommendation, some clinicians perceive a challenge to their knowledge or training. These findings have implications for clinical practice. Patients often want more decision involvement than they receive, whether or not they defer final decision making to their clinicians. Screening patients *a priori* could lead to systematically excluding patients from engaging in the SDM process. Involving patients by starting from a place of acknowledging equipoise, offering treatment choices, providing evidence-based information and then assessing role preference can improve patients’ decision quality.
BiliNova: The Next Generation Phototherapy Blanket
Huy Lam, John Prewitt, Yoga Shentu, Matt Speizman, Charles Wu, and Fangzhou Xiao

Mentor: Matthew MacEwan

BiliNova is a novel biliblanket that significantly improves the effectiveness and accessibility of treatment for neonatal jaundice caused by the accumulation of bilirubin, the most significant cause of newborn hospitalization worldwide. BiliNova uses electroluminescent material which is more energy efficient and reduces its cost 20-fold compared to current biliblankets. A microcontroller automatically controls a grid of battery-powered EL panels, optimizing power-use and allowing incorporation of extension modules, e.g. colorimeter monitoring trend of blood bilirubin level. Lightweight design allows flexible en-route-treatment essential for home-borns, common in developing countries. These distinctions provide lower cost, treatment en-route, phototherapy control, higher comfort, and extensibility.
Protein misfolding results in the accumulation of aggregated β-sheet-rich structures in Parkinson’s disease (PD) and Alzheimer’s disease (AD). The aggregation process is related to neural cellular toxicity and therefore responsible for the patient’s mental decay. The toxic oligomer hypothesis stipulates that prefibrillar assemblies of amyloid β (Aβ and α-synuclein) such as soluble oligomers and protofibrils rather than end-stage, mature amyloid fibrils are the toxic species in AD and PD, respectively, which cause neuronal decay. This notion suggests that reducing the amount of prefibrillar assemblies and increasing the amount of mature fibrils may decrease neuronal cell toxicity.

We previously demonstrated that an orcein-related small molecule, O4, directly binds to Aβ fibrils and stabilizes protofibrils to become mature fibrils. O4 also accelerates the aggregation kinetics of Aβ toward end-stage mature fibrils. Here we demonstrate a similar phenomenon in the aggregation kinetics of α-Synuclein in the presence of O4 and preliminary support for the toxic oligomer hypothesis. O4 accelerated the aggregation kinetics of α-Synuclein and promoted the formation of SDS-resistant aggregates, an indicator for mature fibrils. We also demonstrate evidence for reduced toxicity to human neuronal model cells in aggregated samples of α-Synuclein in the presence of O4 compared to the aggregated samples of α-Synuclein in the absence of O4. These preliminary and promising results suggest that stabilizing mature fibrils may be a new general strategy for detoxifying amyloid assemblies in multiple diseases, and support the use of O4 as a new approach to combating Parkinson’s disease.
Event segmentation is an automatic cognitive process that helps humans break up the flow of everyday experience into temporal units that we call events. Without the ability to segment, one’s memory and comprehension of events would decline. Two key components of the event segmentation process are event models and event schemata. Event models are working memory representations of what is currently happening; event schemata are long-term knowledge about events. Event models are influenced by event schemata. Event models and current sensory information together guide perceptual processing. Based on functional imaging during event segmentation, two defined brain regions—the dorsolateral prefrontal cortex (dLPFC) and the ventromedial prefrontal cortex (vmPFC)—have been implicated in the event model and event schema systems, respectively. To investigate the roles of these brain regions directly, we will assess event segmentation and memory performance in Vietnam War veterans with brain lesions in these areas. In the first stage of the study, participants viewed videos of everyday activities and consciously identified boundaries between both small (fine segmentation) and large (coarse segmentation) meaningful units. Next, we will use x-ray computed tomography (CT) scans to precisely define the limits of brain lesion in each subject. We hypothesize that, compared to combat veterans who did not sustain brain injuries, subjects with dLPFC lesions will have impaired coarse and fine segmentation, and memory performance, due to damage to the event model system. We also expect subjects with vmPFC lesions will have impaired coarse segmentation and memory performance due to damage to the event schemata system. It is our hope that identification of brain areas relevant to event segmentation will help identify the cellular basis of memory deficits and can thus provide insight into future therapies.
It has been speculated that violet cone photoreceptors mediate the magnetic sense in chickens; a conclusive test for this suggested pathway would be to test chickens lacking violet photoreceptors for magnetoreception. Additionally, eliminating the green photoreceptor population would allow further functional testing of avian vision. Our goal was to use the RCAS-BP virus to drive the expression of short hairpin RNA (shRNA) to knock down either the violet or green opsin, in their respective cells. The RCAS-BP virus was replication competent in birds and lacked the sarcoma gene while expressing transgenes for shRNA driven by the constitutively-expressing U6 viral promoter. The RCAS-BP viral genome also coded for GFP transcribed with polyadenylation sequence. We injected the virus into chicken embryos’ neural tubes at stages 9-11. However, post-injection, we found no viral particles in the embryos and no knock down of opsins. We propose that the GFP polyadenylation sequence interfered with the production of viral particles from the RCAS-BP plasmid and consequently, preventing viral particles production. Additionally, survival of injected embryos to day E21 did not occur, likely due to harsh experimental procedures.
The accurate trafficking and transport of membrane proteins plays an essential role in maintaining the function of numerous body processes. In renal cells, understanding the mechanism of assembly and polarized sorting of proteins is essential to elucidating the etiology of associated diseases and symptoms (SeSAME/EAST). In polarized Madin Darby canine kidney (MDCK) cells, we found that the potassium channel Kir4.1 does not traffic to the plasma membrane unless coexpressed with Kir5.1. To identify domains that govern oligomerization and/or delivery to the plasma membrane, we used PCR to construct a chimera Kir4.1 channel with a cytoplasmic C-terminal domain substituted with the homologous Kir7.1 channel sequences. By constructing this chimera between Kir4.1 and Kir7.1, we hope to identify the domain of Kir4.1 that is important in its oligomerization and delivery to the basolateral membrane in polarized MDCK cells. By inserting this chimera (Kir4.1/Kir7.1) and its wild types (Kir4.1 & Kir7.1) into the vector pcDNA, we were able to express these channels in polarized MDCK cells. Analysis with immunofluorescence microscopy revealed 3 major findings: 1) Kir4.1 did not traffic to the basolateral membrane as expected from previous research and other similar investigations 2) Kir7.1 did traffic to the basolateral membrane 3) Kir4.1/Kir7.1 did not traffic and remained intracellular. These results suggest that the cytoplasmic C-terminal domain does not drive self oligomerization and trafficking to the basolateral membrane. Future experiments will involve examining different domains of Kir4.1, such as the N-terminal domain. These results will be useful to dissect the protein motifs that are important for assembly and trafficking of K channels in polarized MDCK cells. Identification of these signals will be important in further understanding the polarized sorting of membrane proteins.
A Tale of Two Countries; Northern Japan Meets Jersey Shore in Post-Storm Rebuilding Efforts

Samuel Leder

Mentor: Lori Watt

After traveling to Japan and the Jersey shore to view the impact of the recent tsunami and hurricane, the goal of my research was to report my findings and critically analyze the rebuilding and reconstruction efforts as seen through the lens of architects, consultants, and government officials involved in the reconstruction and recovery efforts. By studying the varying but sometimes similar approaches used to protect, rebuild, restore and reconstruct communities, I was hopeful to begin to develop a roadmap for future preparedness against natural disasters. Particularly in a world where most populations are not self-sustaining and are totally dependent upon the infrastructure of communities for telecommunication, food, power, water, transportation, and roads, it is vital that corrective measures from past experiences be taken to ease or eliminate future loss and that any recovery be quick and economically feasible to enable regions to rebound and survive.

Through my travel and research, I was able to observe and examine parallels in the rebuilding and recovery processes ongoing in two areas of the world which are separated by over 6,000 miles with very distinct geographical differences and living conditions. Yet, there are similarities in their recovery efforts to protect and fight against the impact of future flooding and loss. Their recovery and mitigation strategies include: 1) the use of seawalls and sand dunes along the coastlines; 2) housing construction in the form of “container” housing and modular units; and 3) government zoning regulations and related requirements on height and evacuation/safety plans. While I was able to identify and analyze these key components of recovery and preventive actions, there is no “best practices” approach that can yet be recognized.
The Dictyostelids are a group of social amoeba that feed on bacteria during a vegetative cycle, a cycle they go through under a favorable condition where they replicate by binary fission. When starved, these social amoeba aggregate and form multicellular fruiting bodies where some of the cells sacrifice themselves to become the stalk that lifts up the rest of the cells which develop into spores. Due to the altruistic behavior required in the process, within-species competition occurs in chimeric fruiting bodies when some strains cheat and lessen their contribution to the stalk, thereby taking advantage of the losing strain’s contributions. And the competition between chimeric fruiting bodies is maintained by the secreted substances, such as polyketides. It’s been discovered that an O-methyltransferase DmtA is involved in the synthesis of DIF-1, a polyketide that’s known to affect stalk development. So the social competition may lead to an evolutionary arms race where O-Methyltransferases (OMTs) evolve rapidly to produce novel polyketide compounds to get ahead and continuously coerce other strains to be over-represented in the stalk. We identified candidate O-methyltransferase genes and created the phylogenetic tree to examine if these genes showed lineage specific gene duplication events and subsequent divergence. What we discovered was that the candidate O-methyltransferase genes examined, Methyltransferase 2 and Methyltransferase 3, respectively showed large and intermediate amounts of lineage specific duplication events when compared to the control, DNA methylase. These results support that these genes could be involved in the creation of novel products, and broadly in an evolutionary arms race that drives continuous adaptations and leads to species differences.
Toward a Better Understanding of...

**Can Feeding Preferences of Exotic Snails Contribute to the Success of Invasive Species?**

_Ana Liang_

*Mentors: Scott Mangan and Claudia Stein*

Understanding the processes that drive invasions is a major goal in ecology and crucial to develop successful restoration projects. Many hypotheses concerning success of invasive species focus on their enemies. Here we concentrate on the “enemy inversion hypothesis” which suggests that the invader’s natural enemies may indirectly facilitate the success of an invasive species by having a stronger effect on the native community than on the invader. At the Tyson Research Center in Missouri we determined abundances of _Bradybaena similaris_, an invasive snail from southeast Asia, in forest plots. In the laboratory, we examined feeding preferences of _B. similaris_ for three native and three invasive plant species commonly found in the forest. Overall, the snails showed strong feeding preferences for the native plant species compared to the invasive species. Our results show that invasive plants may benefit from consumer pressure on native plants, in this study a consumer who is also an invasive species.
Many of the most powerful synthetic transformations used to construct molecules are oxidation reactions, which allow for the either incorporation of new functionality or an increase in the existing level of functionality within a molecule. While oxidation reactions are very powerful, they can also be very problematic because they often leave behind excess amounts of transition metal waste like copper, manganese, chromium, palladium, and iron. An oxidation reaction of particular interest is the electrolytic cyclization of malonate derivatives with manganese to form vicinal quaternary carbon centers. This reaction, studied by Dr. Jonathan Burton at the University of Oxford, provided a suitable target to apply our lab’s solar-powered recycling technique because of the use of manganese.

The goals for this research were to synthesize an enol ether malonate derivative and show that the manganese involved in the electrolytic cyclization of this malonate derivative can be recycled by using solar power as the only source of energy. The synthesis proved to be more difficult than expected due to the acid sensitivity of the enol ether functional group. The synthesis pathway that worked the best was to perform an alkylation reaction first, ozonolysis second, and Wittig last. During the cyclization reactions of this malonate derivative, the first attempt was to run the reaction without the use of manganese. Promising results were obtained that point to successful cyclization of the malonate derivative without the use of manganese. While further work will need to be done to characterize all of the products, the possibility of performing the cyclization without manganese is a step forward to greener synthetic chemistry.
Lung cancer is a deadly disease that kills approximately 160,000 Americans each year. Two tumor suppressors frequently mutated simultaneously in lung cancer are ARF and p53. While the canonical ARF-p53 pathway has been well characterized in the literature, the p53-independent functions of ARF are less understood. Our preliminary studies in Mouse Embryonic Fibroblasts (MEFs) demonstrate that one of ARF’s p53-independent functions may include regulating the Janus Kinase (JAK)-Signal Transducer and Activator of Transcription (STAT) signaling pathway, which has been shown to promote tumorigenesis. Immunohistochemistry staining of lung tumor tissue arrays show that low ARF levels correlated with high Interferon-Stimulated Gene 15 (ISG15) levels, which is a product of the JAK-STAT Signaling Pathway. Furthermore, western blot analysis of human lung epithelial cancer cell lines with different alterations in ARF, p53, and PIK3CA indicate an association between low ARF levels and high Interferon-β (IFN-β) levels. In this study, we investigate the effects of inhibiting JAK and PIK3CA on lung cancer cell growth and proliferation. We found that simultaneous inhibition of JAK and PIK3CA on lung cancer cell growth and proliferation more effectively than inhibition of only one of these targets in Arf-null/p53-mutant/PIK3CA-amplified lung cancer cells. This finding can possibly be translated into a novel dual inhibitor therapy for lung cancer patients with these genomic abnormalities.
Toward a Better Understanding of…

**Knowledge and Awareness of Emergency Contraception in Higher-Risk Male and Female Adolescents**

*Emily Lin*

*Mentor: Sophia Yen, Stanford University*

Purpose: To determine the awareness of emergency contraception (EC) among higher-risk adolescent females and males and to assess their knowledge of proper use and access to emergency contraception.

Methods: From 2010 to 2012, the Teen Health Van, which is a mobile clinic program targeting uninsured and homeless adolescents and providing comprehensive primary health care services to adolescents, utilized self-administered anonymous surveys to patients in six partner sites in the San Francisco Bay Area.

Results: Overall, 40% incorrectly identified or were uncertain if emergency contraception was an abortion pill, 40% incorrectly answered or were uncertain if EC could be used as a form of birth control, and 19% incorrectly answered or were uncertain that Plan B could be used to prevent STIs. Forty-four percent (44%) were uncertain or felt that they could not confidentially obtain EC. Seventy-two percent (72%) did not know or did not think that males could receive EC for use by their partner. Twelve percent (12%) incorrectly selected that infertility was an EC side effect. Forty-four percent (44%) did not know the proper window for EC use and were under the false impression that EC had to be taken within 1 day of unprotected sex to be effective.

Conclusion: Higher-risk adolescents have high rates of EC awareness but low rates of knowledge on the purpose, access, and proper usage of emergency contraception. Male and female adolescents need more education to alleviate misconceptions about EC and increase practical knowledge on the proper use of and access to EC. Specifically, physicians and society need to provide more education about: male access to EC, that EC does not cause infertility, that EC is available over the counter for young men, and that EC’s window of use is up to 120 hours.
Amplification of a well-known transcription factor, the E2F3 gene, combined with the loss of tumor suppressor retinoblastoma, Rb, is commonly found in invasive bladder cancer patients and associated with poor prognosis. However, it is unclear how the particular combination contributes to tumor initiation and progression. By knocking down E2F3 expression level in HT1376 human bladder tumor cell line, which has amplified E2F3 and loss of Rb, we found expression of a subset of chemokines, cytokines and their receptors are significantly changed. We hypothesized that these cytokines, chemokines and their receptors driven by overexpressed E2F3 might have novel function in tumor microenvironment beyond regulation of the cell cycle. Formalin-fixed, paraffin-embedded tissue samples taken from bladder cancer patients were analyzed using immunohistochemistry. The results suggested that could be a correlation between elevated expression levels of E2F3 and reduced recruitment of CD-4 helper cells and CD8 cytotoxic T-cells into the tumor microenvironment. Thus, overexpressed E2F3 may play an important role to help tumor cells escape from immunosurveillance.
Toward a Better Understanding of...

