NEW SYNTHETIC STRATEGIES TOWARDS TOTAL SYNTHESIS OF (-) AZASPIRENE

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As the demand for non-invasive cancer therapies grows, drugs targeting specific hallmarks of cancer with few side effects are crucial. Azaspirene, a natural product isolated from the fungus Neosartorya sp., has been shown to be a potent angiogenesis inhibitor. However, research is limited by the low quantity of azaspirene naturally produced, and more investigation is required to understand the physiological effects which make it a desirable treatment. Therefore, it is important to develop novel asymmetric synthetic methods that are reliably scalable to large quantities. The previous method of synthesis used a Fleming oxidation to install a secondary alcohol with retention of stereochemistry. However, the oxidation procedure currently requires the use of stoichiometric amount of mercury (II) acetate, which is highly undesirable because of its toxicity. Our current synthetic procedure produces environmentally hazardous waste which entails costly disposal procedures. To circumvent the use of mercury, our lab is exploring the use of complementary oxidation conditions to convert a different silyl group into the corresponding alcohol by exposing it to a fluoride source in the presence of bicarbonate and hydrogen peroxide. Preliminary results show that Tamao oxidation can successfully be applied to oxidize the silyl group to the alcohol towards the synthesis of the molecule, but further optimization is required to produce a scalable yield. From this strategy, we are closer to a synthesis of azaspirene with low-toxicity.

This project is currently taking place in the lab of Dr. Mikael Bergdahl, with partial funding by the NIH through the Initiatives for Maximizing Student Development Program – Grant # 5 R25 GMO58906-18.
Atropimerism is a form of chirality that arises from the hindered rotation about a bond, resulting in rotational enantiomers. BINOL and BINAP are two examples of privileged ligands in enantioselective catalysis that contain a stable chiral axis. The mild, enantioselective synthesis of these ligands has only recently been reported; and few general strategies exist to enantioselectively synthesize diverse atropisomeric scaffolds. A general enantioselective synthesis towards diverse enantioenriched atropisomeric ligands would provide access to catalysts with unique geometries and structural properties. Herein, we disclose a dynamic kinetic resolution of biaryl naphthoquinone atropisomers via the nucleophilic addition of thiophenol proximal to the chiral axis. Various biaryl naphthoquinone atropisomers were amenable to this strategy, often yielding enantiomeric ratios of greater than 90:10. The resulting enantioenriched 1,4-dimethoxynaphthoquinone atropisomers can be further modified to contain desirable functional groups in catalysis (i.e. amines, phosphines) with high enantioretention.

This project is currently taking place in the lab of Dr. Jeffrey Gustafson, with partial funding by the NIH through the Initiatives for Maximizing Student Development Program – Grant #5 R25 GMO58906-18.

BIOLOGICAL APPLICATIONS OF ATROPISOMERS
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A wide variety of kinase inhibitors exist in the form of atropisomers, an extended form of chirality that compromises of at least one rotational axis between two aromatic centers. Many of these kinase inhibitors exist as rapidly interconverting atropisomeric racemic mixtures. From these mixtures only a single atropisomeric conformation binds to the targeted active site, while the other conformation binds to off-target sites.

In research done by the Gustafson lab, atropisomerism is exploited to increase kinase inhibition selectivity of Pyrrolopyrimidine based compounds. In the report, they rigidified a biaryl axis by adding steric bulk adjacent to the axis and found the (R)-conformer to be 5x more selective towards RET kinase than the (S)-conformer after subjecting the conformers to a partial kinome screen. One drawback to this work was a loss in potency from the parent compound (no steric bulk).

To fully exploit the strategy of spatial pre-organizing an inhibitor as a selectivity filter, the analogs need to be optimized for both potency and selectivity. To accomplish this, we first identified potential analogs by screening various substituent combinations (Figure 1) of the (R)-configuration against RET using MOE, a molecular modeling software. The docking results sorted by dihedral angles (determinant of R and S) and then ranked by both binding score (potency) and ΔR/S (atropisomer preference) in order to establish priority molecules to synthesize. The optimized molecules were synthesized and their R and S conformers (separated via HPLC) were screened in vitro against RET using ADP-Glo kinase inhibition assay. Preliminary in vitro data (consistent with in silico studies from MOE) demonstrated that any loss of potency from the parent compound may be regained while maintaining RET’s atropisomer preference.

