WiSE Undergraduate Summer Research Mini Symposium

Friday, August 5, 2022

9:00 am – 11:30 am

Schedule

9:00 – 9:05	Introductory Remarks
9:05 – 9:20	Alayne Morrel *Professor Maral Mousavi*
9:20 – 9:35	Sofija Radulovic *Professor Daniel McCurry*
9:35 – 9:50	Shreya Agrawal *Professor Julien Emile-Geay*
9:50 – 10:05	Mengdi Chai *Professor Jazlyn Mooney*
10:05 – 10:15	**Break**
10:15 – 10:30	Aditi Jagannathan *Professor Sarah Bottjer*
10:30 – 10:45	Nettie Serena Ndjuissi Pawa *Professor Andrew Gracey*
10:45 – 11:00	Wanqing Pan *Professor Adam MacLean*
11:00 – 11:15	Mel Persell *Professor Suzanne Edmands*
11:15 – 11:30	Closing Remarks

Understanding Cholinergic Signaling in Alzheimer's Disease; Designing a Neural Probe for *In-Vivo* Recording of Acetylcholine

Alayne Morrel, Shahd Bawarith, Farbod Amirghasemi, Maral Mousavi

Alzheimer's disease (AD) is the most common form of dementia and the 6th leading cause of death in the US. The primary characteristic of AD is the accumulation of amyloid proteins to create neurofibrillary tangles that disrupt the neural network. Cholinergic signaling of acetylcholine (ACh), a neurotransmitter responsible for learning and memory, is also affected. As such, monitoring and understanding changes in ACh concentration in the brain and how it degrades will lead to a better understanding of AD and relevant therapeutic interventions, which are often cholinergic drugs. This project aims not only to develop a reliable ACh sensor, but one that is physiologically selective and sensitive to function in an animal model. We created a yarn-based electrochemical probe that detects ACh at physiological range of concentrations from 10mM to 0.1uM, significantly selecting AChCl over other similar ions such as ChCl, NaCl, and KCl all while retaining a quick response time. We aim to further improve the spatial resolution by nanopatterning conductive carbon fiber and developing a reference electrode to complete the potentiometric circuit. Finally, we will conduct *in vivo* studies on brain homogenate and mouse models before attempting to embed these electrodes in microfluidic devices for brain-on-a-chip applications for cholinesterase inhibitor drug screening and real-time drug interaction.

Development of Headspace GC-MS/MS Method for Simultaneous Determination of Trihalomethanes and Haloacetic Acids

Sofija Radulovic, Marella H. Schammel, Xinle (Grace) Yao, Keith P. Reber, John D. Sivey, Daniel L. McCurry

Over 700 compounds have been identified as byproducts formed during water disinfection; however, only 11 classes of compounds are currently regulated by the EPA. The most commonly detected classes of disinfection byproducts are haloacetic acids (HAAs) and trihalomethanes (THMs). Due to regulatory requirements, accurate and efficient quantification of THMs and HAAs is of great concern to water treatment plants. THMs can be readily measured via gas chromatography mass spectrometry (GC-MS), but HAAs require an additional derivatization step to their methyl ester form prior to analysis. The EPA recommended derivatization method is time intensive and alternative methods have been proposed. Previous research has been conducted to develop a quick method for simultaneous derivatization and extraction of HAAs via headspace gas chromatography. Further work has been conducted to create a method to measure both THMs and HAAs. The proposed method, however, does not consider the possibility of artificial THM formation via decarboxylation of HAAs. This work seeks to develop a headspace GC-MS method to accurately and simultaneously quantify THMs and HAAs in source waters. Previously proposed methods were replicated to demonstrate artificial formation of THMs and ongoing work is being conducted to further optimize the headspace GC-MS method to minimize decarboxylation (and potential hydrolysis) of HAAs.