**IFNγR Signaling Regulates Trafficking of Regulatory T cells after Allo-HSCT**

*Theodore Lin*

Mentor: Jaebok Choi

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) with regulatory T cells (Tregs) contributes to the maintenance of self-tolerance and maximizes the graft-versus-leukemia (GvL) effect while minimizing graft-versus-host disease (GvHD) in patients with relapsed leukemia and marrow failure. However, the number of Tregs obtained from the isolation process is very low, typically around 1% of mononuclear cells in whole peripheral blood mononuclear cells or PBMCs). It has been demonstrated that interferon γ receptor-deficient (IFNγR/-) conventional T cells (Tconv) induce significantly less GvHD than the wild type Tconv in animal models. This effect is believed to be mediated by an altered trafficking of IFNγR/- Tconv to the spleen, away from the typical target GI organs, such as the GI tract, liver, skin, and lungs, due to an up-regulated CXCR3, a chemokine receptor, in IFNγR/- Tconv. In order to determine if IFNγR/- Tregs have a similar defect in trafficking to the GvHD target organs *in vivo*, we performed allo-HSCT in which T cell-depleted bone marrow cells (TCD BM) and Tconv obtained from B6 mice (H2b) along with Tregs obtained from either WT or IFNγR/- B6 mice were transplanted into lethally irradiated Balb/c (H2-d) mice. The mice were imaged continuously for three weeks, using *in vivo* bioluminescence imaging technique. We found that the IFNγR/- Tregs were more abundant in the spleen than in the GI tract, compared with WT Tregs. These data suggest that Tregs and Tconv share the same IFNγR/CXCR3 axis for trafficking to GvHD target organs. Our preliminary results indicate that IFNγR signaling is also necessary for Tregs to up-regulate CXCR3 *in vitro*. More experiments are under way to show the reproducibility of our findings.
Nanoparticles have been shown to enhance the efficiency of therapeutics (e.g. RNAi) by delivering them to a target site, while protecting against degradation and clearance. Current nanoparticles include but are not limited to cationic lipids, cationic polymers, anionic polymers, lipid/polym er hybrids, and functionalized gold nanoparticles (AuNPs). Among these varieties, the cationic polymer polyethylenimine (PEI) is one of the most highly characterized and studied, due in large part to its high transfection efficiency. To its detriment, PEI suffers from significant cytotoxicity. Thus the goal is to strike the optimal ratio of transfection efficiency to cytotoxicity. It has been previously shown that the shape of a given nanoparticle can significantly affect its transfection efficiency. Therefore, our approach is to modulate the size and shape of cross-linked PEI nanoshells using gold nanoparticle templates.

In our synthetic approach to PEI nanoshells (PEINS), gold nanoparticles are first coated in branched PEI (25kDa). The PEI strands are then cross-linked. Finally, the gold nanoparticle is dissolved, leaving behind a PEI nanoshell. We will report on the impracticality of a PEI-capped AuNP approach and our current progress using a cap displacement approach.
The Dirichlet space is a Hilbert space of holomorphic functions on the unit disk. It is a central object of study in function theory and is now well understood. Less is known about weighted variations of the Dirichlet space. I discuss the history of these spaces, give some partial results, and outline my plans for future research. Throughout, I emphasize the importance of dyadic techniques in the study of weighted Dirichlet spaces.
Histological analyses of the large size of the human pancreas require a practical stereological approach. In organs such as the liver or spleen in which different cell populations are relatively homogenously distributed, a localized analysis may accurately represent the whole organ. In the pancreas, however, the unique distribution of endocrine cells among exocrine tissues makes a representative analysis difficult to obtain. Pancreatic islets are unique micro-organs comprised of several endocrine cell types with dense vascularization that are scattered unevenly throughout the pancreas, and they constitute only a small percentage of the total pancreatic mass. Sampling of a small number of specimens, whether done randomly or systematically, as it has been done in most studies in the past does not provide detailed analyses of the human beta-cell/islet distribution. Moreover, large islets (~100 μm or larger in diameter) in humans do not form a beta-cell core as is observed in rodent islets, and non-beta-cells (e.g. alpha- and delta-cells) are intermingled throughout the center of an islet making it difficult to assess the size of a human islet based on beta-cell count alone as is done in the point-counting morphometry method. In the present study, we validated our large-scale, computerized analysis method by comparing its quantification results to those of the commonly used point-counting morphometry and panel-by-panel selection methods of quantification. The results of our simulations show that these widely used methods tend to overestimate the frequency of endocrine cells in the pancreas up to several folds.
The production of a bio-fertilizer could benefit the agricultural industry by decreasing the need for energy intensive nitrogen fixation processes. The nif cluster of *Cyanothece* 51142 consists of 29 genes that construct and regulate a nitrogenase protein complex, which catalyzes the fixation of atmospheric nitrogen. This year, our iGEM team aims to harness the power of nif to produce ammonia in *Escherichia coli*. After synthesizing a nif-containing plasmid (28 kbp) using the DNA assembler method and transforming that plasmid into *E. coli*, our team tested for nitrogenase activity using the acetylene reduction assay. The transformed *E. coli* were then compared to wild-type under limited nitrogen conditions to check for a competitive advantage. Future tests will evaluate the expression of various nitrogenase subunits, such as *nifD* and *nifK*. Our team also aims to further characterize the promoter sequences of the *Cyanothece* 51142 nif cluster. Between the cysE and nifB genes, there is a 958bp uncharacterized, bidirectional promoter region of particular interest. We are currently using fluorescent reporters to identify key regions within this promoter sequence, and plan to test its function in various environmental conditions.
Obesity is a well-established risk factor for adverse health outcomes including HF. While obesity impacts the progression to HF, the obesity paradox in HF refers to the findings that overweight and obese patients have lower cardiovascular mortality than those patients of normal weight. Thus, we aimed to explore the effects of elevated body mass on genetic remodeling in human HF. We hypothesized that gene expression patterns would vary depending on body mass in normal and failing human hearts. Left Ventricular (LV) tissue was obtained from 17 failing hearts from transplant recipients and 18 nonfailing donor hearts rejected for transplantation. These hearts were subsequently classified based on the body mass index (BMI) of the patient or donor: normal BMI (18.5-24.9 kg/m²) and elevated BMI (≥ 25 kg/m²). Following mRNA extraction, cDNA was synthesized and used to run customized TaqMan arrays using RT-PCR with 96 target genes. Gene expression data was obtained and analyzed using the false discovery rate (FDR) method with the Significance Analysis of Microarrays software (Stanford University). A FDR of 3.66% as the threshold for significance resulted in 66 significant genes with d scores from 0.190 to 0.513. Post-hoc t-testing revealed 14 genes of particular interest due to differences in expression patterns between normal BMI and elevated BMI hearts. These genes of interest can be grouped into three general groups: potential arrhythmogenic remodeling (CACNA1D, KKBPIB, KCNJ11, KCNJ5, KCNJ3, and FKPB1B), metabolism (MYH6, LPL, and PLA2G6), and general cell signaling (ADRB1, ADRB2, MAPK11, CAMK2B, and PRKCA). These results may help us understand remodeling that contributes to the obesity paradox, which could direct future therapy.
The collaboration between medicine and art forms is an exciting crossroads with great potential. This research looks at this intersection and its implications; the project explores the efficacy and methods of dance as healing. I looked at dance and healing specifically within the model of an existing program, Dance for Parkinson’s Disease which is now active in over 100 communities worldwide. To evaluate methods of dance healing, I attended a workshop in New York presented by the founders of the original Dance for PD group and conducted an anthropological analysis of the program and its methods of healing. I found that it is the entire culture of the program along with the complex mind-body connection and joy present in dance that is responsible for its success. To gauge the program’s effectiveness, I formulated a questionnaire and collected data by phone interviews with Parkinson’s patients who attend the weekly Dance for PD class in Berkeley, California. The interviews affirmed the effectiveness of dance as an all-around healing treatment, with the strongest factors being the creative mentality when dancing, the music, the atmosphere and the element of enjoyment. The Dance for PD model is highly effective when considering dance as healing, however ironically the purpose of the Dance for PD is specifically not centered on viewing itself as a healing method. Along with nearly a decade of previous and ongoing research on this topic, the knowledge that this class is a powerful healing tool establishes a path for me to begin a dance class for those with Parkinson’s in St. Louis and to possibly collaborate with the Washington University Medical School on a comparative study with other Parkinson’s exercise models in the community.
Explorations in PTR1 and Targeting of Human Beta-Globin BAC Transgene in Nucleus

T. Anthony Maltbia

Mentor: Andrew Belmont, University of Illinois, Urbana-Champaign

Increasing evidence suggests that nuclear compartmentalization is a contributing mechanism for gene regulation. Genes found at the periphery of the nucleus are, in general, repressed; those found at the center of the nucleus are often expressed. However, the factors required to target loci to specific nuclear compartments remain largely unidentified. Molecular dissection of the human Beta-globin gene has identified stretches of DNA needed and sufficient to target linked DNA to the nuclear periphery and typically repress gene expression. Upstream of the human Beta-globin gene, a 6kb peripheral targeting region (PTR) has been shown to target the locus to the nuclear periphery, as removal of the PTR results in the Beta-globin locus targeting to chromocenters. The mechanism and interaction behind how exactly the PTR1 sequence targets Bac transgenes to the nuclear periphery is unclear, and the focus of this research. The goal of the project was to identify a minimal element within the 6Kb PTR1 sequence that is sufficient to target DNA to the nuclear periphery. To do this, I sought to create 6 1Kb fragments from the PTR1 sequence to and inserting these fragments into a cloning vector with the long term goal of using the vector/fragment for future experiments (deletions, replacements, transductions, etc.) to better understand the underlying mechanisms behind nuclear periphery targeting of Bac transgenes. Although the initial cloning experiments were not successful, this project and future experiments are promising in uncovering the underlying mechanisms for how PTR1 interacts with the 200 Kb Human beta-globin Bac transgene and targets to nuclear periphery.
Toward a Better Understanding of...

**Variation in GATA1 Moderates the Association between Childhood Adversity and Amygdala Habitation**

*Seth Margolis*

*Mentor: Ryan Bogdan*

Stress, particularly when occurring early in life, is amongst the strongest predictors of depression. However, the mechanisms underlying this relationship remain poorly understood. A wealth of non-human animal research suggests that stress might disrupt synaptic plasticity as well as brain structure and function. A recent study in rodents has shown that chronic stress is associated with increased *GATA1* expression. Because *GATA1* is a transcription factor that suppresses the expression of synaptic-function-related genes, this stress-induced increase in *GATA1* expression is one potential etiologic mechanism underlying the depressogenic effects of stress. In this study we examined whether genetic variation in *GATA1* moderates the effects of childhood adversity on amygdala habituation, a neural phenotype linked to reduced stress reactivity. For the present study, genetic and neuroimaging data were available from 322 participants who completed the Duke Neurogenetics Study, an ongoing protocol assessing a wide range of behavioral and biological phenotypes among young adult volunteers. We selected the only *GATA1* SNP on our genome-wide array, rs5906709, to examine its association with amygdala habituation, in the context of childhood adversity. To measure amygdala habituation, participants completed a canonical threat-related fMRI task. Amygdala habituation was defined as a decrease in activation over time with repeated presentation of threat-related stimuli. *GATA1* genotype interacted with childhood adversity to predict amygdala habituation in the left dorsal and ventral amygdala (ps<0.003). In the right amygdala, this interaction predicted habituation at a trending level (p=0.07). Post-hoc testing showed that minor allele carriers had reduced left amygdala habituation in the context of elevated childhood adversity (p=0.01), while there was no relationship in major allele homozygotes. Because increased amygdala habituation has been linked to more adaptive responses to stressors, these data suggest that minor allele carriers at rs5906709, may be more susceptible to stress-related psychopathology, including mood and anxiety disorders.
Toward a Better Understanding of...

**Structural Characterization of Amorphous Cu_{46}Zr_{54} using Molecular Dynamics Simulations, Reverse-Monte Carlo Simulations, and Weighted Voronoi Diagrams**

*Zachary E. Markow*

**Mentor: Kenneth Kelton**

Metallic glasses have unique properties that hold great promise for engineering applications. To fully harness these materials, it is critical to advance the understanding of the links between metallic glasses’ bulk properties, microscale atomic configurations, and formation from rapidly cooled metallic liquids. However, the characterization of these materials’ atomic structures is not straightforward because in metallic glasses and liquids, the atomic configurations are disordered or amorphous compared to those of a crystal. A weighted Voronoi diagram (WVD) is a descriptive, chemically specific, precise tool available for characterizing short-range atomic configurations in amorphous materials. In this study, WVDs were used to study the local atomic structures in computer-modeled glass and liquid samples of the alloy Cu_{46}Zr_{54} whose atoms’ positions had been generated by three different computer simulation methods: molecular dynamics, unconstrained reverse-Monte Carlo, and constrained reverse-Monte Carlo simulations. Although all simulation results showed a distinctive increase in icosahedral and nearly icosahedral clusters during cooling below the glass transition, discrepancies in the formation rate and raw prevalence of these clusters across simulation methods raise questions that require further study about which method is most accurate for Cu_{46}Zr_{54}. 
The evolutionary warfare between plants and their pathogens has led each to evolve highly modified strategies for gaining an advantage over the other. Geneticists have been using the model plant system Arabidopsis thaliana and the pathogen Pseudomonas syringae pv. tomato strain DC3000 to identify the genes that govern the interaction between the two, leading to the discovery of various mutants that alter plant susceptibility to infection. The Kunkel lab recently discovered that afb4-2, a novel mutation in Arabidopsis, results in greater susceptibility to DC3000 as well as altered plant morphology. These phenotypes do not appear in the null mutant afb4-8, suggesting that afb4-2 confers some neomorphic function, the mechanism of which remains largely unknown. Using a genetic approach, we have further characterized the afb4-2 mutation in an effort to better understand how it modulates plant immunity. First, dominance between afb4-2 and the wild type (WT) AFB4 allele was determined by crossing plants homozygous for afb4-2 with WT plants and infecting the resulting offspring. In spite of being a gain-of-function mutation, we found that afb4-2 was recessive to the WT allele. Next, afb4-2 plants were crossed with plants containing the afb4-8 null mutation to see if gene dosage plays a role in producing the morphological and susceptibility phenotypes. The results of this experiment will be summarized on my poster. Overall, these results reveal that afb4-2 is a very complex allele. Gaining a better understanding of it will lead to a greater understanding of the intricacies of plant immunity.
The absolute binding free energies of organic ammonium ligands to cucurbit[7]uril were investigated using the AMOEBA polarizable force field with explicit water solvent and molecular dynamic simulations. The free energies were computed via the double decoupling method in which the ligand is decoupled from water and from the cucurbit[7]uril-ligand complex, and then the difference in free energy between these two processes computed. Eleven of the ligands contained a single ammonium group. Two of the molecules contained two ammonium groups and one the ligands contained three-ammonium groups. Compared to experimental results, our results were good for most of the singly protonated species, six of which we were able to predict within 0.9 kcal mol$^{-1}$. The gold standard for computation chemistry is to predict energies to within 0.5-1.0 kcal mol$^{-1}$ often referred to as “chemical accuracy.”
The Peace Corps’ mission incorporates two different goals—foreign assistance and public diplomacy. The agency enlists predominately recent college graduates to volunteer abroad, providing a form of technical, as opposed to financial, foreign assistance to interested countries. While the agency is bureaucratically independent from the State Department and intelligence agencies, its funding is allocated through the Congressional appropriations process. Is the Peace Corps, then, constrained at all by the foreign policy objectives of the executive or legislature? To what extent is the agency’s decision-making process directed by strategic considerations? There is a great deal of scholarship in political science that attempts to measure whether bilateral foreign aid is leveraged as an attempt to “buy” foreign policy allegiance, usually using UN voting patterns as a metric of political alignment between countries. This research seeks to engage with this set of modeling techniques, and situate the Peace Corps along a spectrum of strategic foreign policy objectives and altruistic development goals. I supplement quantitative analysis with primary document research—primarily declassified government and intelligence reports—to address to what degree the Peace Corps functions as an agent of U.S. foreign relations.
Infertility is an emotionally taxing condition, freighted with guilt and self-blame. In order to overcome this personal anxiety, and the potential for social stigma, women often go to great lengths in order to conceive. These include painful self-injections of progesterone and invasive surgical procedures involved with biomedical assisted reproductive technologies (ART) such as in vitro fertilization (IVF). As an alternative or complement to these uncomfortable biomedical treatments, women in the United States and other Anglo countries have pursued traditional Chinese medical therapies such as acupuncture and herbal prescriptions. This study explores the pervasiveness of this phenomenon in China, where the medical paradigms of biomedicine and traditional Chinese medicine (TCM) coexist, and often converge. Specifically, this study compares the explanation and understanding of female infertility in the biomedical and TCM models, and the corresponding approaches to treatment. This study also investigates beliefs held by women undergoing infertility treatment, and their experiences in Western-style and TCM clinics. Findings come from semi-structured interviews, observations at three clinics in Shanghai, and printed materials accompanying herbal remedies purchased at a TCM pharmacy.
Toward a Better Understanding of…