This project is currently taking place in the lab of Dr. Jeffrey Gustafson, with partial funding by the NIH through the Initiatives for Maximizing Student Development Program – Grant #5 R25 GMO58906-18.
Atropisomerism is a mode of chirality that arises due to sterically hindered rotation about an axis. The axis of chirality may rapidly interconvert from one conformer to another depending on the amount of steric bulk proximal to the axis. One overlooked class of atropisomers are diaryl ethers, which are ubiquitous in drugs and natural products, such as the antibacterial vancomycin and mammalian hormone thyroxine, Seminal work has shown that the different atropisomer conformations of diaryl ethers possess different pharmacological properties. However, in depth medicinal chemistry studies on diaryl ethers have been hindered by a lack of asymmetric routes to homochiral diaryl ethers.

To address this issue we have begun development of a chemical methodology that utilizes a dynamic kinetic resolution on a hindered, yet freely rotating, diaryl ether naphthoquinone. Preliminary results have shown that a urea-based quinine derived quaternary ammonium catalyst can effect the enantioselective alkylation of these quinones using nitroalkanes as the alkyl source with enantiomer ratios up to 85:15. This poster will discuss our recent efforts to further optimize this chemistry as well as apply it to the synthesis of atropisomeric analogs of diaryl ether based kinase inhibitors.

This project is currently taking place in the lab of Dr. Jeff Gustafson, with partial funding by the NIH through the Initiatives for Maximizing Student Development Program – Grant #5 R25 GMO58906-18.
THE MOLECULAR CHARACTERIZATION OF TIE2

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Nearly one-third of human kinases are implicated in disease, and this enzyme class has proved to be an enormously successful drug target for combating many diseases. Kinases are key regulators in signaling pathways responsible for such processes as growth and proliferation. Tie2 is an endothelium-specific receptor tyrosine kinase (RTK) responsible for angiogenesis and vasculature maintenance. Mutations in this enzyme can cause venous malformations for which no current therapies are available. Tie2 has also been proposed to be a target for anticancer therapies. However, the molecular mechanisms of Tie2 activity are not well understood. In this work, we will develop robust purification strategy using heterologous expression in insect cells. Preliminary data shows that the optimum multiplicity of infection (MOI) is 12 and the optimum incubation time post infection is 72 hours while using the High Five insect cells. Autophosphorylation assays will be used to establish catalytic rates of wild-type and mutant Tie2. We hypothesize that mutant Tie2 will have faster rates of autophosphorylation, likely through stabilization of the active conformation of the protein. These studies in kinase activity can improve our understanding of the catalytic features of wild-type and mutant Tie2, and can inform the development of therapeutic targets for vascular disease.

This project is currently taking place in the lab of Dr. Christal Sohl, with partial funding by the NIH through the Maximizing Access to Research Careers (MARC) Program – Grant #2T34GM008303-28
FUNCTIONALIZATION OF PYROGALLOL[4]ARENE HEXAMERIC CAPSULES

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Pyrogallol[4]arene is a curved, hydrogen-bonding molecule that is capable of self-assembling in solution to form molecular capsules. These capsules enclose approximately 1300 Å³ of space, enough to trap up to seven or eight small molecules and isolate them from solution. As a part of our studies on these capsules, we hypothesized that a new way to control guest release could be engineered by attaching polymers to the capsules. With this design, mechanical forces pulling on the polymers would be transduced to the capsule, releasing the contents. But to attain such a new molecular capability; the capsule must be modified with chemically reactive handles for polymer attachment. We developed a new synthesis to enable these modifications. The synthesis of mono-functionalized pyrogallol[4]arene begins with attaching 0–4 terminal alkenes to the capsule. What follows is an olefin metathesis with benzyl acrylate. Finally, hydrogenation of the esters results in pyrogallola[4]arenes with carboxylic acids on the lower rim of the capsule. However, because the molecule may contain 0–4 carboxy footed chains, it is important to be able to separate the capsules that only contain one terminal carboxylic acid. Attempts have been made to separate monofunctionalized pyrogallol[4]arene with conventional methods such as flash chromatography and the use of DIOL columns. This approach has been unsuccessful so far. We have been able to protect and deprotect the capsule effectively, providing different separation routes, and experiments to purify the protected compound are underway.