Using Data from Corals to Strengthen Current Paleoclimate Records

Shreya Agrawal, Julien Emile-Geay

Most instrumental records of Earth's climate only stretch back to about CE 1850. For paleoclimate evidence, research relies on documentary evidence of past climate events, which comes from natural archives like tree rings, corals, ice cores, lake and marine sediment cores, and others. Such paleoclimate "proxies" provide indirect evidence of climate fluctuations in the pre-instrumental era, some with nearly monthly sampling. This research project leverages such records to reconstruct climate conditions over the past 2,000 years using a technique called paleoclimate data assimilation. The Last Millennium Reanalysis (LMR) fuses information from such proxies and the output of physically-based climate models. Recent efforts have assembled a larger collection of coral datasets that could be leveraged to augment the published LMR dataset. We apply the LMR framework to these two data sources (CoralHydro2k, early instrumental data) to better characterize the climate of the early 19th century through a Climate Field Reconstruction. Assimilation of paleoclimate data through LMR will strengthen our understanding of past climate variability as well as our predictions of future climatic patterns.We assess similarities and differences between the information provided by those two independent sources and use instrumental data to help validate the proxy-based LMR.

Identifying Genes Associated with Coat Color in Tigers

Mengdi Chai, Jazlyn Mooney

Seeing a snow-white coat in tigers is a very rare occurrence. Previous work has hypothesized that the snow-white coat is a result of multiple recessive loci, *SLC45A2* and *CORIN*. However, recent work identified an individual that is heterozygous at one of these loci, suggesting a more complex genotype to phenotype relationship. Thus, the goal of our work is to identify candidate regions for coat color genes by utilizing shared genomic segments between parent-offspring trios. We focus specifically on a parent-offspring trio where the mother (Zhara) and offspring (Kylo) are white with stripes, and the father (Assad) is snow white. By intersecting shared identity-by-descent (IDB) segments and runs of homozygosity (ROH) we identified 20 genomic regions that overlap seven loci potential candidate loci. One of these candidate loci, *TRIM8*, has previously been shown to be associated with coat color in cattle. We believe this loci may be responsible for coat color in tigers as well and requires further functional validation.

Investing Basal Ganglia Pathways that Mediate Vocal Learning in Songbirds

Aditi Jagannathan, Mira Nigudkar, Sarah Bottjer

Vocal learning in songbirds provides a powerful experimental model for motor skill learning, a term that refers to the acquisition of a stereotyped behavior through the refinement of variable actions. The neural pathways that mediate vocal learning are localized in two parallel circuits that traverse the cortical region LMAN, the basal ganglia, and the thalamus. The basal ganglia are known to have both a "direct" and an "indirect" pathway to the thalamus that are thought to have different roles in motor cognition and performance. "Direct" neurons send projections directly to the thalamus, whereas "indirect" neurons send projections onto the thalamus-projecting neurons. The direct pathway may be associated with positive reinforcement of

behavior since it increases the activity of thalamic neurons while the indirect pathway inhibits thalamic activity. This study focused on a region of the basal ganglia essential for song learning called Area X. We used neuroanatomical and immunohistochemical techniques to identify "direct" neurons in Area X with one fluorescent label and expression of the transcription factor FoxP2 using a different fluorescent label. FoxP2 plays an important role in human language development, with mutations leading to speech disorders such as childhood apraxia. Knockdown of the FoxP2 protein in Area X of juvenile songbirds has also been shown to impair vocal learning. Based on previous research, we predicted that "direct" neurons that send a projection to the thalamus would not express FoxP2. Our initial results support this hypothesis: FoxP2-positive neurons in Area X do not project to the thalamus, indicating different subpopulations of neurons that likely correspond to a direct and indirect pathway. Future studies will test how these distinct pathways mediate different functions during the song learning process in juvenile songbirds.

Determination of Cytoplasmic Viscosity Trends using Thermal Adaptation in C.elegans