The Japanese Famine of 1946

Benjamin Misch

Mentor: Lori Watt

Having been at war for nearly fifteen years, the Japanese people experienced shock, relief, and shame all at once on August 15th, 1945, the day of Emperor Hirohito’s first-ever radio broadcast announcing Japan’s unconditional surrender to the Allied powers. Within three weeks of this date came an army of American bureaucrats and specialists whose mission was to remake Japan in the mold of demilitarization and democratization. The nature of unconditional surrender and foreign occupation devastated the Japanese psyche. The rapid deterioration of the country leading up to and following defeat left many Japanese feeling destitute, derelict, and dejected. Using newspaper sources translated into English by the occupation authorities, this paper argues that the summer of 1946 represents the turning point of Japan’s defeatist condition from a disenfranchised and fractured population focused on the crimes of the past to an engaged and variegated populace focused on the building of a bright future. During the period of May through August, Japan witnessed its first steps towards its present political system with the opening of the first “democratic” Diet; it witnessed a mushrooming of newspapers, journals, books, periodicals, and other forms of uncensored and popular literature; it witnessed an unparalleled increase in the number of labor unions and union participants; and it witnessed the worst famine to hit the country in forty-five years. In these few short months, the Japanese population took survival into its own hands and focused on a New Japan of the future.
The nematode *C. elegans* is a useful model organism for studying the genetics of aging. Several mutations, and independent signaling pathways, have been identified that dramatically alter lifespan in worms. Many of these have also been found to alter the ability of animals to resist internal and exogenous stressors, suggesting that the rate of aging and stress-resistance are intrinsically linked physiological traits. In worms, the elimination of germ line stem cells increases lifespan and enhances stress resistance. This lifespan extension is a precisely, genetically regulated process and requires the function of several transcription factors, including DAF-16/FOXO and TCER-1/TCERG1. In an effort to understand how these proteins interact functionally, our lab has used massively parallel RNA sequencing (RNA-Seq) to identify shared, as well as individual, downstream targets of DAF-16/FOXO and TCER-1/TCERG1. We found that these proteins share about a third of their transcriptomes and increase the transcription of many genes that are functionally essential for longevity. In addition, we also noticed that TCER-1/TCERG1 independently suppresses the expression of genes that are likely to promote reproduction and inhibit a long life. We have tested the hypothesis that TCER-1/TCERG1 promotes the expression of “pro-longevity” and “pro-stress-resistance” genes, and suppresses the expression of “anti-longevity” and “anti-stress-resistance” genes. We devised an assay that examines the resistance of wild-type worms to an oxidative stress inducing agent, tertiary-butylhydroperoxide(t-booh), and to test the effect on the worms’ lifespans. We have used RNAi to knock-down the expression of genes that our RNA-Seq data showed were repressed by TCER-1/TCERG1 and tested the effect on the worms’ oxidative stress resistance.
Investigation of the Role of a KCNN3 Small Nucleotide Polymorphism in Prematurity

Neha Mukunda

Mentor: Sarah K. England

Preterm birth (birth before 37 weeks gestation) is the leading cause of infant mortality globally and is increasing in its prevalence. Alterations in ion channel expression and regulation are critical to maintaining uterine quiescence during early gestation as well as increased uterine excitability at the time of labor. One channel in particular, the small-conductance calcium-activated potassium (SK3) channel, is downregulated in late-pregnancy corresponding with the onset of contractions. Mice overexpressing SK3 demonstrate weakened uterine contractility and defective or delayed parturition; this led us to hypothesize that premature downregulation of SK3 activity can lead to an excitable, overly contractile uterus. Genotyping and sequence analysis revealed that several single nucleotide polymorphisms (SNP) within the gene encoding SK3 (KCNN3) are associated with preterm birth. One of these SNPs (rs1218585) is located in a highly conserved region near the promoter for SK3-1C, an isoform that suppresses the native (1A) form of the SK3 channel by reducing channel activity at the cell surface. Here, we investigated the mechanism by which the KCNN3 SNP rs1218585 contributes to preterm birth. Due to its unique genomic location, we examined whether the SNP acts as an alternative promoter or enhancer to drive transcription of the inhibitory SK3-1C. Using luciferase reporter assays of transfected human embryonic kidney (HEK293T) cells, we found a 7-fold decrease in enhancer activity of KCNN3 exon 1C upstream sequences containing the SNP as compared to KCNN3 exon 1C with the wild type (WT) sequence. The loss of SK3 enhancer activity upon inclusion of the SNP suggests that the KCNN3 upstream sequences may not have direct promoter activity for 1C; the SNP may instead be altering enhancer elements that modulate the expression of either SK3-1A or 1C. The results emphasize the need for a full-gene model of KCNN3 regulation to definitively elucidate its role in preterm birth.
While the reaction mechanisms of organic compounds containing first-row elements are fairly well-understood, the same cannot be said for compounds containing elements below the first row of the periodic table. Studying the pericyclic Diels-Alder reaction of disilenes can help elucidate the nature and reactivity of covalent bonds to silicon, an important group 4 analog to carbon. Previous research suggests that the pyrolysis of tetramethyldisilacyclohexene to form butadiene and Me2Si=SiMe2 occurs via a diradical intermediate rather than a synchronous, concerted transition state. The hypothesis is that the symmetry (or lack thereof) of the HOMO and LUMO of the silicon dienophile determines the mechanism of a cycloaddition reaction. Here we employ computational methods to determine the mechanism of the retroaddition of the butadiene and 9,10-disilannaphthalene adduct, the latter of which has been shown to be planar and have the necessary symmetry to allow for a concerted reaction. A coordinate driving profile calculation was run in the Spartan computational chemistry software at the Hartree-Fock 3-21G level, constraining the Si-C bonds involved in the retroaddition in order to model the reaction coordinate. Transition state optimization and frequency animation of a local maximum on this coordinate at the B3LYP/6-31G* level clearly illustrated a synchronous, concerted mechanism with a relatively low activation energy. This calculation was compared to the predicted activation energy leading to a hypothetical diradical intermediate that would be involved in an asynchronous, stepwise mechanism. Geometry optimization of three different conformations of the diradical intermediate at the B3LYP/6-31G* level yielded a predicted activation energy that was higher than that of the concerted mechanism. This result appears to confirm the hypothesis about the rules of symmetry governing the mechanism of the Diels-Alder reaction, leading to greater insight into how compounds containing heavier elements behave.
In the vertebrate nervous system, the myelin sheath is important for rapid conduction of action potentials, and providing trophic support essential for the proper function of neurons. Myelinating glia iteratively wrap their plasma membrane around axons to form the myelin sheath; in the peripheral nervous system (PNS) and central nervous system (CNS), these specialized cells are Schwann cells and oligodendrocytes, respectively. Our research aims to elucidate the molecular mechanisms governing myelination by utilizing a three-generation forward genetic screen in zebrafish. We have induced random mutations in the genomes of zebrafish using the chemical mutagen N-ethyl-nitrosourea (ENU), and have crossed these mutants to a strain of double transgenic zebrafish. We utilize two transgenes, which are fluorescent reporter proteins, driven by the neuronal promoter Lhx and the glial promoter myelin basic protein. These transgenes enable us to rapidly screen for potential mutants exhibiting disruptions in fluorescence intensity. Phenotypes observed by transgene are then confirmed via whole mount in situ hybridization. Thus far, we have identified 24 putative mutants with a variety of defects in both CNS and PNS myelination that are at various stages of the re-screening process, and one confirmed mutant, stl64. We are currently confirming that the observed phenotypes are heritable, and preparing to use next generation sequencing to determine the specific genes and mutations responsible for each phenotype. Further follow up of these mutants will entail experiments such as marker analysis of genes that define different stages of glial development, in addition to transmission electron microscopy to determine the stage at which myelination is disrupted and the specific ultrastructural consequences. If verified, these mutations may provide insight into diseases in which myelination is disrupted, such as multiple sclerosis, Guillain Barré Syndrome, and other myelin disorders.
Plants are largely immobile. To adapt to rapidly changing environments, plants evolved the ability to produce specialized compounds. The production of these compounds is key to their survival. For the production of these compounds, biochemical pathways evolved from primary metabolism. For example, the model plant *Arabidopsis thaliana* contains three genes for putative isopropylmalate dehydrogenases (AtIPMDH1-3). Recent studies show that AtIPMDH2 and AtIPMDH3 are involved in leucine synthesis, an essential amino acid produced by plants, and that AtIPMDH1 is involved in the production of glucosinolates, important anti-herbivory compounds. Of these three enzymes, we have obtained the crystal structure for AtIPMDH2. Using the crystal structure and knowledge of bacterial IPMDH, a mechanism for IPMDH was proposed. To test this model, eighteen different point mutants of AtIPMDH2 were generated to change specific active site amino acids. Each mutant will be expressed and purified for kinetic analysis. By assaying the activities of each of these mutants, we can gain novel insights into the mechanisms of not only AtIPMDH2, but also AtIPMDH3 and AtIPMDH1. The IPMDH activity assay monitors the reduction of NAD⁺ to NADH as the enzyme converts 3-isopropylmalate to 4-methyl-2-oxovalerate. Using this assay, the activity of each AtIPMDH2 mutant will be tested and kinetic parameters determined. This data will enable us to assess the roles of specific active site residues in the reaction mechanism of AtIPMDH2.
Toward a Better Understanding of...

Effects of Ritalin in rcTBI Animal Models

Scott O’Brien

Mentor: David Brody

Traumatic Brain Injury (TBI) is the single leading cause of permanent disability in people under the age of 45 in the United States. Patients often experience depression post-TBI, and very little is known about the best way to treat depression in this population. Animal models, more specifically mouse models, are used for testing different therapies for human injuries and diseases. Previous published literature demonstrates that TBI, when paired with fear conditioning, leads to increased depression-like behavior as well as decreased social interaction in these animal models. We hope to build upon these results by testing possible therapeutics that may have an effect on the depression-like and anxiety-like behavior that ensues post-TBI. Certain drugs, for example Ritalin, are often prescribed to patients suffering from cognitive decline due to previous TBI. Ritalin is a central nervous system stimulant and is known to have a wide range of side effects including nervousness, agitation, anxiety, insomnia, loss of appetite, nausea, vomiting, and dizziness. This experimentation focuses on Ritalin and its effects on the depression-like and anxiety-like behavior that ensues following TBI.
For low-lying Pacific Islands, the question is not if climate change will affect their nation, but how it will. With grim projections for increased frequency of extreme weather events, rising sea-levels, and changing rainfall patterns being supported by credible entities such as the IPCC (Intergovernmental Panel on Climate Change), Pacific Islands are taking seriously the need for adaptation strategies. Because it is not known precisely what form the effects of climate change will take, or when and where exactly they will strike, preparing to respond to these effects is a complex and difficult task.

One of the primary facets of life that will be affected by climate change is food production and acquisition. As climate change adaptation is a broad topic, this study focuses specifically on issues surrounding food security as well as investigating the current food system that exists. The objective of this study was to qualitatively assess both the perceived and anticipated effects from global warming on the Kingdom of Tonga, as well as investigate the myriad of approaches that exist to address these effects. This study consists of both semi-structured and in-depth interviews with key informants, collection of site-specific data about major stakeholders in the area, and analysis of secondary data obtained while living in Tongatapu, Tonga. Although the overarching objective of this research study is to understand the ways in which Tonga will be affected by global warming as well as how it is preparing to adjust, much of the data collected during the research period this summer is specifically about the present state of food systems on the main island. This information is useful in analyzing levels of resilience or vulnerability in relation to climate change, as well as formulating and evaluating future climate change related adaptation strategies.
Toward a Better Understanding of…

**Tenacity within Transience:**
**Factors Affecting Youth Homelessness and Stability Incorporated into Health**

*Nicholas Okafor*

*Mentor: Shanti Parikh*

The state of being homeless compounded with other marginalizing agents, such as disadvantaged sexualities and minority status, increases one’s vulnerability to a variety of health risk factors. This social status and as well as the lack of emotional, mental, and residential stability could worsen the situation and the condition of being HIV-positive, putting one at risk of being in poorer health. Likewise, being HIV positive raises the likelihood of losing stability and puts one at risk of being homeless. Many queer transient youth struggle with a variety of other issues involving identity, lack of familial acceptance, self-acceptance, and safe sexual habits. This study analyzes elements that initiate and propagate youth homelessness and transience in St. Louis and how organizations intervene to address issues surrounding their health. For this study, the definition of health has been broadened, encompassing sexual health, mental health, and housing as a means of health, incorporating how such stability can affect one’s overall well-being. This research has the translational aim of identifying gaps within the services being offered to allow such organizations to better serve this population. The overall objectives of the research project are to: 1. examine the structural, psychological, social, and household factors that make St. Louis youth vulnerable for homelessness, 2. analyze existing services and intervention models to reduce youth homelessness and sexual health risk factors, and 3. identify gaps in services for youth who are at risk for HIV transmission, morbidity, and mortality and opportunities to reach this population.
A left ventricular assist device (LVAD) is an artificial implant that is used in patients suffering from severe congestive heart failure to pump blood in place of the weakened heart. Despite the life-saving benefits that this device can have, LVAD placement can have serious complications, one of which is the formation of clots within the pump. To address this issue, it is necessary to develop a diagnostic imaging method that can help guide clinical management decisions regarding intra-pump thrombosis. In this particular experiment, a fibrin-specific radiolabeled tetrameric probe, $^{99m}$Tc-F4A, was selectively bound to clots placed within a functioning HeartMate II LVAD. While $^{99m}$Tc-F4A had been previously shown to possess a strong affinity for fibrin in *in vivo* mouse studies, LVADs generate enormous shear stresses that adversely impact the binding ability of most homing ligands. Because of this, it was necessary to show that the probe could still bind to the fibrin clots under the hostile conditions produced by the LVAD. Synthesized clots were placed into a specially designed phantom LVAD loop. When running the experiment, the loop was flushed with a mixture of plasma and PBS and the tetrameric probe was injected through one of the tubing connectors. After the pump was run, the loop was drained and the clot was removed and inserted into a gamma ray counting device. The measured radioactivity was over 5 $\mu$Ci, thus demonstrating that the agent is able to bind under the high flow rates of the LVAD. As such, future studies will focus on optimizing the radioactive dose and time for targeting while keeping the target thrombus stable and the pump blockage-free. The ultimate goal will be to develop specialized imaging devices that can externally detect the binding of the probe and to translate these findings into a clinical setting.
The Effect of LHX9 Levels on HCRT Neurons

Euna Park

Mentor: Joseph Dougherty

This research was largely based on reproducing the work found in the Muschamp et al. (2007), in which the HCRT/orexin neuron cell counts and protein levels were observed to increase during copulation and decrease with castration. The decrease caused by castration can be reversed with the treatment of estradiol benzoate (EB), a hormone replacement. The goal was to determine the effects of this same kind of study done in mice.

Hypocretin (aka orexin) (HCRT) encodes a hypothalamic neuropeptide precursor protein that codes for Orexin A and Orexin B. It plays a confirmed role in sleep and arousal regulation, and may also play a role in feeding behavior, metabolism, and homeostasis. The LHX9 gene is a transcription factor essential for the formation of gonads. Loss of this gene was predicted to cause a 30% decrease in the HCRT neuron count in a mouse model. This gene may also be important for normal development of HCRT neurons and normal sleep behavior.