This project is currently taking place in the lab of Dr. Byron Purse, with partial funding by the NIH though the Initiatives for Maximizing Student Opportunities Program – Grant # 5 R25 GMO58906-18

OXIDATION OF PHENYLENEDIAMINES IN THE PRESENCE OF ADDED BASES

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This study focuses on p-tetramethylphenylenediamine, H₂PD, in the presence of H-acceptors. Phenylenediamines, which are weakly basic to begin with, undergo two successive oxidations to form an increasingly acidic radical cation, then quinoidal dication. Little changes in wave shape and small negative shifts are observed when slightly more basic guests are added such as cyanopyridine or trifluoromethylpyridine, but, unlike these bases, with just 1 equivalent pyridine guest, a significant shift in the potential of the second oxidation is observed, followed by smaller shifts with additional equivalents. We believe that this behavior signals proton transfer between the pyridine. In this case, the observed E₁/₂ should depend on the pKₐ of the Hpyr⁺. To test this hypothesis, the voltammetry of H₂PD is currently being studied with different pyridines that cover a range of pKₐ values. If correct, the explanation for the continued shift in potential with increasing concentrations of pyridine is well-accounted for simply by applying the Nernst equation to the overall reaction. This can explain proton transfer, but not reversibility. The simulations of the voltammetry show that proton transfer by itself cannot explain the observed reversibility of the second oxidation wave in the presence of increasing amounts of added pyridine. This is where H-bonding can play a role. By including H-bonding steps, and allowing electron transfer to occur through the H-bond complex formed between H₂PD²⁺ and pyr. The simulations can nicely explain both the observed potential shifts and the reversibility of the waves.

This project is currently taking place of Dr. Diane L. Smith, with funding by NIH (IMSD Grant 5 R25 GM058906-18) and the NSF (CHE-1611585).
Muscle function depends on the assembly of myosin molecules into thick filaments and organization of the sarcomere. Genetic studies have shown in a variety of species that the unc-45 (uncoordinated mutant number 45) gene encodes for a protein, UNC-45, that is essential for the proper assembly, folding, and function of myosin thick filaments in developing skeletal muscle. The amino-terminal tetratricopeptide repeat (TPR) domain of UNC-45 has been identified to interact with the ATP-dependent molecular chaperone Hsp90 (heat shock protein 90). However, the consequences of the interaction between UNC-45 and Hsp90 proteins on the assembly and function of myosin remain unclear. In order to improve understanding of the UNC-45:Hsp90 protein-protein interaction, we used hydrogen-deuterium exchange-mass spectrometry (HDX-MS). Purified, recombinant UNC-45 and Hsp83 proteins from the fruit fly, Drosophila melanogaster, were prepared and subjected to HDX-MS. With the data collected from HDX-MS we were able to obtain the relative uptake difference for both UNC-45 and Hsp83, which can provide insight into the protein-protein interaction and conformational changes upon interaction. The results revealed that when UNC-45 is in the presence of Hsp83, the TPR and central domain experienced a decrease in deuterium uptake. This suggests that UNC-45 relies upon more than the TPR domain to interact with Hsp83. In addition, Hsp83 experiences significant protein conformational changes in the presence of UNC-45. Further work in understanding the UNC-45 and Hsp90 protein interactions will lead to a greater understanding of its role in myosin thick filament assembly.

This project is currently taking place in the lab of Dr. Tom Huxford, with partial funding by the NIH through the Maximizing Access to Research Careers (MARC) Program – Grant #2T34GM008303-28

As a result of the legacy of contamination onset by abandoned Cold War uranium mines and mill waste sites, many Navajo communities have unregulated water sources that exceed established maximum contamination levels for uranium and other toxic metals. This research investigates a phosphonic acid silica polyallylamine composite (SPC) material, BPAP, for the adsorption of uranium in solutions modeling average conditions of drinking wells. Water quality measurements and samples were collected from 17 well sites in the Tsétah Area of Navajo Nation. Each water sample was analyzed using IC and ICP-OES analysis for various ion concentrations, including arsenic and uranium. The capacity of BPAP to adsorb uranium (UO$_2^{2+}$) and Zirconium-BPAP to adsorb arsenate (As(V)) and arsenite (As (III)) was measured at equilibrium. Using ICP-OES analysis we found BPAP to adsorb 0.30 mmol of uranium per gram of composite and Zr-BPAP to adsorb 0.35 mmol As(III) and 0.46 mmol As(V) per gram of composite. Further investigations for testing the working capacity of BPAP and Zr-BPAP with water samples collected from wells in the Tsétah Area are currently being studied.