Nettie Serena Ndjuissi Pawa, Andrew Gracey

In U.S adults 65 years+, the rate of chronic diseases is as high as 73.% and is projected to rise with life expectancies. Because aging has been identified as a genetically hereditary, mediated, and shapeable trait, organisms with conserved evolutionary pathways such as Caenorhabditis elegans are ideal to observe. The goal of this experiment is to establish the role of cytoplasmic viscosity adaptation in Caenorhabditis elegans' thermal tolerance, therefore, the expression of the genes relating to homeoviscous response of nematodes using genetic tools with aging. During a 'homeoviscous response', organisms adapt lipid composition of their membrane to adjust to the existing environmental temperature, therefore matching the fluidity of the membrane at that temperature and thus its aging process. The role of this process in an organism's thermal adaptation was previously unexplored and its implications deepen the understanding of human aging and co-morbidities through conserved evolutionary pathways. Previous research on cytoplasmic viscosity with aging has been done on other organisms in research papers such *Yeast As A Tool to Identify Anti-Aging Compounds,* and *Nanoscale Viscosity of Cytoplasm Is Conserved in Human Cell Lines.* This experiment explores the correlation between cytoplasmic viscosity adaptation and aging by measuring the thermal tolerance of Caenorhabditis elegans against a constant cold environment. Our results showed a negative correlation between the percentage of survival in cold challenged regular strand N2 Caenorhabditis elegans and time, suggesting that their viscosity of the cytoplasm decreases. The change in thermal tolerance of continuously challenged cold tolerant worms over multiple generations shows that thermal tolerance at cold temperatures is also a product of genetic adaptation.

Investigating How Differentiation of Myeloid-Derived Suppressor Cells are Altered in Cancer

Wanqing Pan, Jesse Kreger, Adam MacLean

Myeloid-derived suppressor cells (MDSCs) are pathologically activated neutrophils and monocytes (subtypes of immune cells) with immunosuppressive activity. They are implicated in the regulation of immune responses in many pathological conditions and are closely associated with poor clinical outcomes in cancer. Recent studies have indicated key distinctions between these MDSCs and classical neutrophils and monocytes. Amongst other pathologically activated microenvironments, long-term intensive production of cytokines, chemokines and growth factors by cancer and stroma creates a tumor microenvironment that induce the formation of MDSCs. MDSCs can not only inhibit anti-tumor immune reactions but also directly stimulate tumor growth and metastasis. Therefore, understanding the mechanisms of their generation, differentiation, and activation based on environmental cues is required for the development of novel strategies for tumor therapeutics. A small-scale mathematical model was proposed based on ordinary differential equations (ODE) to describe cell differentiation of myeloid c origin in healthy versus tumor microenvironments. The model has initially investigated the differentiation pathways from MDSC's progenitor hematopoietic stem cell (HSC), to granulocyte-monocyte progenitor cell (GMP), to monocytic (M-MDSC) and polymorphonuclear myeloid-derived suppressor cells(PMN-MDSC). I analyzed the 4 populations' proposed model's fixed points and stable states, possibility of oscillations and bifurcations that represent conditions of the system that induce stability, direction, and diversion in cell lineage. Based on initial results, cancer alters myeloid-derived cellular differentiation by significantly increasing the rate of polynuclear myeloid cells deriving from progenitors of the mononuclear cellular lineage instead of the regular granular progenitor cells. As the model is being further developed and refined with increased databases, future studies will improve upon the biological accuracy of the mathematical model and test how different cancers provide different computational context for the model, and how the myeloid-derived cellular differentiation pathways are influenced by the context.

Effects of Dietary Restriction in Early Life on Survivorship of *Tigriopus Californicus*

Mel Persell, Suzanne Edmands

Dietary restriction (DR) is thought to increase lifespan in many organisms. Under the disposable soma theory, in reduced food conditions, there is a tradeoff between survival and reproduction. This was a pilot study over the summer that examined *Tigriopus californicus*, a copepod (zooplanktonic crustacean), as a model organism to explore ideal and lethal food concentrations. This information will allow for larger studies on survivorship and reproductive success, using concentrations determined in this pilot study. Copepods are a good model organism because they are easily and affordably raised under laboratory conditions. Their lack of sex chromosomes, which can produce sex specific mitochondrial effects, allows the sex differences in aging and dietary restriction to be studied while controlling for mitochondrial influence. Preliminarily, a lower threshold for food was determined which will be used in subsequent studies. In the coming weeks, two studies will stem from the results of this pilot study, one an expansion on DR and lifespan, the other an examination of DR's impacts on reproduction. This data will also allow for a more complex study to study dietary restriction and mitochondrial effects, controlling with

mitotypes. This information on dietary restriction and lifespan would be applicable to many other organisms, including humans.