Wild-type (WT) and LHX9 knockout (KO) mice were treated with either oil or EB injections. Out of the the WT mice, a few were castrated from both the oil-treated and EB-treated groups. I used a combination of immunofluorescence and microscopy to mark the HCRT neurons near the third ventricle in animals that were about a year old. The slide labels were covered so that the counts could be conducted blindly, and then ANOVA was used to analyze the data’s significance. Surprisingly, the results were different from those of the Muschamp study. While the LHX9 knockouts showed the expected decrease of HCRT, neither castration nor the EB treatment gave the expected results.
We report novel fabrication of amorphous titanium dioxide (TiO$_2$) microgoblet and microdisk whispering gallery mode resonators using sol-gel processes. A microgoblet demonstrated a Q-factor as high as $7.5 \times 10^4$, higher than any Q-factor previously demonstrated by TiO$_2$ based resonators. Microgoblets formed microdisks during XeF$_2$ etching with the release of the stress built up in TiO$_2$ thin film of 600nm thickness during deposition and HF etching. XeF$_2$ etching, which decreases the contact area of TiO$_2$ microdisk and the silicon substrate, released the built-up stress causing the disks to lift up. The angle of the microgoblet uplift increased with the extent of XeF$_2$ etching. Microdisks fabricated from TiO$_2$ film with a larger thickness of 1.2μm were able to resist the stress-release and maintained its disk shape regardless of the extent of XeF$_2$ etching. A given microgoblet or microdisk exhibited higher Q-factors when XeF$_2$ etching was minimal. Due to the negative $dn/dt$ value of TiO$_2$, resonance modes in these devices exhibited a linear blue-shift upon heating, opposite the red-shift of resonance modes in common silica microresonators. In water, due to high refractive index of TiO$_2$ (2.5–2.6), the TiO$_2$ resonators were able to closely maintain their Q-factors in air, while those of silica resonators degrade by a factor of at least 10 in water. As TiO$_2$ is a semiconductor with strong absorption of ultraviolet, the TiO$_2$ microresonators fabricated and studied here have future applications to UV sensing and potentially to photocatalysis and dye-sensitized solar cells.
In an increasingly globalized world, invasive exotic species pose one of the greatest threats to native ecosystems. However, not all exotic species are invasive, which leads to a pressing question: what traits do certain exotic plants have that lead to invasiveness? One challenge that any potentially invasive species must face is competition with other plants in the community. As part of a larger study of invasive plants at the Tyson Research Center, we study the role of competition in reducing fitness of six invasive plant species. Then we assess the plant traits that allow these species to overcome competition with differing degrees of success. For each species, we compare the fitness of individuals in a competitor removal treatment and a control treatment. For the competitor removal treatment, we remove all competitors from in and around the plots, and measure the dry biomass of competitors removed from each plot. For each species, we expect the amount of removed biomass in the competitor removal treatment to correlate positively with an increase in fitness over the control group. However, many of our species are not strongly affected by the competitor removal treatment. To investigate why, we examine two plant traits: (1) the chemical inhibition of one plant by another, and (2) disturbance adaption. We use a literature search to assess allelopathy. Then we measure specific leaf area—the leaf area per dry mass unit, for our six invasive species compared to the local community and use it as a proxy for rapid growth and disturbance adaption. Our results suggest that there are multiple mechanisms that allow exotic plants to become invasive, and that more work is needed to understand trends in how exotics exploit these mechanisms.
Dominant, perennial grasses are often used in early restoration because they are believed to play a critical role in maintenance of grassland systems. Despite their widespread use, past research is conflicted over whether grasses have a positive or negative effect on native and invasive plant diversity and population growth. Furthermore, grasses’ effects on native plants may change during extreme climate events (e.g. droughts), switching from facilitation to competition or vice versa. The objective of this study is to examine the effects of a dominant, perennial grass on co-occurring native and invasive plants under varying moisture conditions to better develop restoration methods that increase diversity while decreasing nonnative invasions. We hypothesize that dominant, perennial grasses will initially increase diversity before shifting from facilitation to competition, with stronger competition with invasive species and during drought conditions. In a greenhouse experiment, seeds of four native species were sowed in 40 pots. Pots also contained a perennial grass, *Schizachyrium scoparium*, and/or an invasive legume, *Lespedeza cuneata*. Half of the pots experienced drought conditions. We found interaction between the presence of grasses and water availability, which resulted in a relationship characterized by competition rather than facilitation. Grasses suppressed growth of both native and invasive herbaceous plants but did not affect diversity. We conclude that dominant, perennial grasses likely maintain their dominance in grassland ecosystems by out-competing all other species, not just invasive ones. This suggests that, while they are useful in preventing invasive plants, grass introduction is not the best tool for restoring diversity.
Engineering Human Embryonic Stem Cells to Provide Antibody-Mediated Immunity

Kranti Peddada

Mentor: Deepta Bhattacharya

Developing an effective vaccine against HIV and dengue continues to remain a formidable challenge. Recently discovered broadly neutralizing antibodies (BNA), however, provide a promising avenue for research. The goal of this project is to integrate BNA genes into the immunoglobulin (Ig) loci of embryonic stem (ES) cells so that individuals injected with derivatives of these modified cells can acquire long-term immunity. Currently work has focused on testing RNA-guided genome editing with the CRISPR-Cas system as a reliable method of knocking in BNA genes while deleting regions of the endogenous Ig loci critical to VDJ recombination. This strategy is being applied to influenza A and tested in 293 cells. Guide RNAs (gRNA) targeting regions in the Ig locus; a nickase vector co-expressing green fluorescent protein (GFP); and a targeting construct containing the influenza A BNA (FI6) heavy chain gene with homology arms complementary to regions of the Ig locus were synthesized and transfected into 293 cells. Fluorescence Activated Cell Sorting (FACS) was used to collect GFP positive cells, and a polymerase chain reaction (PCR) with primers flanking the endogenous and insert sequences of the genomic DNA of these cells was run. Visualization through gel electrophoresis indicated proper integration of FI6. When the assay was repeated for a second transfection without the gRNAs, however, proper integration of FI6 was still observed. This indicated that homologous recombination of the targeting construct with the Ig locus was possible without the gRNAs. Further testing should be done to determine if the gRNA system enhanced the level of homologous recombination or had no significant effect.
Some organic compounds are chiral, i.e. exist in the form of nonsuperimposable mirror images called enantiomers. The two enantiomers of the same compound often have different bioactivity, and therefore need to be prepared individually (in enantiopure form). Asymmetric catalysis is the most attractive approach to accomplishing this goal. As part of ongoing efforts in the Birman group, I have synthesized several axially chiral thiazolylidene carbenes, which are a new class of asymmetric catalysts. I have also demonstrated their efficacy in benzoin condensation. My preliminary results are expected to pave the way to improving the enantioselectivity in this and related reactions.
Increasing numbers of U.S. adults and children suffer from obesity, which places them at a higher risk for cardiovascular disease and diabetes. Understanding the mechanisms underlying diabetes-related cardiovascular disease is essential for developing future treatments. The peroxisome proliferator activated receptor-gamma coactivators (PGC-1a, b and PRC) are known to regulate mitochondrial biogenesis and function. Mammalian models suggest that the PGC-1 coactivators play significant roles in mitochondrial function in diabetes. However, knock-down of both PGC-1α and β is associated with neonatal mortality, so the loss of PGC-1 in older diabetic models has not been studied. This project aims to study the role of Spargel, the only Drosophila PGC-1 homologue, in the fly heart at baseline and in the context of diabetes. We examined the impact of Spargel knock-down in the fly heart tube on a control diet using optical coherence tomography (OCT) and found that Spargel-knockdown heart tubes have systolic and diastolic dilation, decreased fractional shortening, and higher heart rates. Interestingly, when we performed negative geotaxis, an exercise test, the Spargel-knockdown flies displayed more erratic behavior, which was inconsistent with our hypothesis that exercise tolerance would be impaired. To evaluate the impact on mitochondrial number and morphology, heart tube samples from larvae and adults have been prepared for mitochondrial imaging. In order to assess the impact of diabetes, Spargel-knockdown flies have been placed on a high sucrose diet, which is known to cause a diabetes-like phenotype. We will then reassess heart function by OCT, exercise capacity by geotaxis, and mitochondrial number and morphology by confocal imaging. Our data demonstrates that, similar to mammals, Spargel plays a significant role in maintaining cardiac function in Drosophila. We are particularly interested in loss of Spargel in diabetic flies; these studies are ongoing.
The sciences aim at discovering truth and disseminating knowledge. Do their practices as social systems complement these epistemic aims? One noteworthy feature of the sciences today is that distribution of results often depends on their direction: positive or statistically significant results are significantly more likely to be published (and thus widely distributed) than negative or statistically insignificant results. How does this affect the likelihood that the community will reach the correct answer? To investigate this, computer simulations of community learning were performed, with surprising results: moderately biased communities outperformed unbiased communities. These results challenge an assumption behind much of the publication bias discussion: Positive bias does not necessarily decrease accuracy. It can, in fact, increase it. This is because suppressing the flow of negative information encourages some individuals to continue experimenting in situations where fully informed, epistemically motivated, individually rational agents would stop—at the community’s expense.
Previous studies have shown that odors can be represented with a unique neural code of ensemble projection neuron (PN) firing patterns in the olfactory processing area of the brain. These firing patterns can be represented as a three-dimensional odor trajectory using standard dimensionality reduction techniques. In collaboration with a graduate student and a post-doctoral fellow, an experiment was implemented to determine how ensemble PN activity correlates with behavior. Neural data showed that the odor trajectory for a binary mixture of two odors typically lies between the individual odor trajectories. Behavioral tests were also performed in order to correlate with neural data. One behavioral task utilized appetitive conditioning to test a locust’s ability to recognize and respond to the conditioned odor. Both the neural and behavioral data suggests that locusts can differentiate between odors in a variety of mixtures. However, one odor pair, citral and geraniol, had a mixture odor trajectory that closely followed the geraniol trajectory instead of staying in between the two single odor trajectories. To address this issue, we developed a T-maze paradigm to test innate locust behavior to various odors. This assay showed that locusts were innately attracted to geraniol but repelled by citral. When a mixture of geraniol and citral was presented in the maze, locusts were primarily attracted to the mixture, which was consistent with our neural results. These results suggest that geraniol masked the locust’s responses to citral when they were presented in an overlapping fashion. Furthermore, these results indicate that ensemble PN firing patterns correlate well with both conditioned and innate preferences for insect olfaction.
The ongoing endangered species epidemic has led to an increased interest in preserving and protecting the earth’s threatened species. This attention has come at the expense of so-called “thriving species,” such as species that are not federally listed under the Endangered Species Act (ESA). Since one criticism of the ESA is that species are often not listed until they become extremely rare and thus difficult to manage and conserve, work on common species is crucial to keep them from becoming endangered.

Through a case study in the endangered species capital, Hawaii—where one-third of all of the United States’ endangered species call home—I studied a declining, native, common seabird species, the wedge-tailed shearwater (*Puffinus pacificus*). Our team tracked their nesting success on a preserve established by the Hawaii Audubon Society. The timing (mean, median, minimum, maximum) of the dates when eggs were laid for the colony were computed and analyzed. Interestingly, the peak in the number of eggs laid coincided with a full moon, a previously unknown phenomenon. We conducted preserve-wide censuses during the brooding and chick-rearing periods to study the long-term colony progress over time and confirmed the colony’s ongoing success. This study contributes to necessary research on the country’s declining but not yet listed species to maintain their current population levels and continue to provide important ecosystem services.
Proper heart function requires heart cells to efficiently generate energy. Ketone bodies are an energy source that is produced by the liver and used in the heart, muscle, and brain when other energy sources are unavailable. Ketone bodies are oxidized in myocardial cells in part by the mitochondrial enzyme SCOT before entering the tricarboxylic acid cycle. In our lab, we genetically blocked ketone body oxidation in myocardial cells of mice (SCOT-Heart-KO mice) and observed increased fatty acid oxidation and signatures of oxidative stress. However, cardiac function in these mice at baseline was normal. In our lab, we investigated possible compensatory mechanisms that support normal cardiac function under conditions of oxidative stress. Akt is a protein that plays cardioprotective roles when phosphorylated (activated), including inhibition of apoptosis and cell proliferation. To determine whether Akt signaling played cardioprotective roles in SCOT-Heart-KO mice, we quantified the phosphorylated-Akt to Total-Akt ratios through Western blot. We observed nearly a 2-fold increase in Akt activity in SCOT-Heart-KO mice, suggesting that Akt signaling is increased in SCOT-Heart-KO mice to maintain normal heart function. To quantify the phosphorylation of Akt target proteins, we ran another Western blot and found that, indeed, phosphorylation of Akt targets also increased 2-fold in SCOT-Heart-KO mice. To determine specifically which Akt target proteins were phosphorylated, we tested Bcl2 Associated Death Promoter (BAD) and Hexokinase II (HK2), two known targets of Akt. Akt phosphorylates and inhibits BAD, a pro-apoptotic protein to promote cell survival and Akt phosphorylates HK2, which prevents mitochondrial swelling by maintaining membrane potential. Although BAD was below the detection limit of the Western blot and HK2 was difficult to test, through mitochondrial swelling assays, we determined the swelling rate of the mitochondria using CaCl₂ as a catalyst and observed increased swelling in SCOT-Heart-KO mice mitochondria.
Rice is a popular staple crop around the world and is vital to the economy of many countries such as the United States and China. However, rice has not always been an edible crop that farmers controlled to plant and harvest. Thousands of years ago rice was more like a weed that took over fields; unfortunately, today rice has begun to evolve into its weedy relative and studying this change is important to farmers.

Determining weed traits in rice is important because weeds are responsible for negatively impacting farmers’ crop yields. Weedy rice has developed immunities to herbicides, making it a nuisance. Since weedy rice seems to adapt easily to new herbicides, it might be easier to understand why the rice is weedy in the first place. Studying weedy characteristics in rice could create better crop yields, thus saving farmers billions of dollars.

One way to tell the difference between rice and weedy rice is to look at the tiller angle (the way the plant grows upright). A greater tiller angle is a characteristic of weeds while a smaller angle is common in rice. Using the pcr product, I am able to sequence the gene that is helpful in determining the different coding regions of the TAC1 gene. The enzyme EcoN1 cuts at an A site but not a G site; this is important because one can tell whether the plant has a wider tiller angle (A nucleotide) or if it has a small tiller angle (G nucleotide). Knowing which nucleotide codes for tiller angle is a great advancement; soon scientists may change wide tiller angle for small tiller angle and possibly stop weedy rice from spreading from farm to farm.
Cerebrospinal fluid (CSF) is a complex biological fluid produced primarily by the choroid plexus, a vascular structure within the cerebral ventricular system. In a condition known as hydrocephalus, excess CSF builds up within the brain ventricles due to either poor CSF absorption or blockage within the ventricular system. While a number of variants of hydrocephalus exist, perhaps the most common and debilitating is congenital hydrocephalus (congenital HC). Congenital HC affects infants and young children at a critical time in neurodevelopment and thus has potentially devastating implications. At present, neurosurgical management of congenital HC remains constrained by significant limitations in diagnostic and therapeutic capabilities; indeed, the most basic question—Is this hydrocephalus?—is often difficult for clinicians to answer, as ventriculomegaly resulting from other conditions is common in this age group. The lab of David Limbrick has shown a strong increase in APP (and some of its isoforms), tau, and other proteins in the CSF of children with post-hemorrhagic hydrocephalus, changes that are associated with ventricular size. Using Elisa kits we measured the levels of APP, sAPPα, sAPPβ, Aβ1-40, Aβ1-42, tau, and p-tau in CSF obtained from 25 age-matched human infants and children in each of 4 different groups: 1) no known neurological disease; 2) congenital hydrocephalus; 3) ventricular enlargement without hydrocephalus (VEWOH); and 4) Chiari type I malformation. Our results showed significant elevations in APP, tau, and p-tau but not Aβ1-40 or Aβ1-42 in patients with congenital hydrocephalus thus leading us to believe that these proteins can be used as detection methods for the disease.
Approximately 900,000 Americans have little to no control over their hands due to motor neuron diseases (MNDs), such as multiple sclerosis. Advanced-stage MNDs result in significant loss of voluntary motor control, excluding many existing assistive technologies. However, brain computer interfaces (BCIs) that use brain signals do not require muscular control. However, BCI technologies are expensive and mostly restricted to research uses. We endeavor to design a BCI using commercially-available components that allows subjects to navigate an eBook hands-free.

The eyeReader uses steady-state visually evoked potential (SSVEP) signals found in the brain’s occipital lobe. Concentrating on a blinking stimulus in the visual field induces an SSVEP brain signal that oscillates at the same frequency as the visual stimulus, which can be detected with electroencephalography (EEG). To use the eyeReader, the subject concentrates on one of two squares (representing a left or right page turn) blinking at different frequencies. The SSVEP signal is recorded with the inexpensive, non-invasive, and easy-to-use Emotiv EPOC EEG headset. A decision tree machine learning algorithm was used to determine if the user was concentrating on one or neither of the blinking stimuli. The algorithm constants were determined by training data collected over 10 minutes, in which the user is asked to concentrate on each blinking stimulus and nothing. Choosing to concentrate on one of the blinking stimuli served as control signals to flip pages of the eBook left or right. The eyeReader was tested on two healthy subjects to validate our detection method for 101 trials total. The eyeReader had 86.2% detection accuracy and could detect a control signal at least every 10 seconds (a 5.2 bits/minute information transfer rate).
The current study is a truncated replication of McDaniel, Howard, and Einstein (2009) in which the Read-Recite-Review strategy (3R) was validated. 3R is a study strategy wherein students read a text, immediately recall as much as they can, then review the text again. This strategy was compared with a read, then re-read, and note-taking strategies. On one-week delayed tests, the 3R method proved robustly beneficial to free recall assessments, as well as requiring less time than the other strategies. In the current study, read-recall and read-explain conditions were compared in order to determine the best form of retrieval practice. We hypothesized that the essay condition would elicit superior performance on inference questions compared to the standard recall condition, with both having equally large free recall benefits. The results indicated that the predicted manipulation was not in any way successful, as the read-recall manipulation yielded significantly better assessment scores than read-explain.
Toward a Better Understanding of...