This project is currently taking place in the lab of Dr. Edward Rosenberg, with partial funding by the NSF through the Research Experience for Undergraduate Program at University of Montana.
EFFECTS OF Mn(II) ON SURFACE CHEMISTRY OF CeO$_2$ NANOPARTICLES IN COMPLEX NATURAL WATER SYSTEMS

Daniel Delgado, Xuanhao Wu, Doyoon Kim, Dr. Young-Shin Jun

Cerium oxide (CeO$_2$) nanoparticles (NPs) are widely used as fuel additives and catalysts. The wide applications of engineered CeO$_2$ NPs have increased their presence in natural and engineered aqueous systems. After being released into environments, CeO$_2$ NPs are a potential health risks to humans and other organisms. Through interacting with aqueous species in water systems, the surface chemistry of the colloidal nanoparticle may be altered by adsorption of charged species, thus tremendously affecting their transport and environmental risk of these nanoparticles.

The purpose of this study is to investigate the co-effects of Mn(II) and UV on CeO$_2$ NP’s stability and surface properties in complex aqueous systems. To test these effects CeO$_2$ at 50 mg/L was prepared with 10 mM NaNO$_3$ and placed in 50 mL reactors with and without Mn(II) and with and without UV light. The reactions ran for 6 hours, during which particle settling was tested via UV-visible spectrometry, surface properties and morphology of CeO$_2$ NPs were tested with transmission electron microscopy and dynamic light scattering. Finally, oxidation states of Ce and Mn were tested with X-ray photoelectron spectroscopy. Results have shown that without UV light, increase in Mn(II) concentrations increases the colloidal stability of CeO$_2$; however, under UV light conditions, increase in Mn(II) concentrations decreases colloidal stability. At higher pH, nearing the isoelectric point, the Mn(II) effect without UV light becomes less noticeable.

This project was performed over the summer of 2017 in the lab of Dr. Young-Shin Jun, with partial funding by the NIH through the Maximizing Access to Research Careers (MARC) Program – Grant #2T34GM008303-28 and the Leadership Alliance SR-EIP.
Sewage leaks are a prominent contributor to water quality compliance failures, and their immediate detection is imperative to minimizing the risks of introducing large quantities of pathogens in urban watersheds. Dissolved organic matter (DOM) is an energy source to promote bacterial growth, and can influence biogeochemistry of a body of water. A portion of DOM is colored, called chromophoric dissolved organic matter (CDOM); these components have unique, fluorescent properties that facilitate their identification when they emit radiation in the ultraviolet and visible spectrum. Fluorescence has proven to be successful in discriminating between microbial and terrestrial sources of organic matter and a positive correlation exists between bacteria counts and fluorescent DOM. Preliminary research has demonstrated that tryptophan-like fluorescence intensity is significantly correlated with total aerobic bacteria counts ($R^2$ of 0.71 and $p < 0.01$) and total coliforms ($R^2$ of 0.65 and $p < 0.01$) during storm events from February 2017. The next step in the research evaluates whether an in-situ fluorometer can yield similar relationships with bacterial numbers in surface water and rapidly detect the presence of wastewater in riverine environments. Ongoing research introduces wastewater to surface water collected from Alvarado Creek, mimicking a sewage spill, and subjecting the sample to fluorescence and microbial analyses. The data collected is essential to understanding the extent to which fluorescence spectroscopy can be used as a warning system in the event of a sewage spill by monitoring water quality in real time.

This project is currently taking place in the lab of Dr. Natalie Mladenov. Funded by a grant from the National Institute of General Medical Sciences (NIGMS) of the National Institutes of Health (NIH): SDSU MARC U*STAR 5T34GM008303-28
Membrane ultrafiltration (UF) is on the rise in the water industry because it provides good removal of turbidity, particulates, and organic matter. However, membrane fouling has been seen as a limitation to the wide usage of membranes. Fouling necessitates periodic chemical cleaning and as a result, causes an increase in the amount of energy and in the overall cost for operation. Dissolved organic matter (DOM) has been identified as one of the major causes of fouling during membrane ultrafiltration, specifically the protein-like constitutes. There is a need in the water industry to understand the changes in the DOM due to fouling during membrane ultrafiltration. In this study, we are using a pilot scale UF membrane and two different forms of milk powder based synthetic wastewater solutions as feed water to compare how well the membrane performs. We are also evaluating the effects of biofilm formation on the retention of different organic compounds by the UF membrane, as well as investigating the possibility of using DOM fluorescence to characterize the feed, permeate, and backwash during UF membrane fouling. By preparing a disinfected milk powder solution and a milk powder with bacteria solution and running several cycles of each through the UF membrane, we have been able to use fluorescence spectroscopy and bulk protein analysis to gather measurements and interpret our findings. Preliminary results so far indicate that ultrafiltration for both solutions preferentially removed the protein-like components compared to the humic-like components. In addition, despite the feed water source, the backwash results portrayed a biofilm that is predominantly made up of protein-like components and as a result, has an effect on the DOM removal by the UF membrane. In regards to utilizing a modified Lowry protein assay microplate procedure for bulk protein analyses, it was concluded that generally the amount of protein detected is low right after backwash, but increases with time. However, with the experiment that incorporated a disinfectant, results were more variable. These initial results and findings are critical in further studying what exactly is in these protein-like components that are a major cause for fouling. Current and ongoing work is being conducted in the Water innovation & Reuse Laboratory to identify exactly how the protein concentration varies. Hopefully, with more analyses, more conclusive results can be determined with.

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A NUMERICAL STUDY TO INVESTIGATE THE EFFECTS OF IMPACT DAMAGE IN BUCKLING-CRITICAL HONEYCOMB SANDWICH

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Current heavy launch vehicles use curved honeycomb sandwich composite panels due to their high stiffness and lightweight. Low-velocity impact damage may cause damage to the facesheet and core of these shell structures causing local degradation of the material properties. Increasing the instability due to the dent created after impact may cause early onset buckling in the curved honeycomb sandwich composite panel. A parametric finite element model is developed to study the role of residual dents from low-velocity impact damage in global buckling of curved sandwich panels. The 3 ft. x 5 ft. sandwich panels had a 1-inch-thick, 3.1 pcf aluminum honeycomb core and 8-ply IM7/8552 facesheets. Linear eigenvalue buckling analyses were conducted with a wide range of residual dent diameters and depths to evaluate the influence of impact dents representative of barely visible impact damage (BVID) on buckling load. The analyses showed that dents representative of BVID yielded a knockdown in buckling load of less than 1%. A nonlinear post-buckling analysis was conducted to investigate the local stress state near the dent to assess the likelihood for a residual impact dent to trigger other failure modes prior to panel buckling, e.g. core crushing. Analysis results indicate bending of the dented facesheet leads to higher compressive core stresses in pre-buckling and tensile stresses in post-buckling.

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ELECTROANALYTICAL INSTRUMENT FOR ELECTROCHEMICAL IMPEDANCE SPECTROSCOPY

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The ability to both test and analyze various electrochemical interactions using electrochemical impedance (EI) spectroscopy has been of major research interest for some time. We present the design, construction, control, and application of a potentiostat electrometer electroanalytical device and how it can be used for such analysis and tests. The device is based on a small scale Complementary metal-oxide-semiconductor (CMOS) potentiostat coupled with an electrometer. The potentiostat electrometer device is sent a signal from a signal generator of 45Hz, 40mVpp, the potentiostat electrometer then amplifies the voltage signal into the +100 mVpprange. The device also filters out any noise artifacts that may be present in the prerecorded ECoG signal. The signal is then passed to the electrochemical cell and recorded by a solartronanalytical galvanotactic impedance meter Model 1070E (AMETEK, Oakridge, TN) to validate the potentiostat’s operation. The small set up, and inexpensive components make this electroanalytical device ideal for rapid development of microelectrodes and other electrochemical devices. The utility of the instrument was assessed for EI spectroscopy (5 mV RMS amplitude from 1 M Hz to 1 Hz frequency sweep) on different microelectrodes, and applied to the determination of electrical and neurotransmitter signals in neural communications at the synapse level.

This project is currently taking place in the lab of Dr. Samuel Kassegne, with partial funding by the NIH through the Initiatives for Maximizing Student Development Program – Grant # 5 R25 GMO58906-18.
When an airplane is in flight, a turbine blade is rotating or a truck is being driven, flow separation can occur. This phenomenon increases the drag making vehicles less efficient: increasing time, fuel usage and runtime. Studies show that flow can be controlled with active or passive form. Active form would include an apparatus that reacts to changing conditions in the flow. Passive form devices have a constant state. The past two years Synthetic Jet actuators (synjets) are studied at the San Diego State University. The focus is flow over an airfoil using separation control. The synthetic jet actuator is a piezoelectric diaphragm encased by a 3D printed cavity. A sinusoidal voltage applied to the piezoelectric disk oscillates it, creating a jet of air used to control the suction side of the airfoil. A NACA 65(2)-415 with a 5-inch chord and a 29.25-inch span is tested with 12 synjets in place. A series of experiments within the subsonic wind tunnel is conducted using particle-imaging velocimetry (PIV), recording aerodynamic loads and hot wire anemometry testing.