**3D Sensing for Automatic Robotic Control**

*Joshua Remba and Andrew Schoer*

*Mentor: Arye Nehorai*

With the advent of more advanced robots, the need for robots to interact with their environment through visual stimuli is increased. Our project utilizes the 3D sensing technology of the Xbox Kinect to allow a Fanuc robotic arm to automatically see and pick up a target. Our overarching goal was to create a framework for future projects, allowing the Kinect and the robot to interact. Through utilization of pre-written C++ code for the Kinect, a memory sharing DLL, and a LabVIEW framework, we were able to accomplish that goal. Technology such as this can be utilized in factories to speed up production rate and lower manufacture cost by allowing the process to be more dynamic. When the robot has sensing capabilities, it can move to pick the target up however is necessary regardless of its orientation. Because this was the first project of its type done in the ESE department at Washington University in St. Louis, we started from scratch. While the project is not yet completely automated, we have successfully located a target marker using the Xbox Kinect with enough accuracy that the robot could pick it up. We hope that our work with the Xbox Kinect and the robotic arm will help future undergraduate research projects. The possibilities range from the immediate next step of automatically picking up a randomly oriented marker to playing catch with the robotic arm. The code we developed for the interface between the Kinect and Fanuc arm allows the robot to interact with its environment, which will expand the available applications of the robot.
The cholesterol trafficking pathway is highly regulated by the cell and is important to metabolism. We suspect a novel role that noncoding RNA, specifically small nucleolar RNAs (snoRNAs), play in this pathway. We used a mutant Chinese Hamster Ovary (CHO) cell line isolated from a genetic screen which showed a decrease in esterification of plasma-membrane derived cholesterol. The I5 mutant was identified to be haploinsufficient in the U17 H/ACA snoRNA. Previous studies have shown that Box H/ACA snoRNAs assist in rRNA pseudouridylation. We used a microarray to identify genes whose expression change between U17 knockdown and wild type cells and found potential non-rRNA targets. We found that a decrease in U17 correlates to an increase of these target mRNAs as well as protein levels. The goal of the project was to establish this relationship in the context of cholesterol trafficking, in particular by determining the effects of U17 on target mRNA half-life and the effect of target mRNA overexpression to the cholesterol esterification phenotype.
The chemistry and reactivity of Pd(0), Pd(II), and Pd(IV) have been well characterized and show great versatility of the Pd metal center in synthetic organic chemistry. They allow one to generate C-C bonds and functionalize C-H bonds. However, the Mirica group has synthesized and isolated a ligand, which stabilizes an unprecedented, mononuclear Pd(III) complex that has been shown to form carbon-carbon bonds with just air and light. The two “arms” of this “N4” ligand can be almost any alkyl group and the group has synthesized a whole series of such ligands, that have been used to extensively study the Pd(III) center as well as other metal centers. However, they have had trouble synthesizing asymmetric derivatives of the N4, in which the two “arms” are different. To accomplish this, we altered one step at the beginning of the synthesis to produce 2-hydroxymethyl-6-(bromomethyl)pyridine, as opposed to the symmetric 2,6-bis(bromomethyl)pyridine.

The synthesis of this intermediate has been reported by literature in approximately 40% yield, but we were able to optimize the procedure by utilizing a bi-phase as the solvent. With this intermediate, we added t-butylamine in excess to selectively produce the secondary amine, with which there are two schemes to explore: brominating the alcohol group and adding another equivalent of the intermediate to produce the tertiary amine.

In parallel with these experiments, we also attached Ts-NH₂ by a literature procedure in 63% yield and used an improved column procedure to isolate not only the tertiary amine, but also each side product as well. Then, we brominated it using thionyl bromide, which required high excess of thionyl bromide, but the desired product was isolated in 81% yield, leaving us only a few steps away from closing the pyridinophane ligand and producing the group’s first asymmetric ligand.
Currently, there is a lack of public awareness about the importance of plant conservation and the methods that are used to preserve critically rare species. This project focuses on the central role and importance of plant micropropagation in the conservation of Hawaiian flora and the techniques used in this process. Micropropagation is the tissue culture and cloning of plant materials. This practice increases the population size of individual species in a relatively short time, thus saving dwindling species from the brink of extinction. In the lab at the Lyon Arboretum, which houses the only micropropagation facility in Hawai‘i, I worked with taro (*Colocasia spp.*), a culturally significant crop plant, as well as with an endangered species of mint. Varieties of taro are being cultivated in order to safeguard genetic variations and preserve crucial elements of Hawaiian culture, whereas the mints are micropropagated to proliferate them. Since the two species have different growing points, I used distinctive practices on each that catered to their unique methods of growth. Using Murashige and Skoog medium, I successfully cloned these plants via *in vitro* cultivation and allowed them to thrive. Through these processes, I was able to effectively propagate around 300 plants, thus increasing the numbers of these species. The use of micropropagation in the conservation of endemic endangered species in places like Hawai‘i will preserve millions of years of floristic evolutionary history.
One of the most effective methods of evaluating how neural circuits work is to compare their response (e.g. extracellular activity) before and during disruption of signal transmission through specific information pathways using pharmacological agents. One drawback to this method is that drug spread could influence the activity of nearby cells and indirectly affect the measurements. Thus, it is essential to understand the effective spread of the drug in tissue.

Here we measure the effective spread in nervous tissue of two widely used GABA receptor antagonist drugs: SR-95531 (gabazine) and Phaclofen. Gabazine is a GABA$_A$ antagonist, and Phaclofen is a GABA$_B$ antagonist. We used custom made electrodes consisting of compound multi-barrel and single glass electrodes to inject the drugs iontophoretically while recording the activity of a cell located at a known distance from the injection site. Neuronal activity was recorded in the anesthetized mouse through one of the barrels of the multi-barrel electrode during injection of Gabazine or Phaclofen through the single (distant) glass electrode.

We found that Gabazine spread can be fit by a logarithmic function with a time constant (distance from injection site at which effect was reduced by 63.2 %, which we call it here “space constant”) of 149 μm and 162 μm when 50 μA and 100 μA were applied respectively. Phaclofen spread with a space constant of 114 μm and 59 μm when 50 μA and 100 μA were applied respectively. Overall, these results provide important quantitative information to interpret the data obtained by studies using this type of injection in nervous tissue. Our choice of drugs makes these results relevant for a large number of studies; GABA is a ubiquitous inhibitory neurotransmitter in the central nervous system and GABA$_A$ and GABA$_B$ are two of its most abundant receptor types.
Toward a Better Understanding of...  

**SEM Analysis of Stardust Analogue Craters**  
Charles Schlaepfer

*Mentor: T. Kevin Croat*

The NASA Stardust mission aimed to gather particulate from the nucleus of the comet Wild-2—a comet that was formed ~4.57 billion years ago during the birth of the primitive solar system—to determine the composition of comets and to find presolar grains held within Wild-2 unchanged from the time of its formation. Due to the high impact speed of the probe through the tail of Wild-2, the aerogel assembly failed to safely capture smaller grains for analysis; however, the Al foil between aerogel holders proved adept at capturing at least some of these grains in bowl shaped craters. Our primary goal is to continue to lay the foundations for analysis of these craters in the Al foil by using analogues of those impacts to determine the survival rate and impact characteristics of refractory presolar grain compounds against other cometary materials. Field surveys were conducted on an analogue that contained a refractory mix of projectile materials, G080709 South foil 2, and an analogue of meteoritic projectile material, Acfer 094 2B. Certain phases of minerals and amorphous material were indistinguishable without FIB cutout and TEM analysis. However, now armed with a large sample selection, FIB-TEM can be conducted on analogues furthering the results of this study to develop relationships between known impacting materials and primary characteristics of craters—depth to diameter ratio and EDX Spectra. Our results are not conclusive definitions of fine presolar grain impact characteristics but do provide a large data set to draw upon when searching true Stardust foils for craters containing presolar isotopic and chemical data.
Mosquito-borne disease is (re)emerging worldwide and is becoming an increasing public health threat, particular in urban areas. However, many factors influencing the larval dynamics that regulate biting adult populations in urban landscapes are still unknown. This study evaluated how a common urban water pollutant and the sequence of larval hatching in container habitats influence the competitive interactions between two urban disease vectors, *C. pipiens* and *A. albopictus* larvae. The study demonstrated strong evidence of asymmetrical competition, where *A. albopictus* developed faster and had higher pupation rates in all treatments. Higher nitrate levels in the larval environment resulted in larger *A. albopictus* females and higher emergence and faster time to emergence for *C. pipiens*. There were also indications of possible interactions between nitrates and priority effects. These results give insight into the abiotic factors important to each species and each species’ life strategy, while also providing vital information that can be used to predict future disease risk from these vectors on a local scale.
Toward a Better Understanding of…

Crowdsourced Cross-Cultural Accounts of World War II: Is Wikipedia an Agent of Collective Memory?

Ruthie Shaffer

Mentor: Henry L. Roediger III

This project sought to use WWII entries on Wikipedia pages of various languages to identify key events in the timeline of the war that were common to the Wikipedia pages of many countries, as well as key events that were idiosyncratic to the pages of specific countries. The purpose of this project was to evaluate Wikipedia as an agent of collective memory (“a form of memory that transcends individuals and is shared by the group” [Roediger et al. 2009]). Because Wikipedia serves as a fairly open online forum for which many people can contribute and where people often look for basic information on a subject, it appears that Wikipedia may in part reflect and shape collective memory. In order to collect information about what events in WWII were emphasized on the various pages (defined as percent of word count), information was first translated into English using online translators. Word counts were then obtained for each event (for example, a battle) that was discussed on the Wikipedia page. Finally, relative word count for each event (percent of total word count on the specific Wikipedia page) was used to identify the top 15 events within each language’s Wikipedia page. Results show that certain events or time periods tended to receive more emphasis across many of the language’s Wikipedia pages (e.g., the German invasion of the USSR was in the top 15 most emphasized events in seven out of the ten language’s Wikipedia pages), but each language page also contained major events not emphasized by pages in other languages. This pattern suggests that the Wikipedia pages in different languages reflect somewhat varying collective memories across countries, and that these pages may in turn influence collective memory within those languages for current and future generations.
By looking at network formation and risk associated with creating relationships, Blume et al. (2011) were able to model cascading failure over multi-step paths using graph theory. Applications of such failure include financial contagion, modeling epidemic disease, and the exposure of covert organizations to discovery, among others. In graph theory terms, the goal in all of these applications is to form graphs in which cascading failure is unlikely. Blume et al. were able to prove that the formation of disjoint cliques, or subsets of a graph in which all vertices (participants) in each subset do not form edges (relationships) with vertices not in the subset, has this property.

This research focuses on how Blume’s model of financial contagion, the transmission of financial shock from one participant to another, can be applied to recent macroeconomic events. The Financial Crisis of 2008 was an event that demonstrated the consequences of contagious risk in networks. It is commonly accepted that higher risk yields higher reward. Higher risk taken by banks in 2008 posed a threat not only to the two primary participants in the agreement, but also all participants in the network of agreements that could be reached via multi-step paths. In addition, we show how social optimality affects payoffs and the stability of economies by analyzing banking systems in countries with centralized and decentralized governments. Lastly, we explore an application related to market structure. Electronic, digital currencies, such as Bitcoin and Canada’s Mintchip, are commonly used as a form of investment. However, these investments solely rely on the willingness of users to accept this form of currency. It has been shown that a large portion of Bitcoin investments default due to the anonymous nature of the transactions.
Glades are fragmented desert ecosystems that historically burned at least once a decade. They have thinner soils and higher median temperatures than the surrounding forest. In fire-dependent systems such as the Ozark glades, fire is necessary to maintain the richness and diversity of flowers and thus the native bees that depend upon them, and may open the forest surrounding glades, allowing for the further dispersal of seeds and bees. However, fire also destroys the woody-stem resources that cavity-nesting bees require for reproduction. Therefore, in flower rich areas where bees have plentiful food but little habitat suitable for reproduction, fire may restrict bee populations. As bees decline across the globe, it becomes more vital to determine how to manage bees so that they have the best chance of survival. In order to determine if fire limits bee and flower diversity in glades we sampled ten glades, quantifying the amount of flower resources, suitable nesting resources and the bee diversity in each site. Five transects were used in each glade for bee netting, flower sampling, and quantifying the available amount of woody stems. Bee bowls were also used to fully sample the bee population. United States government canopy cover data will be used to see how dispersal has been effected in systems where fire is present. While this experiment has not yet been completed, after the data has been analyzed the results can help us improve the flower and bee populations in Missouri. If fire does limit bees, land managers can alter their restoration techniques to allow for an increase in these native species by adding more suitable habitat, such as nesting blocks, helping restore declining populations.
Toward a Better Understanding of…

M2 Macrophage Purification and Investigation of Its Role in IL-13 Pathway of COPD Pathogenesis

Niki Song

Mentor: Michael Holtzman

Chronic obstructive pulmonary disease (COPD) is the third leading cause of death in the U.S., with its incidence increasing every year. Characterized by chronic bronchitis and emphysema, this disease progresses slowly and is often fatal. Unfortunately, there is still a lack of research being done to investigate the causes and treatments of the disease. We are studying the inflammatory pathway that leads to COPD in order to define the contributions of different immune cells and signaling pathways to chronic airway disease.

The immune system has long been known to drive the acute response to infection, but only recently has it been found that this acute response can translate viral infection into chronic inflammatory disease such as COPD. Analysis of the response to infection by parainfluenza Sendai virus in a mouse model showed that levels of IL-13 increased in mice with COPD. IL-13 is a cytokine (signaling molecule) involved in the inflammatory pathway, which induces airway hyper reactivity, mucus cell differentiation, and overproduction of mucus. These effects combined lead to obstruction of the airways and development of COPD. Production of IL-13 is largely driven by monocytes, which differentiate into macrophages, amplifying IL-13 production.

We have confirmed the contribution of M2 monocytes/macrophages to IL-13 production in mice, and are hoping to characterize the same pathway in humans. Thus, our goal is to isolate M2 cells from whole lung tissue and conduct in vitro studies and genomic analysis. We can also compare M2 cell populations between healthy and sick lung tissue to observe for significant differences in size and number.

Ultimately, we hope to better understand the contribution of M2 macrophage in the development of COPD.
Ebola virus, one of the Filoviridae family, is a highly contagious virus that has a mortality rate approaching 90%. Ebola virus often goes undetected in the first stages where its symptoms resemble those of flu and even the common cold. However in the later stages Ebola infections cause hemorrhagic fevers and systemic multi-organ failure. Despite its devastating effects, Ebola is understudied and little is known about how it evades the immune system and replicates inside human cells. Consequently, no approved vaccines or treatments are available for Ebola virus infecting to humans.