This project is currently taking place in the subsonic wind tunnel. This material based upon work partially supported by the CSU-LSAMP program funded by NSF under Grant HRD-1302873 and CSU Office of the Chancellor.
DEVELOPMENT OF A LOW-COST MURINE AEROSOL DELIVERY SYSTEM

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Lung diseases are among the leading causes of death in the United States, claiming more than 240,000 lives per year. Due to the anatomical and physiological similarities between murine and human respiratory systems, as well as their ease of handling, and cost-efficiency, mice have become a widely-utilized model for human lung diseases. Because of this, murine pulmonary drug delivery systems play a critical role in research and therapeutic development of lung diseases. Drug delivery to the murine airway involves inhalation or insufflation. Insufflation is not suitable for hydrophobic drugs and is not efficient in ill or respiratory-compromised animals. There are commercially available aerosol delivery systems available, but at prices beyond the reach of many labs. We have devised an inexpensive aerosol exposure chamber that allows for repeated pulmonary delivery of aerosolized drugs. The aerosol exposure chamber can be used to deliver targeted anti-inflammatory drugs to treat pulmonary inflammation associated with infectious lung disease. Animals are exposed to the aerosolized drug without restraints or anesthesia, allowing rapid drug delivery to the airways. This aerosol exposure chamber will allow laboratories to utilize aerosol drug delivery for research and therapeutic development at a low cost.

This project is currently taking place in the lab of Dr. Joy Phillips, with partial funding by the NIH through the Initiatives for Maximizing Student Development Program – Grant # 5 R25 GMO58906-18.
CREATING A VIETNAMESE NONWORD TASK:
ADULT RATINGS OF WORD LIKELINESS AND PHONOLOGICAL PROPERTIES
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The Nonword Repetition (NWR) task was created to investigate Vietnamese children’s language development and disorders. The purpose of this presentation is to explain the procedure of creating the NWR task, including (1) the selection of consonants and vowels; (2) the adults’ feedbacks; and (3) the correspondence of the nonwords’ frequency. We presented a set of nonwords that produce similar sounds in different Vietnamese dialects to create a set of NWR stimuli to satisfy their phonological properties. We, then, combined the consonants and vowels into a set of stimuli that consist of one to four syllables length. Vietnamese adult native speakers were asked to identify if the nonwords sounded like real Vietnamese words. Then, we verified the frequency of each syllable to be consistent across each consonants and vowels to ensure equal effects. Vietnamese NWR was accessible to examine bilingual Vietnamese-American children’s ability to repeat certain nonsense words. It allowed participants to express their listening and speaking skills and function their short term memory.

This project is currently taking place in the lab of Dr. Giang Pham, with partial funding by the NIH through the Initiatives for Maximizing Student Development Program – Grant # 5 R25 GMO58906-18.

MODELING PHAGE SURVIVAL IN LIMITING BACTERIAL GROWTH CONDITIONS
Nicole Tomassi and Dr. Antoni Luque
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Phages are viruses that infect bacteria and play a key role in ecosystems, including the human body. The resources available in the environment affect bacterial growth, which controls the production of phage particles. The impact of this pipeline in the ecological coexistence of phage and bacteria, however, remains unclear. Here we address this problem introducing a new mathematical model for E. coli bacteria and T4 phage—two reference model systems found in humans. First, experimental data is analyzed using linear regressions to determine the dependency of the phage production parameters as a function of the bacterial growth rate, which led to high R-squared values and statistically significant p-values. Then, a Lotka-Volterra predator-prey model was extended to include the bacterial dependency on resources as well as the phage dependency on bacterial growth. Standard tools in dynamical systems were applied to study the equilibrium and stability of the system analytically and numerically. Our preliminary analysis suggests that the coexistence of phage and bacteria depends on the initial conditions of the system, contrary to the classical Lotka-Volterra model. Additional analysis will be necessary to determine the biological implications of this result and its potential biomedical application, for example, in phage therapy.

This project is currently taking place in the lab of Dr. Antoni Luque, with partial funding by a grant from the National Institute of General Medical Sciences of the National Institutes of Health: SDSU MARC U*STAR 5T34GM008303-28
Amyloids play a central role in many neurological diseases and are formed from a wide variety of proteins in solution, including those in the nuclear pore complex (NPC). The NPC is a channel in the nuclear envelope regulating traffic into and out of the nucleus. Nucleoporins with repeating phenylalanine and glycine residues (FG-nups) fill the central channel of the NPC. FG-nups can aggregate to form amyloids in vitro. Here, we investigate the differences in the aggregation structure of FG124 in the presence of PEG and PVP crowders. Building from previous knowledge that PEG and PVP demonstrate unique aggregation rates, we further explore the subsequent formation of aggregate structures. Using x-ray scattering to investigate the difference in aggregate structures we found no significant peaks. The aggregate structures studied demonstrate amorphous structures. Next, we will grow heavy labeled protein to study the differences between PEG and PVP using Nuclear Magnetic Resonance spectroscopy.

This project took place in the lab of Dr. Loren E. Hough, with funding by a grant from the National Institute of General Medical Sciences of the National Institutes of Health: SDSU MARC U*STAR 5T34GM008303-28
QUANTIFYING SENSORY INPUT TO RODENTS ENGAGED IN COMPLEX BEHAVIORS

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Complex behaviors are abundant in every-day life but are difficult to study in the laboratory setting. Because rodent brains have some analogous structures with similar functions as human brains, it is possible to understand the neural bases of complex behaviors using rodents. Many complex behaviors in rodents are guided by olfaction. Quantifying the real time olfactory information sensed by the animal while it executes complex behaviors, such as odor-guided navigation, will allow for better interpretation of the underlying brain mechanisms involved during complex sensory-guided tasks in humans. Using CAD programming, a design was developed to hold an odor-tracking device in place while rodents used plumes to navigate through an arena. The odor-tracking device produced recordings that were highly correlated with the neural activity within the olfactory bulb of a rodent as it was exposed to odor-plumes in a wind tunnel. The developed design then allowed for accurate recordings of the odor plume as the rodents freely navigated through the arena, indirectly indicating the probable sensory input to the rodents during the trials. Tracking the odor plume at the same rate the rodent experiences the odor provides insight into the underlying brain mechanisms involved while rodents engage in complex sensory-guided tasks. Using this information, complex behavior in rodents can be better quantified and used to try to understand the physiology of human brains as they engage in similar intricate behavior.

This project took place in the lab of Dr. David Gire at the University of Washington, with partial funding by the NIH through the Maximizing Access to Research Careers (MARC) Program – Grant #2T34GM008303-28
Current pioneering research has indicated midlife obesity as a risk factor for Alzheimer’s Disease (AD). The processes of food initiation and termination are fundamental contributors to obesity that are dependent on the regulation of several hormones. One such critical gut hormone integral in the process of satiation and energy expenditure is leptin. This hormone serves as a neuronal communicator and may potentially hold neuroprotective properties. With females accounting for two thirds of the 5 million Americans battling AD, it is also increasingly important to investigate gender differences in physiological wellness and brain health. This study aims to investigate variance in the endocrine system between males and females by investigating leptin and ghrelin regulation in middle aged adults. Participants were 20 middle-aged adults, 7 of whom were males and 13 of whom were females. Blood samples were collected from participants after a 12-hour fasting period prior to experimentation. The metabolic manipulation enabled comparison between baseline leptin levels and baseline ghrelin levels. Results demonstrate a significantly greater difference in leptin to ghrelin ratio in females in comparison to their male counterparts, p = .002. In addition, leptin levels exclusively in relation to gender are approaching significance at p = .051, with females displaying exceeding levels. This reflects the contrast in endocrine function between males and females. With the rise in obesity and dementia prevalence observed in the United States, particularly in females, it will be increasingly important to consider hunger and satiety hormones in the investigation of healthy aging in the human brain.

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The integrative role that brain rhythm and noise serve in memory is not well understood. To better comprehend such mechanism, it is pertinent to observe how these metrics vary across brain regions and memory performance. Therefore, the behavior of neural noise and theta power was documented during free recall, as a function of subsequent memory outcome at frontotemporal cortical sites. Human electrocorticographic (ECoG) recordings were obtained from University of Pennsylvania's Restoring Active Memory (RAM) publicly available dataset. ECoG signal was analyzed in frequency domain with a multitapered Fast Fourier Transform. Neural noise was measured as the 1/f slope of the ECoG power spectrum within 80-150 Hz across 1.6 seconds-long memory encoding trials, while theta power was computed as the average power within 4-8 Hz. Independent samples t-tests were conducted with 1/f slope or theta as the dependent measure and subsequent recall (successful or unsuccessful) as the independent variable for each electrode across two subjects. 1/f slope was less negative during encoding trials that resulted in unsuccessful recall among 40% of frontal and 72.2% of temporal electrodes. Higher theta power was observed in trials with successful subsequent recall in 60% of frontal and in 55.6% of temporal electrodes. These results may provide insights into the spatial properties of neural noise and theta rhythm during memory formation, and could potentially inform hypothesis formulation regarding the dynamics of neural communication subserving memory.