The genomes of filoviruses typically code for only 7 proteins. One of these proteins, VP24, a matrix protein, has been identified to inhibit the immune response by blocking interferon signaling. Thus, the goal of this project is to determine the interactions between VP24 with proteins from the interferon pathway. To reach this goal, the structure of VP24 was studied to identify protein-protein binding domains in VP24, and to explore whether these binding domains interact with immune-response proteins. Completion of these goals will clarify how Ebola and likely other filoviruses evade the immune response, essential information that will help lead to treatments or cures for Ebola.
The ciliated protozoan *Tetrahymena thermophila* maintains both germline and somatic copies of its genome in functionally distinct micro- and macronuclei, respectively. During conjugation, they discard the existing somatic macronucleus and replace it with an undifferentiated copy derived from their germline micronucleus which is then subject to genome wide rearrangement; a process that cuts out nearly 50MB of DNA. Prior work in the Chalker lab has demonstrated that there is a vital role for small RNAs in the excision of the germline-limited sequences, called Internal Eliminated Sequences (IESs), from the developing *Tetrahymena* genome. These small RNAs, called scnRNAs, are generated from meiotic transcription of the micronuclear genome and are responsible for the sequence recognition of IESs, facilitating their excision. Many of these IES’s contain repetitive regions that, when scnRNAs are mapped onto their sequence, match these repetitive sequences most abundantly. Current experiments aim to test the hypothesis that the scnRNAs generated in the micronucleus during meiosis target the homologous IES in the developing macronucleus in trans. It has been found that removal of genomic R IES decreases the excision in a plasmid-based copy. Most of the deleted regions show little to no rearrangement in the knockouts, a result that can likely be attributed to the loss of production of the scnRNAs unique to that sequence. However, some rearrangement still remains. Currently, experiments are being done to test whether removal of these repetitive sequences from the plasmid copy abolishes all excision, as is hypothesized. This result will show that scnRNAs produced during meiosis target IESs, in trans, in the developing macronucleus.
Toward a Better Understanding of…

Surrealism as a Uniting Force:
How Two Estranged Artists Found Their Identities and Attempted to Communicate through a Trans-Atlantic Art Movement

Annie Stanford

Mentor: Ignacio Infante

This project is an investigation of Salvador Dalí and Federico García Lorca, a Surrealist artist and poet respectively, and how their relationship with one another grew and was ultimately fractured through their embrace and rejection of Surrealism during the Avant-Garde in Spain and the United States. The two met as students in Madrid, Spain, a time during which both focused on a traditionally academic artistic style, with Lorca adhering to the gypsy culture of his native Granada, and Dalí focusing on the aesthetic canon of Western art with influences especially from the Northern Renaissance. As the two became close and ultimately inseparable friends, their styles and influences on one another began to blend, with Lorca priding Dalí’s adherence to the traditional and Dalí praising the balladic nature of Lorca’s poems. However, Dalí’s thirst for fame, as academic art was slowly being replaced by a desire for the new and the Avant-Garde, combined with Lorca’s homosexuality ultimately pushed both of them towards Surrealism, with Lorca relocating to New York and Dalí remaining in Europe. With Dalí’s style change came a complete rejection of Lorca as an individual, with Dalí sling many personal and private insults towards him, many of which are difficult to understand for scholars today. Despite these insults, Lorca attempted to use Surrealism to attract Dalí’s attention and rekindle the relationship, though he was ultimately unsuccessful even after his return to Spain up until his assassination in 1936. Through a thorough investigation of Lorca’s poems and personal drawings, Dalí’s art and published essays, and the personal letters the two exchanged throughout their lives, I will trace the personal motivations behind their changing styles and the reason why this once powerful duo fell so quickly into estrangement.
Informal science education encompasses the science learning that takes place outside the traditional formal classroom environment, such as explorations that occur in museums, apprenticeships, or participation through social media. This type of education tends to be more engaging by nature, as it does not pressure the student for a grade but rather piques curiosity and allows them to freely explore a subject that interests them. Because informal does not mean unstructured, the engagement of the educator can be just as necessary as that of the students. I explored the role of the educator in an informal science education setting at the Tyson Research Center. One project involved the creation and execution of a lesson plan for a weekly high school student-directed discussion to encourage dialogue that connects the students’ ongoing projects in their research apprenticeships to current concepts in the field of ecology. A second project was the adaptation of an existing board game, which uses Missouri plant species to demonstrate displacement in an ecosystem, to a Spanish-language version in which Ecuadorian species demonstrate the same concept for use in Galapagos National Park. A third project focused on strategy for the social media presence of a current movement ecology study to promote awareness and interaction, creating an interface between researchers and the public. Informal science education communicates knowledge in a manner that is engaging for the student and hopefully results in increased and sustained interest. I explored how different approaches to informal science education can be implemented to encourage student interest and participation in order to promote science literacy.
RNA interference—an endogenous system in eukaryotic cells by which double-stranded RNAs mediate the degradation of complementary mRNA—can be exploited by small interfering RNAs (siRNAs) to silence any gene in the human body. However, siRNA faces a host of delivery barriers that have limited its clinical translation. Our recent work has shown safe and effective delivery of siRNA using PEG-shielded, pH-responsive, endosomolytic, siRNA-loaded NPs (siNPs) formed from copolymers (poly(EG-b-[BMA-co-DMAEMA])). In this study, we have synthesized and tested a nanocarrier variant based on a new polymer (poly(EG-b-[BMA-co-DMAEA])) that was designed to increase siRNA intracellular bioavailability through a combination of endosomal escape and improved siRNA release based on polymer charge reversal via self-catalyzed hydrolysis of the cationic monomer DMAEA into anionic acrylic acid.

The polymers were synthesized with 50 mol% BMA content in the second block. Förster Resonance Energy Transfer (FRET) spectroscopy was used to measure release of siRNA. FRET confocal microscopy was used to image siRNA intracellular release within cancer cells. Gene knockdown was assessed following delivery of luciferase siRNA to luciferase expressing cells.

We found that HDG siNPs showed an increased rate of siRNA release when compared to non-HDG siNPs. Similarly, FRET confocal microscopy revealed increased intracellular release of siRNA following delivery with HDG versus non-HDG siNPs. Cellular uptake of HDG and non-HDG siNPs was similar, but HDG siNPs produced significantly greater gene silencing relative to non-HDG siNPs, achieving approximately 75% protein level silencing.

In conclusion, HDG siNPs showed increased intracellular siRNA release, which, importantly, yielded significantly increased gene silencing bioactivity. These data confirm that intracellular siRNA release is a major barrier limiting the bioactivity of cationic siRNA delivery systems and suggests that HDG siNPs are a promising delivery platform that warrants further development toward use in vivo.
Sediment deposition has adverse effects upon coral reefs-disrupting the sunlight’s path into the ocean and hampering the process of photosynthesis, coating the coral in layers of silt and other pollutants, and negatively altering the overall water quality. This research was part of a larger project conducted by staff of The Nature Conservancy (TNC) and was located in Kane‘ohe Bay, Hawai‘i. We quantified whether or not the presence of a wetland reduced sediment deposition in a marine ecosystem. To test the utility of wetlands (specifically taro patches, commonly known as lo‘i fields) we measured levels of turbidity via a 650A and a SONDES device. One SONDES was submerged under water and placed at the entrance of the Taro field and the other device received the same treatment, but was placed at the exit of the field. The SONDES devices remained in these positions for weeks at a time. To collect the data we connected the 650A to both of the SONDES and recorded the turbidity levels for the water from noon of each day at the entrance and the exit of the lo‘i fields. Results showed the opposite of what we expected, turbidity out was higher than turbidity in. This diversion from our hypothesis might be explained by the lack of pulse rain events and a high level of construction and manual labor in the fields that disrupted the sediment during the time of our data collection. A previous study by TNC showed that the taro wetlands did effectively reduce sediment levels, most significantly during pulse rain events. Looking at this larger data set and the general trends, we conclude that wetlands are most critical to lessening sediment deposition immediately following major rain falls and are a crucial “barrier” for protecting and preserving coral reefs.
Toward a Better Understanding of…

Preliminary Survey and Studies on the Spray Technology for Oxy-coal Combustion Systems

Biao (Toby) Tong

Mentor: Benjamin Kumfer

Despite rapidly growing interest in harnessing energy from various unconventional renewable sources in recent decades, coal, along with other conventional fossil sources of energy, remains significant in global energy generation. With the goal of reducing pollutants and boasting energy production efficiency of coal-based processes, I sought to advance coal-based combustion technology development. The project was focused particularly on spray technology for Coal-water Slurry Fuel (CWSF) and coal-biomass co-firing experimentation under oxy-fuel conditions, and the design of associated equipment. In addition, a literature survey of previous studies on a novel coal-biomass slurry fuel was conducted to examine its feasibility. Subbituminous Powder River Basin (PRB) coal was used in the study. Preliminary experimental results were obtained for the coal-biomass co-firing studies. Though the CWSF project is still largely in progress, I have been able to amass, design and manufacture the required experimental equipment, and am ready to move on to the next step—the characterization of CWSF flame in “Junior”, a cylindrical, horizontally-fired 30 kWth combustor with a 14 cm x 78 cm combustion section, followed by a 37 cm x 120 cm burnout section.
NAD+ is a critical component of both energy and signaling pathways. Here we investigated the link between NAD+ and glioblastoma multiforme (GBM) stem cells (GSCs) through NAMPT, the enzyme that catalyzes the rate-limiting step in the NAD+ salvage pathway by converting nicotinamide to nicotinamide mononucleotide (NMN). We found NAMPT to be over expressed in patient derived GSC’s lines of varying subtype. Inhibiting NAMPT with the administration of drug inhibitor FK866 had little effect on cell death but caused a decrease in proliferation. Most striking, was FK866’s inhibition of self-renewal, accompanied by a decrease in the expression of ID-1 and rescued by NMN administration. We have established a link between the levels of NAD+ and a cancer stem cell’s potential for self-renewal, possibly in a pathway that involves ID-1.
For people with insulin-treated diabetes, severe hypoglycemia can be fatal. Sudden deaths due to hypoglycemia are thought to be mediated by lethal cardiac arrhythmias. It has been shown that rats previously treated with recurrent moderate hypoglycemia have remarkably less mortality than untreated rats during severe hypoglycemia. To test the hypothesis that recurrent moderate hypoglycemia has a pre-conditioning effect to prevent cardiac arrhythmias during severe hypoglycemia in a diabetic model, 9-week-old Sprague-Dawley rats were injected with streptozotocin to induce diabetes two weeks prior to a 3 hour hyperinsulinemic (0.2 U kg\(^{-1}\) min\(^{-1}\)) severe hypoglycemic (10-15 mg/dL) clamp with simultaneous electrocardiogram monitoring. For three consecutive days prior to the clamp, diabetic rats were injected with insulin to maintain moderate hypoglycemia (30-60 mg/dL) for 90 minutes (RH-recurrent hypoglycemia; n=5) or with saline (CONT-control; n=4). Compared to CONT rats, RH rats required significantly higher glucose infusion (3.5±0.7 vs. 1.6±0.7 mg kg\(^{-1}\) min\(^{-1}\)) during severe hypoglycemia (indicating a blunted counterregulatory response). RH rats had 7-fold less episodes of 2nd degree heart block during severe hypoglycemia than CONT rats (4±2 vs. 26±4 per min) and had 10-fold less premature atrial contractions (0.03±0.02 vs. 0.3±0.2 per min). RH rats had significantly fewer seizures than CONT rats (1.5±0.2 vs. 3.4±0.1 per hour). Mortality was reduced in RH rats compared to CONT rats (0% vs. 33% mortality). In conclusion, recurrent moderate hypoglycemia had a pre-conditioning effect and significantly reduced severe hypoglycemia-induced cardiac arrhythmias in diabetic rats. The reduction in cardiac arrhythmias due to recurrent hypoglycemia is likely due to a diminished catecholamine surge associated with a blunted counterregulatory response. The results from these experiments demonstrate potential mechanisms for preventing life-threatening arrhythmias unique to people with diabetes.
Parkinson’s Disease (PD) is a severe neurodegenerative disorder that affects the central nervous system. The disease specifically targets dopaminergic (DA) neurons in the substantia nigra, a region of the midbrain. PD can be studied using the environmental toxin MPP⁺ (1-methyl-4-phenylpyridinium ion), which selectively targets DA neurons by entering cells through dopamine transporters and then interfering with complex I of the electron transport chain in those cells. This causes the depletion of ATP and the buildup of free radical species, which leads to further cell damage and eventually cell death.

Neuroprotectin D1 is a docosahexaenoic acid derivative that has been shown to protect brain and retinal cells against oxidative stress. In human neural cell cultures, NPD1 seems to work by upregulating anti-apoptotic proteins and downregulating pro-apoptotic proteins. We sought to investigate whether NPD1 has a neuroprotective effect on damage done by MPP⁺ on DA neurons, and if yes, then at what concentration it has the most effect. We treated murine midbrain cultures with MPP⁺ and differing concentrations of NPD1, and quantified cell death using stereological software. Our results show that NPD1 does in fact rescue cell death caused by MPP⁺, although there does not seem to be a definitive relationship between NPD1 concentration and degree of rescue. By studying the potential mechanisms by which NPD1 can rescue DA cell death, we hope to better understand NPD1 as a potential PD treatment.
Osteoclasts are cells responsible for resorption of organic and inorganic components of bone. A key molecule, receptor activator of NF-κB ligand (RANKL), was found to cause osteoclast differentiation from marrow macrophages in culture, as well as in vivo, giving the first look at the pathway required for osteoclastogenesis. Downstream of RANKL, activation of the alternative NF-κB pathway, mediated by the proteins NIK and RelB, is important for osteoclastogenesis. Precursors deficient in either protein fail to form osteoclasts in culture, yet successfully form osteoclasts in vivo. Previous studies have shown that transforming growth factor β (TGF-β), an abundant protein found in vivo, promotes RANKL-induced osteoclastogenesis, leading us to hypothesize that TGF-β could be the factor responsible for rescuing NIK and RelB deficient osteoclasts in vivo. We have found that TGF-β rescues RANKL-induced osteoclastogenesis in NIK- and RelB- deficient cultures. Since recent studies have shown that the Smad signaling pathway is important for RANKL-induced osteoclastogenesis in the presence of TGF-β, we used two different strategies to knock down Smad4 expression. Smad4 is a co-mediator Smad that is required for the transcriptional activation of Smad2 and 3, the Smads specific for TGF-β. Bone marrow macrophages (BMMs) were infected with a virus containing shRNAs that bind to and cause the degradation of the mRNA of the target gene, Smad4. Immunoblotting revealed that Smad4 was completely knocked down in the first 24 hours of infection. BMMs were also harvested from Smad4(flox-flox) mice, and underwent viral cre infection in vitro. Experiments with both types of Smad4 knockdown BMMs thus far show no effect on TGF-β or RANKL induced osteoclastogenesis, although experiments are still ongoing to confirm these results. In the future, alternatives such as mitogen-activated protein kinases will be explored to further understand the pathways resulting in the rescue of osteoclastogenesis in vivo.
Individuals with obsessive-compulsive disorder (OCD) experience symptoms like intrusive obsessive thoughts (e.g. thoughts of checking, contamination, safety, etc.) and are known to have deficits of cognition, like working memory processing. Working memory is a complex cognitive process critically dependent upon the ability to store information in active memory for future use. This storage ability is a limited resource such that when capacity is fully taxed working memory performance decreases. Individuals with active OCD symptoms have intrusive thoughts that may compete with demands on task related working memory capacity, thus impairing working memory performance. To test this idea we evaluated working memory assessments of healthy undergraduates prior to and after reading one of two articles: one valenced article that was meant to induce obsessive thoughts and another that was meant to be neutral. Subclinical OCD was assessed using the Maudsley Obsessive Compulsive Inventory (MOCI). We hypothesized that there would be an association between symptom severity, working memory load, and experimental condition where higher symptom severity elicited by the valenced article would result in worse working memory performance at higher loads. We found a significant interaction between pre- and post-test scores and condition for performance in the highest working memory load, such that accuracy of high OCD symptom participants was worse from pre- to post-test for the valenced condition. However, accuracy of high OCD symptom participants was numerically higher from pre- to post-test for the neutral condition. Our findings suggest that access to working memory capacity is impaired by the activation of OCD symptoms, which may contribute to cognitive deficits of individuals with this disorder.
One common misconception is that learning only occurs during study and that testing is useful only for evaluation. However, studies show that testing improves memory; this is known as the testing effect. One specific type of test that has been continually studied and under scrutiny is the multiple-choice test. One of the main criticisms of multiple-choice tests is that by providing the correct answer as one of the options, the tests promote recognition processes rather than the more effective retrieval processes that strengthen connections to enhance later recall. It’s a well-known fact that retrieval-induced learning is a powerful tool, strengthening the connection to the recalled information and making it more recallable in the future. Many studies have shown that the testing effect is greater under conditions in which the initial test is more difficult, strengthening the connection even further. We were interested in whether multiple-choice tests could incur retrieval processes if the alternatives provided were competitive enough to compel test-takers to think of not only why the correct alternative was correct, but also why the incorrect alternatives were incorrect. We also studied if answering multiple-choice questions could improve both accuracy and response speed on a later test. Multiple-choice tests, however, can lead to misinformation effects, which are when presented-alternatives intrude as incorrect responses to later questions. Thus, we also researched the possible presence of a misinformation effect and if the benefits outweigh the potential costs. In two experiments, we found that well-constructed multiple-choice tests can indeed incur retrieval processes, but also that they enhance recall of information related to incorrect alternatives better than cued-recall tests. We also found that multiple-choice testing did increase intrusions, but just as much as multiple-choice questions did. However, both intrusion rates were significantly lower than their respective increases in accuracy due to prior testing.
Male-Young Interactions in Kinda Baboons in Kasanka National Park

Emily Walco

Mentor: Anna H. Weyher

Kinda baboons, previously considered a subspecies of yellow baboon but now recognized as a distinct species, demonstrate social interactions that are unique to other baboons. The Kasanka Baboon Project, founded in Kasanka National Park, Zambia in 2010, is the first project to conduct a long-term behavioral study on Kinda baboons. While previous studies have focused more on the unique interactions between adult males and adult females, this study focused on interactions between adult males and young. These interactions are outstanding both in their frequency and in their affiliative nature. I collected both behavioral data and fecal samples for genetic and hormone data. While research is still being collected and data is being analyzed, it is evident that these interactions are occurring far more frequently than in other species and are non-aggressive in nature. The genetic samples will provide insight into the relationships between the males and the young with which they engage. Current theories propose that males interact with young either to protect their offspring from aggression or to use the young to protect themselves from an aggressive interaction with another male, who is not motivated to harm the infant. Because aggression is limited in Kinda baboons, neither of these theories seem sufficient. Future studies will look to determine possible causes for these interactions and will compare current findings to the behavior within other troops of Kinda baboons.
Participatory Empowerment and Sexual Health: Development of Biomaterials to Understand Axonal Guidance in Neurodevelopment

John Walker

Mentor: Joshua Maurer

The growth and development of the nervous system involves a complex network of neuronal cues that help guide axons to specific locations. To help better understand this process, we are developing biomaterials that facilitate the reconstruction of the microenvironment seen by the neuron during development. We utilize self-assembled monolayers (SAM) on gold to provide defined surface chemistry for the creation of guidance cue maps. In these studies, the background surface needs to be protein resistant so that specific neuronal cues can be spatially localized; however, the surface must also support cell attachment and motility so that neurons are able to grow and move across the entire surface. The development of this surface was achieved through the synthesis of a long chain alkyl thiol molecule with a short zwitterionic peptide. The identity of this molecule was verified using matrix-assisted laser desorption/ionization (MALDI) mass spectrometry and infrared (IR) spectroscopy. Protein resistance was determined using fluorescence microscopy and surface plasmon resonance imaging (SPRi) relative to a glycol control, while the support of cell attachment and motility was determined with phase contrast microscopy using both CHO-K1 and 3T3-Swiss cells. This surface will allow us to use chemical techniques to specifically attach neuronal guidance cues, such as the Slit 2 protein, and characterize the response of developing neurons under various conditions.
The mammalian Suprachiasmatic Nucleus (SCN), located in the hypothalamus, is the master clock responsible for maintaining circadian rhythm. SCN neurons express many regulatory clock genes in maintaining these rhythms, such as the \textit{per2} gene. However, it is unclear how these neurons connect and communicate with each other. My aim is to determine how wiring connections among SCN neurons regulate and establish circadian synchrony. I hypothesized that local, short-distanced connections are necessary to synchronize the intrinsically circadian cells of the SCN. Furthermore, I predicted that cells in the ventral SCN initiate the daily, synchronous wave of \textit{per2} gene expression.