This project took place in the lab of Dr. Brad Voytek, with funding by the NIH through the Maximizing Access to Research Careers (MARC) Program – Grant #2T34GM008303-28
San Autism spectrum disorders (ASDs) are a range of neurodevelopment disorders involving impairments in social communication, and repetitive and restricted behaviors. A growing body of evidence suggests that atypical sensory processing is also highly prevalent in children with ASDs. While questionnaires such as the Sensory Profile (SP) capture abnormalities in sensory behavior, how these measures relate to symptom severity remains unknown. We hypothesize that children with ASDs with more severe sensory processing issues will also show greater symptom severity in the core domains. To examine this, data from children and adolescents with ASDs and typically developing (TD) peers, matched in various demographics, were collected. Sensory behaviors were assessed using the SP care-giver questionnaires. Scores indicating low registration were used to subdivide the ASD cohort into “moderate” and “severe” subgroups. Statistical analyses were run to compare measures of autism symptomatology, including the Autistic Diagnostic Interview (ADI) and the Social Responsiveness Scale (SRS), between the three groups. An Analysis of Variance (ANOVA) of SRS sub-scores showed a main effect of group; independent samples t-tests indicated significant differences between the severe ASD subgroup and the TD group, as well as between the moderate ASD subgroup and the TD group. Results showed significantly higher ADI communication, SRS autistic mannerisms, and SRS communication sub-scores in the severe ASD subgroup as compared to the moderate ASD subgroup.

This project is currently taking place in the lab of Dr. Ralph-Axel Müller, with partial funding by the NIH through the Initiatives for Maximizing Student Development Program – Grant # 5 R25 GMO58906-18.
Parent-child bookreading (BR) is a key context for promoting language development and early literacy. Yet, although BR interactions are viewed and performed differently between income groups and cultures, there is limited study of BR interactions in low-income Latino families, particularly in 2-mo-old infants. The families were recruited from a study of a pediatric-based intervention delivered in a public hospital. Daylong audio recordings were collected using LENA™, a digital recorder and software system that records infants’ audio environments and conducts automated analysis of sounds and speech. On recording day, caregivers completed a logbook indicating the activities taking place during each 1-hour interval. There are two specific aims: 1) To examine differences in the quantity of language interactions between BR and non-BR contexts during a typical day in the home; 2) To describe the types of interactions taking place during BR. For aim 1, there were no significant differences in adult words (AW), conversational turns (CT), or child vocalizations (CV) between families who reported BR and those who did not. Among families who reported BR, BR segments were significantly higher in AW, CT, and CV, than non-BR segments. During BR segments, parents engaged in different types of interactions including teaching, playing, singing, reading, and asking questions. This suggests that booksharing in Latino families involves a variety of interaction types, including but not exclusively reading, and interactions involving books result in high quantity and quality of language input that may stimulate children’s language development.

This project is carried out in the context of an ongoing project led by Dr. Adriana Weisleder, with partial funding by the NIH through the Initiatives for Maximizing Student Development Program – Grant # 5 R25 GMO58906-18.
Cannabis is the most commonly used illicit drug among pregnant women. Moreover, over half of pregnant women who report consuming cannabis also report consuming alcohol. It is well established that prenatal alcohol exposure, by itself, can lead to long-lasting impairments in motor coordination. However, the effects of prenatal cannabis exposure or combined cannabis and alcohol exposure on motor development have not been well-characterized. The current study examined motor coordination following exposure to ethanol (EtOH) and/or CP-55,940 (CP), a cannabinoid receptor agonist, using a 2 (EtOH, Sham) x 2 (CP, Vehicle) x 2 (male, female) design. From postnatal days (PD) 4-9, a period of brain development equivalent to the third trimester, Sprague-Dawley rats received EtOH (5.25g/kg/day) or sham intubation, as well as CP (0.4 mg/kg/day, i.p.) or vehicle. All subjects performed a parallel bar motor coordination task during PD 30-32 (a period of development equivalent to human adolescence). Developmental EtOH exposure significantly increased the number of trials to the first successful traversal across the bars and decreased the maximum width reached between bars. However, the combination of developmental EtOH and CP exposure significantly decreased the overall success ratio and ability to complete the task, an effect seen in females but not males, although combination effects in males may have been masked by a floor effect. Importantly, these data suggest that combined prenatal exposure to alcohol and cannabis may be more damaging to the developing fetus, which has implications for the lives of prenatally exposed individuals and their families.

This project is carried out in the context of an ongoing project led by Dr. Jennifer Thomas, with partial funding by the NIH through the Initiatives for Maximizing Student Development Program – Grant # 5 R25 GMO58906-18.