To observe and quantify these circadian rhythms, I monitored a bioluminescent reporter of PER2 protein production in SCN cells cultured on slices surgically removed from mice brains. With a highly sensitive camera, I took images of bioluminescent activity every hour. I first established a baseline for 4 days, treated the slice with Tetrodotoxin (TTX) for 6 days, and then washed out the TTX and watched the resynchronization process for 12 days. TTX inhibits sodium channels in the neurons, blocking action potentials and intercellular communication. Afterwards, I constructed a movie from the images, and tracked bioluminescence levels from Individual neurons over time to create a wiring map that will be analyzed through computer algorithms for connectivity. From the preliminary data, we found that local connections are indeed necessary for synchrony, and that the cell regions leading the synchronization process, although distinct, differ among SCN slices.
Toward a Better Understanding of…

Navigating the Patient Experience: A Qualitative Study on Patient Satisfaction in the Rush University Emergency Department

Samuel Wein

Mentor: Peter Benson

This study aims to explore an anthropological assessment of patient satisfaction in the Rush University Medical Center Emergency Department. Welch explains that “a working definition of patient satisfaction includes the following: (1) overall satisfaction (usually solicited by survey) (2) likelihood to recommend and (3) willingness to return.” Administrators at Rush’s Emergency Department are particularly interested in raising patient satisfaction scores after receiving record low scores following relocation to a new facility in December, where they have experienced substantial increases in patient volume. This study, in focusing on the patient experience, uses interviews and participant observation as methods to assess patient satisfaction in the Emergency Department. These methods were used to gather data from the front-end processes: specifically, patient experience in the waiting room, through being checked in at the registration desk, and while being assessed by nurses during the triage process. The data collected was analyzed to reveal potential opportunities for the Emergency Department to increase as well as decrease the satisfaction of the patient experience. This study hopes to create a dialogue on cultural aspects of spaces in the healthcare field, especially in emergency care, as a fast-paced, life-saving space. As such, this study represents the greater conversation on the transformation of healthcare in the United States, and how emergency care providers and patients are affected by these modifications.
The Dispersive Optical Model was used as a framework for analyzing $^{12}$C, $^{14}$C, and $^{16}$O in order to learn more about the nuclear drip line. A fitting program was used to analyze data from scattering experiments in order to determine the optimal values for 23 different parameters that describe the given nuclear system. The program was able to quickly and easily produce good fits for $^{16}$O, indicating the DOM’s strength in describing this nuclear system. The program was only able to produce mediocre fits for $^{12}$C, and this was only after months of work, indicating the inability of the DOM to adequately describe the $^{12}$C system with the present forms of the potentials.
In this project, I argue to an audience of playwrights and directors the fallibility of profiling African-American characters of color within a theatrical production. I plan to claim the inadequacy of solely physical character descriptions for African-American roles due to the several articulations of blackness that exist. Because very little is straightforward, my central reason will be supported by a definition of how blackness is perceived by African-American actors and white directors, and how directors distinguish between white and black performativity. I will accomplish this through the analysis of scripts and interviews that demonstrate the superficiality of searching for black actors in an integrated theatrical production. The work addresses the issue of profiling characters of color from a historical and theoretical perspective.
An overwhelming majority of plants, up to 90%, require pollinators for reproduction. Reproductive success is essential for small scale plant population growth and large scale plant diversity. Maximizing plant diversity is the main goal of all restoration projects. Therefore, it is surprising that so little attention has been given to the effects of restoration efforts on bee diversity, abundance and pollination services. Thirty-two experimental glades in three different sizes were restored at Tyson Research Center in Eureka, MO. Smaller habitats are often less diverse than larger habitats, therefore, it is likely that our smaller restorations will have fewer bees or species of bee, and the plants in our smaller restorations will have decreased pollinator visitation. However, plants differ in their number of effective pollinators. Plants with a generalist pollination syndrome (many pollinators) may receive adequate pollination despite differences in bee diversity or abundance, whereas plants with a specialist pollination syndrome (few pollinators) are likely to be effected by depauperate bee communities. Alternatively, if specialist plants rely on generalist bees (visit many plants) even specialized plants might get adequate pollination in smaller restorations because these habitats house generalist bees. Bee communities were surveyed in the experimental glades using bowl traps and smaller restorations were found to have significantly lower bee abundance. However, visitation rates did not differ among glade sizes for any of the seven plants observed (3 pollinator specialists; 4 pollinator generalists). Our data support the hypothesis that plant-pollinator networks are nested; plants that specialize to a habitat type like glades rely on generalist pollinators, insulating plants in smaller habitats from the detrimental effects on reduced bee abundance. Our results are optimistic, suggesting that low initial abundance of bees in small and newly restored habitats might not cause drastic reductions in pollinator services to plants.
Toward a Better Understanding of...

Altered Communication in Mouse Model of Social Deficit Disorders

Kellie Wilson

Mentor: Joseph Dougherty

One in 88 children are diagnosed with Autism Spectrum Disorder (ASD) each year, a 78% increase from 2002. A related disorder, known as 7q11.23 Duplication Syndrome, is caused by the duplication of 30 genes in humans. Individuals with these disorders display severe social and communication deficits, among other health problems. Previous studies have shown that four of these genes, (the 3GN genes), may be involved in regulating the social aspect of these disorders. This research focused on the role of these four genes in social deficits. We hypothesize that having an extra copy of the 3GN genes will result in ASD-like social behavior.

To test this model, we separated 8-day-old mice from their mother. With all mammals, if you take a baby away from its mother, it will cry out, but mouse vocalizations, or whistles, are too high for humans to hear. So, we used a high frequency microphone to record a three-minute sample of ultrasonic vocalizations (USVs) for each pup. Using MATLAB, we were able to analyze the number and duration of whistles for each pup.

We hypothesized that the 3GN+ mice (pups with the extra copy of the genes) would have a lower number of vocalizations than the wildtypes, similar to the social deficits seen in ASD. However, we found that the 3GN mice had a higher number of whistles. This could mean the separation causes more anxiety than in a normal pup. This could be interpreted as a different manifestation of ASD behavior, though further studies are needed. Through this experiment, we hope to gain a better understanding of the genetic and molecular basis of human social behavior in order to apply this knowledge to the diagnosis and treatment of ASD and other social and cognitive disorders.
I investigated and recreated statistical simulations of changes in the amount of frequency splitting from the one-by-one absorption of fixed-sized particles onto a whispering gallery mode (WGM) microresonator’s mode volume. The WGM phenomenon was first observed in St. Paul’s Cathedral’s whispering gallery, where whispers can be heard across the structure from sound waves traveling along the almost perfectly circular walls. This phenomenon can be recreated with light by passing a laser into an optical resonators trapping the light inside for a significant number of revolutions until it is ejected. A mode volume refers to the space that a traverse mode travels through in the micro resonator. A traverse mode is a particular type of electromagnetic field pattern of radiation commonly seen in optical fibers and optical resonators. When particles are placed into the mode volume of a WGM microresonator mode splitting is induced and measured from observations of the exiting laser. These measurements may be used to accurately estimate the size and number of particles in the mode. The statistical simulations that I recreated were first completed by Lina He in a paper titled “Statistics of Multiple-Scatterer Induced Frequency Splitting in Whispering Gallery Microresonators and Microlasers.” The simulations involved finding distributions of multiple-particle induced frequency splitting by varying the number and single size of the particles in the mode volume. Later, I simulated the same distributions, but instead used a uniform and normal distribution for the radius values which is more realistic. I concluded that the standard deviation and the maximum value of the multiple-particle induced frequency splitting are proportional to the polarizability of the particles.
This project focuses on Chinese contemporary fashion photographer Chen Man (陈漫) and the artist’s use of the female body as a national symbol of social progress. Her work often straddles the divide between avant-garde fashion and fine art; her series *Long Live the Motherland* appeared in the October 2009 issue of *Vogue China*, coinciding with the residual fever of the 2008 Beijing Olympics. A focused analysis of this particular magazine spread, which has been exhibited across the globe in enlarged formats since its original publication, reveals a desire to both deplore national ideals of femininity and reimagine the “Chinese” identity in a global context. My main research question examines how the artist used the opportunity offered by a densely concentrated period of national image reconstruction to insert her own ideals and social commentary. Chen’s repetitive use of women situated against national icons reveals how nationalism is utilized as a nostalgic platform on which to restore fashion as not only a site for women’s agency, but also to restore women’s agency to a position that aligns with national desires and utopia-chasing plans implemented by a patriarchal society. Furthermore, the exclusive use of touristic sites implicates the impending pressure of the “touristic gaze” upon Chinese identity. More broadly, this indicates how the permeation of nationalist imagery in the contemporary era has come to not necessarily indicate the actual authoritative presence of the government, but rather how nationalism has become an identifying feature of China as a country without necessarily existing at a local level.
Parkinson’s disease (PD) is a neurodegenerative disorder that affects the central nervous system, causing motor dysfunctions such as involuntary shaking and balance problems. The pathology is characterized by the formation of Lewy bodies which contain amyloid fibrils made from the aggregation of alpha-synuclein. No therapy is available that addresses this underlying mechanism of PD. We recently found that Ezrin, a microtubule-associated protein found in the gut but also in neurons, can inhibit the formation of alpha-synuclein amyloid fibrils.

This study’s purpose is to explore the mechanism of its action in vitro, using purified ezrin and alpha-synuclein that were expressed recombinantly. We quantified the effect of ezrin on the kinetics of alpha-synuclein aggregation by a Thioflavin-T binding assay. Aggregation kinetics were recorded with varying amounts of ezrin. Ezrin decreased the endpoint Thioflavin-T fluorescence and prolonged the lag-phase of aggregation at sub-stoichiometric concentrations (1:20). The stability, structure, and morphology of alpha-synuclein aggregates were probed at different time points of the aggregation process. Filter-retardation assays were done with these time points to show that ezrin prevents the formation of SDS-stable fibrils aggregates. Semi-denatured Western blots exposed that ezrin also prevents the formation of SDS-resistant oligomers. Transmission electron microscopy was used to visualize aggregate morphologies. These experimental results support the hypothesis that ezrin inhibits the formation of amyloid fibers.

However, ultracentrifugation experiments done at the same time-points demonstrated that alpha-synuclein does still form insoluble aggregates in the presence of the ezrin protein. This finding suggests that ezrin inhibits amyloid formation by a new mechanism. Our results support a model in which ezrin inhibits aggregation of alpha-synuclein into amyloid fibers, instead causing it to form nontoxic amorphous aggregates, which may open new avenues to the treatment of PD.
Parkinson’s Disease (PD), the second most common neurodegenerative disease in the world, is a progressive disorder that leads to significant disability. Although motor symptoms like tremor are historically associated with PD, research has shown that mood disorders commonly occur as well. Studies have indicated one mood disorder, apathy, in as many as 60% of individuals with PD. Here, we investigated the neural basis of this condition and focused on the neurotransmitter dopamine and the dopaminergic reward system’s meso-cortico-limbic pathway, a collection of neurons branching from the midbrain to a variety of subcortical and cortical regions. Unilateral infusions of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) were administered to induce parkinsonism in a primate model of PD. Before and after MPTP, we measured apathetic behavior with a validated apathy rating scale and neural activity with MRI and PET imaging. The lack of desire to perform trained behaviors—hallway walking, circle walking, and reaching for fruit—was rated on a scale of 1-4 for apathetic behavior while uptake of three dopaminergic radiotracers—\([^{18}F]FD\), \([^{11}C]DTBZ\), and \([^{11}C]CFT\)—was used to quantify neural activity. MRI and PET scans were transformed into the same coordinate space using Vector Gradient co-registration instead of traditional Automated Image Registration. With this new method, we confirmed previous results relating apathetic behavior to the nucleus accumbens, a central reward structure. More importantly, the increased registration accuracy allowed us to identify correlations between apathetic behavior and \([^{11}C]CFT\) uptake in the reward system’s dorsolateral and ventromedial prefrontal cortices. These primate results support the link between the reward system and apathetic behavior. They suggest that several reward structures are involved in PD-related apathy and should be investigated further.
Reprogramming differentiated cells improves our understanding of regenerative process with significant implications for health and medicine. A general, robust, and easily-transferable method for cell fate reprogramming is important. CRISPR (clustered regularly interspaced short palindromic repeat) and Cas (CRISPR associated) proteins has programmable RNA-guided DNA nuclease activities, found in adaptive immune systems of bacteria and archaea. Recently, the system has been used for gene knock-out or knock-in in eukaryotes.

The goal of this project is to modify the CRISPR/Cas system even further to modularly and multiplexibly control eukaryotic gene expressions in mice and human cells, as a promising general and robust method for cell fate reprogramming.

We generated a version of Cas9, named Cas9Dead, with mutation in both of its nuclease domain. Cas9Dead lacks endonuclaese activity while still binds to the targeted genome loci when guided with sgRNA. We also showed that when transcriptionally linked with activation or repression domains, Cas9Dead can activate or repress genes targeted by sgRNAs. sgRNAs were modified to contain not only loci targeting sequences, but also binding sites for RNA-binding proteins. I also made constructs of PUM and Lmda (RNA-binding proteins) fused with VP16 or VP64 (activation domains) or SID (repression domains).

Theoretically, when Cas9Dead, modified sgRNA, and RNA-binding protein fused with functional domains are all present in a cell, this system could regulate multiple gene expression simultaneously. When combined with a dry-lab project on sgRNA design automation software, this system would not only improve cell transdifferentiation efficiency, but also serve as powerful tools for gene regulation in general. Current experiments have shown that when Cas9Dead fused with VP-64 is targeted by one of the modified sgRNAs, the targeted genes can be significantly activated. The work currently under progress is examining the synergistic effect when multiple sgRNAs are present, and the activation effect using Cas9Dead with PUM fused with VP-64.
Plants lack the nerves and muscles that enable movement in animals, but some plants are still capable of rapid movement. We seek to understand the biomechanical events that drive rapid movement in plants, using the Venus Flytrap (*Dionaea muscipula*) as our system. The Venus Flytrap actively traps prey with a unique snapping mechanism. After two stimulations of the interior trigger hairs, equilibrium within each lobe is upset, causing rapid changes in lobe geometry, from convex to concave, as both halves transitions between stable open states to stable closed states. When stimulation of trigger hairs occurs unilaterally, the stimulated leaf lobe sometimes closes more rapidly than the other leaf lobe. Our research focuses on this asymmetric closure process to further explore the role of intrinsic and extrinsic factors that drive trap closure. Our specific aims were to determine the effects of different trap-triggering stimuli on asymmetric leaf closure and the effects of natural geometric variation between leaf lobes on asymmetric trap closure.

Specifically, we assessed the natural geometry of each leaf lobe and stimulated trap closure mechanically, recording the process at 1000 frames per second. Through a custom program, we manually tracked three material points and calculated the angular speed and acceleration of the distal edge of each lobe. Analysis of videos of trap closure clarified how intrinsic geometric differences between leaf lobes underlie asymmetric deformation and how extrinsic, unilateral stimuli drive asymmetric deformation.

We expected this project to distinguish the relevant impacts of differences in the curvatures of trap halves versus the location of stimuli on asymmetric trap closure. Ultimately, the principles derived from studying the Venus flytrap may inspire designs for bio-mimetic devices, such as sensors and actuators, leading to a wide range of engineering applications.
In plants and microbes, chorismate mutase (CM) is an essential enzyme in the biosynthetic pathway of the essential amino acids phenylalanine and tyrosine. CM catalyzes an intramolecular cyclization reaction of chorismate to prephenate. Yeast CM is the most well-studied CM. CM in yeast is positively (tryptophan) and negatively (tyrosine) regulated. There are multiple isoforms of CM in plants which are differentially regulated by metabolic effectors. In Arabidopsis thaliana allosteric effectors positively (tryptophan) and negatively (phenylalanine and tyrosine) regulate the conversion of chorismate to prephenate catalyzed by AtCM1. AtCM2 is not regulated by these allosteric effectors. We want to understand the molecular basis of regulation in these enzymes specifically why AtCM1 is negatively regulated by phenylalanine and why AtCM2 is unaffected by any known allosteric effectors. We collected x-ray diffraction data on crystals of AtCM1. The 2.3 Å and 2.45 Å resolution structures of AtCM1 in complex with Phe and Tyr, respectively, identifies the regulatory site and reveals key structural differences between yeast and plant CM’s. To probe the contribution of residues in the site to allosteric regulation, a series of mutants of AtCM1 to AtCM2 residues (H145Q, K152E, S153Y, G213P, I273V) and the reverse for AtCM2 (Q76H, E83K, Y84S, P144G, V204I) were generated. Wild-type and mutant AtCM1 and AtCM2 were characterized using steady-state kinetic assays in the presence and absence of allosteric effectors and by isothermal titration calorimetry to analyze ligand binding. Although yeast CM and AtCM1 share high sequence similarity, the crystal structure of AtCM1 reveals key differences in the allosteric site that explain why AtCM1 is regulated by phenylalanine. The AtCM1 mutant G213P prevents effector binding to the allosteric site. The reverse mutant in AtCM2 P144G did not restore allosteric control which suggests that there are other key allosteric residues involved in effector binding and/or allosteric communication.
Toward a Better Understanding of...

Developing ΔsurAΔsmpA as a Pseudo-Gram-Positive Host in Functional Metagenomics Screening

Nancy Yang

Mentor: Gautam Dantas

Functional metagenomics screening is a culture-independent technique used to investigate microbial communities’ functions through the assessment of total genomic DNA. This powerful tool enables identification of novel resistance genes, but has been confined to Gram-negative antibiotics resistance genes because the customary host, E. coli, is Gram-negative and inherently resistant to Gram-positive antibiotics. This greatly limits the scope of resistance gene analysis and impedes understanding of the human gut microbiome, which is heavily populated by Gram-positive species and is potentially a major resistance gene reservoir. The goal of this project was to develop a Gram-positive antibiotic susceptible host, and then confirm its viability by assessing the results from screening fecal samples anticipated to contain resistance genes. We chose to develop ΔsurAΔsmpA E. coli, because it has previously exhibited susceptibility to vancomycin, a Gram-positive antibiotic; we hypothesized that ΔsurAΔsmpA has a disrupted pseudo-Gram-positive cell wall, which would induce susceptibility to other Gram-positive antibiotics. To control for the transformation procedure and establish the MIC (minimum inhibition concentration) of a selection of Gram-positive antibiotics, we transformed ΔsurAΔsmpA with vector pZE21 carrying a known kanamycin resistance gene. Transformants were selected using the known kanamycin MIC for wildtype E. coli; MICs for these transformants were established for the Gram-positive antibiotics vancomycin, clindamycin, and linezolid. Results showed that ΔsurAΔsmpA has slightly elevated MICs for the selected antibiotics compared to true Gram-positive microbes, and exhibited other unexpected resistance behavior. Furthermore, initial sequencing results from library screenings identified genes that potentially complement the knockouts, which restore the cell wall to Gram-negative character rather than providing true resistance. These results demonstrate that the selection pressure is sufficient; however, further work by high-throughput Illumina sequencing of all surviving transformants is necessary to identify true Gram-positive antibiotic resistance genes.
Toward a Better Understanding of...

Estimation of the Presynaptic Spike Trains by the Analysis of Single Membrane Potential Traces

Tansel Baran Yasar

Mentor: Ralf Wessel

The goal of this study is to estimate the time course of the synaptic conductances from single membrane potential traces and ultimately extract the excitatory and inhibitory presynaptic spike trains from the information about conductance traces. First, a neuron model that generates the spike trains of a set of excitatory and inhibitory presynaptic cells and the corresponding subthreshold membrane potential fluctuations is created by Python 2.7; the model includes different features such as correlation, spiking mechanisms, varying post-synaptic current strengths for different cells and zero-mean noising of the membrane potential trace. Then attempts to analyze the membrane potential traces generated by the neuron model are made by taking two approaches: (1) dividing the trace into very small windows; fitting an exponential curve to the change of membrane potential at each window; estimating the time constant of the exponential curve in each window; and as these time constants are the effective membrane time constants of the corresponding time steps, determining the total membrane conductance trace and eventually the excitatory and inhibitory conductance traces by using these time constants and (2) directly extracting the synaptic conductance traces from the change in the membrane potential and the steady-state potential at each time step. After the E & I conductance traces are obtained, the presynaptic spike trains are estimated by peak detection. Real and estimated traces of excitatory and inhibitory conductances and input spike trains are compared under different simulation conditions.
The dystopian literary form is often understood to be rooted in science fiction, depicting a futuristic totalitarian state. In this work, I challenge all three of these assumptions. In examining Margaret Atwood’s *The Handmaid’s Tale*, J.M. Coetzee’s *Disgrace*, and Kazuo Ishiguro’s *Never Let Me Go*, I posit that these contemporary dystopias demonstrate that the dystopian form possesses distinctive internal qualities. These qualities, most apparent in the novelist’s depictions of political societies, give the dystopian form a more substantial definition than that of a futuristic anti-utopia. I argue the dystopian form portrays a state characterized by the extension of justice from the regulation of individuals’ external interactions to that of their internal states. This control manifests as an enforced restriction of the natural human impulses towards meaningful work, romantic fulfillment, and the establishment of a family. I consider how these restricted impulses help make the dystopia dystopian. I also consider the relation of Atwood’s, Coetzee’s, and Ishiguro’s work to classic dystopias such as Yevgeny Zamyatin’s *We*, Aldous Huxley’s *Brave New World*, and George Orwell’s *1984*, arguing that the contemporary dystopia negates the element of futurism essential to these foundational texts. In doing so, the contemporary dystopia provokes a greater social consciousness in its readers, asking them to consider which elements of their own societies might, upon closer examination, be considered dystopian.
Over the past number of years, the culture of medicine has shifted to encourage more patient engagement in health decisions. The growing acceptance of Shared Decision Making (SDM), a process of engaging patients in their health decisions that involve multiple medically appropriate treatment options, reflects this shift. Our study aimed to explore physicians’ attitudes, beliefs, and perceived social norms about practicing SDM through semi-structured, qualitative interviews with physicians in four practice areas: obstetrics and gynecology, internal medicine, medical oncology, and surgery. We concentrated our interviews in the following behaviors: (1) acknowledging a decision to the patient, (2) describing the potential benefits, potential risks and cost of options, (3) eliciting patients’ values and preferences, (4) allowing the patient to review information about the decision and return to the clinic to make a final decision, and (5) disagreeing with a patient’s choice. Our research suggests support for incorporating SDM in medicine and many participants described a cultural shift toward patient engagement in decisions. However, certain systems level barriers can inhibit actually practicing SDM. In addition, many clinicians supported SDM but struggled to incorporate particular components associated with the process. More extensive training on how to navigate discussions of cost and uncertainty, how to balance patient preferences with clinical evidence, and how to engage in SDM with patients across varied socioeconomic background can help increase physicians’ confidence in SDM skills. This process can ultimately lead to more patient autonomy in their health decisions.
ROLE OF THE *Toxoplasma gondii* Secreted Kinase ROP28 in Growth and Virulence

*Tiang Zhang*

*Mentor: L. David Sibley*

*Toxoplasma gondii* is a widespread intracellular parasite that chronically infects ~25% of the world’s human population. It can cause severe disease in individuals with a weakened immune system, such as in developing fetus and AIDS patients. Upon infection, the secretory organelles known as rhoptries secrete protein kinases (ROP kinases) into the host cell cytoplasm where they modulate host functions. Among the highly expanded family of ROP kinases several have been shown to affect virulence in mice, yet the functions of most remain unknown. In the present study, a knockout of the rhoptry protein ROP28 was generated to investigate its role in virulence and parasite growth. Previous failed attempts to knock out *ROP28* led us to hypothesize that it possibly plays an essential role in the parasite life cycle. We undertook an alternative “unbiased” knockout approach in order to eliminate competition with wild-type parasites during clonal isolation and drug selection. This new approach replaces the *ROP28* gene at its endogenous locus with a “floxed” version flanked by LoxP sites. Transient expression of Cre recombinase was then used to recombine LoxP sites and delete the *ROP28* gene. Several independent Δrop28 clones were obtained and compared for growth *in vitro* and for virulence in a mouse model. The KO clones showed normal plaque formation on host cell monolayers *in vitro* and similar virulence to wild-type parasites in mice. These findings are consistent with knockout studies of other ROP kinases, which have shown the majority of ROP kinases to be non-essential, suggesting they either have redundant function or are important in other hosts. The study demonstrates the effectiveness of the Cre-Lox system as a knockout strategy to study other uncharacterized ROP kinases. Alternative roles for ROP28 are suspected to exist and will be the subject of future studies in the lab.
Single-molecule fluorescence resonance energy transfer (smFRET) is widely used in the imaging of dynamics of single molecules including protein and DNA. A typical two-dye scheme in smFRET utilizes a pair of donor and acceptor molecules and attaches them to two sites distant from each other on the molecule. As the molecule varies its conformation, the distance between the donor and acceptor also varies, thus allowing experimenters to detect the real-time transitions between different states of the individual molecule based on the measurement of the energy transferred from the donor to the acceptor. The human cardiac sodium channel (NaV 1.5) can be considered as a potential research subject for the smFRET experiments. However, the smFRET equipments were just set up in the lab and the computer software supplied by the camera manufacturer was only able to generate molecule-scale movies that were not directly analyzable. We introduced a software solution using MATLAB to resolve the issue of data processing which translates raw movie frames recorded by the smFRET CCD camera into analyzable datasets for research purposes. The project is still under steady progress as now we are working on the improvement of mathematical algorithms involved in the data analysis and its reliability, as well as the connections between multiple software packages that may aid in later data plotting.
Toward a Better Understanding of...

Utility of Transmitral Flow in Differentiating Hypertrophic Cardiomyopathy from Physiological Hypertrophy in the Left Ventricle

Simeng Zhu

Mentor: Sandor Kovacs

Both hypertrophic cardiomyopathy (HCM) and athletic training result in hypertrophy in the left ventricle (LV). Their similarities in morphology and clinical indexes make it difficult to distinguish between them. However, the differentiation is important, especially for young athletes. Conventional indexes derived from echocardiographic transmitral flow images (Doppler E-wave) have shown reasonable but not definitive utility in differentiation. In this study, we used kinematic model-derived indexes to assess the LV diastolic function (DF) in 14 HCM patients, 21 canoeing athletes and 21 sedentary controls. MRI data was used to determine LV mass and chamber size, which confirmed the presence of both types of hypertrophy. The model quantitatively assesses DF based on digitized E-wave contours and produces indexes such as relaxation/viscoelasticity \(c\), chamber stiffness \(k\) and load \(x_o\). A total of 1500 E-waves were analyzed: 328 from HCM, 672 from athletes, 500 from controls. We observed marked increase in load \(x_o\) in both types of hypertrophy; moreover, the HCM group displays significantly higher relaxation/viscoelasticity \(c\), and the athlete group shows significantly lower stiffness \(k\). These results show that, with the help of the model-based analysis, transmitral inflow has greater utility indifferentiating the two types of hypertrophy and in revealing the changes in LV properties.
Policy Brief

Children in Poverty: Protecting the Developing Brain
Alison Cesarz

Mentor: Joan Luby

I Problem and Prevalence
It is estimated that one out of five children, about 12-14 million, in America are living below the poverty line.1 In one study, for 4.8% to 15% of children living in poverty, the experience lasted for 10 years or more.1 Whether or not a child enters poverty depends solely on their family’s economic circumstances, since children depend on caregivers to fulfill their basic needs. These rates are disturbing given that poverty is the most robust risk for poor developmental outcomes in children.1,2 Poverty is associated with unsupportive parenting, poor nutrition and education, lack of caregiver education, high levels of traumatic life events and exposure to violence.2 Early interventions should be the highest priority for policymakers who aim to prevent these devastating outcomes. To begin to achieve this goal three steps must be followed: (1) Understand the effects of poverty on children demonstrated by scientific evidence (2) Recognize a specific target for intervention (3) Design and implement feasible and cost effective interventions addressing the target.

II Effects on Childhood Brain Development
In the past 20 years researchers have provided clear and convincing scientific evidence demonstrating the measurable effects of poverty on childhood development in numerous domains. Building on this literature, a recent study by Luby et al. showed that children growing up in poverty had reduced gray and white matter, as well as reduced hippocampal and amygdala volumes in the brain.3 Importantly, the negative effects of poverty on the hippocampus was mediated through parenting support and stressful life events. That is, these factors appeared as the key ingredient in hippocampal health or damage. Since the hippocampus is particularly important for learning, memory, and emotion regulation, the integrity of this region is important for adaptive functioning.4 Therefore findings of an effect of poverty on these areas of brain development are pivotal because they provide physical evidence for the negative effects of early adversity.

III Prevention
The next step in identifying effective interventions is recognizing a specific target. As Brooks-Gunn points out, what the research on childhood poverty has lacked is a clear picture of how the “puzzle pieces” or array of factors associated with poverty fit together to cause poor outcomes.1 The Luby et al. study has begun to fill this gap by highlighting the role of parenting and stressful life events as targets for intervention.3
Specifically, the study found that caregiving behavior, defined as the ratio of parental support/hostility towards a child, and stressful life events, the former a clear and changeable target, mediated the volume reductions seen in the hippocampus. With this mechanism in mind policymakers should now move forward to design targeted interventions to help these rapidly developing children living under high-risk conditions while the long-term goal of alleviating poverty continues to be addressed.

IV  Policy Recommendations

When considering possible interventions, caregiving is a central target since children who receive more nurturing caregiving may also be protected from experiencing stressful life events. Further, we know that changing parenting is both feasible and possible. If early interventions are to be successful in addressing caregiving, they must focus on parenting education and support. An exemplary intervention was conducted by Olds et al. in which nurses visited women in their homes during pregnancy until their child was age two. Compared to mothers not visited by nurses, the mothers who received the intervention displayed positive outcomes such as greater time intervals before having a second child, less domestic violence, and a home environment more conducive to children’s learning. Additionally, children of the mothers who received the intervention displayed more advanced language, superior executive functioning, and better behavioral adaptation to testing. Mothers supported by the nurses during the visits waited longer to have a second child, which allowed them to spend more time with their first child and provide better care. These significant effects were observed only two years after the program ended, and there is no telling how far-reaching they may be. This successful intervention should be used as a model for future programs, especially since the greatest child benefits were observed in the families at highest risk due to sociodemographic and psychological factors. This successful early intervention and others like it, taken together with the new findings on the effects of parenting on brain development, demonstrate that efforts to enhance high quality caregiving in childhood populations living in poverty is now a key next public health step.

Sources

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