



BROWN

SUMMER RESEARCH SYMPOSIUM

2021



Presented by The College

Virtual Symposium

11 am – 1 pm

Thursday, August 5

Life Sciences and Humanities

&

Friday, August 6

Physical and Social Sciences

SUMMER RESEARCH SYMPOSIUM

THURSDAY, AUGUST 5

LIFE SCIENCES AND HUMANITIES PRESENTATIONS

11:00 - 11:05 Welcome and remarks

Oludurotimi Adetunji, Associate Dean of the College for
Undergraduate Research and Inclusive Science

11:05 - 1:00 Research Poster Presentations

FRIDAY, AUGUST 6

PHYSICAL SCIENCES AND SOCIAL SCIENCES PRESENTATIONS

11:00-11:05 Welcome and remarks

Oludurotimi Adetunji, Associate Dean of the College for
Undergraduate Research and Inclusive Science

11:05 - 1:00 Research Poster Presentations

SYMPOSIUM ORGANIZERS

Oludurotimi Adetunji

Associate Dean of the College for Undergraduate Research and Inclusive Science

Linda Sutherland

Co-Curricular Program Manager

Vasudev Agarwal

Symposium Intern

Andrew Creamer

Scientific Data Management Specialist

Lauren Fish

PhD Candidate in Neuroscience

ACKNOWLEDGEMENTS

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President

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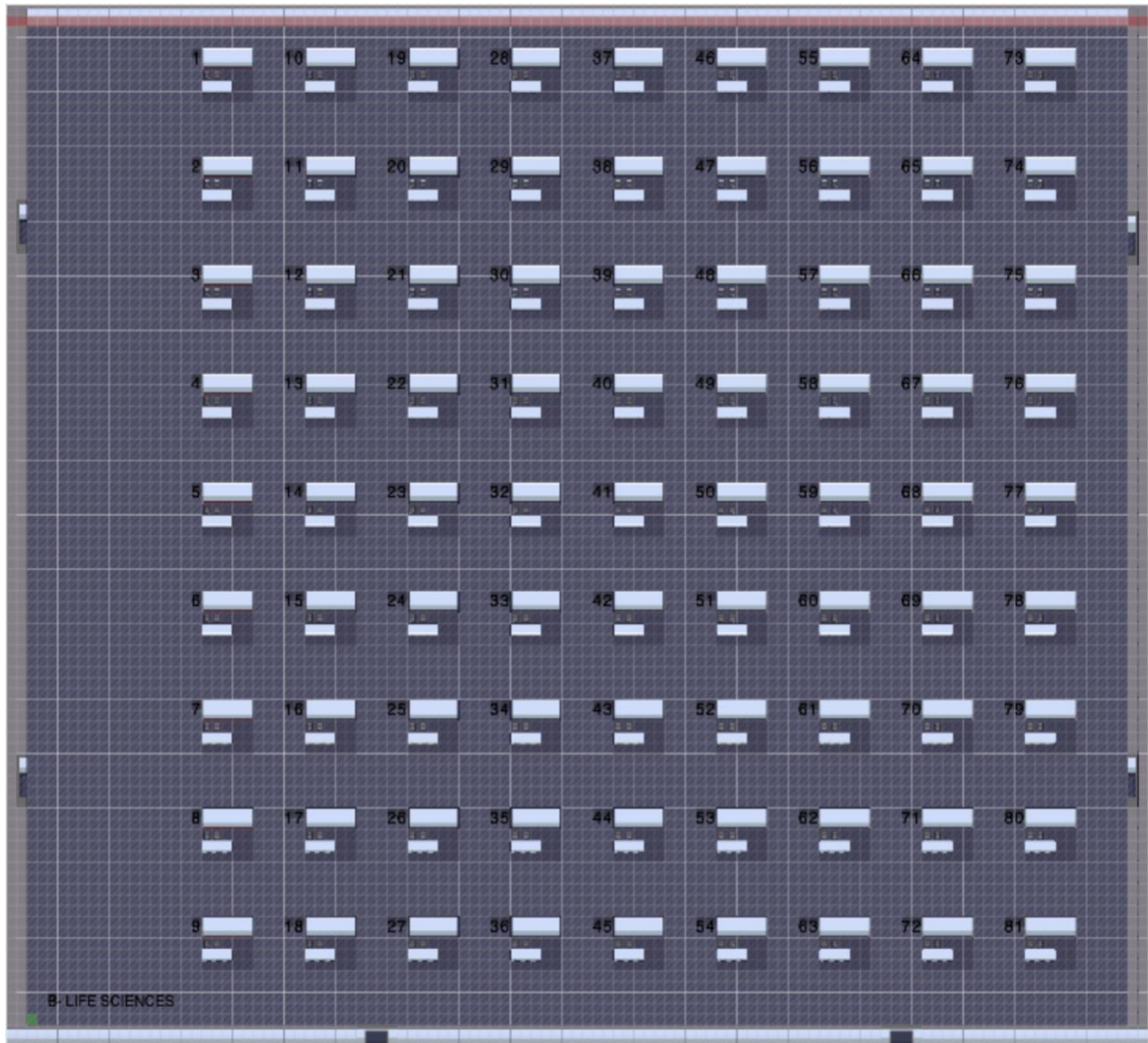
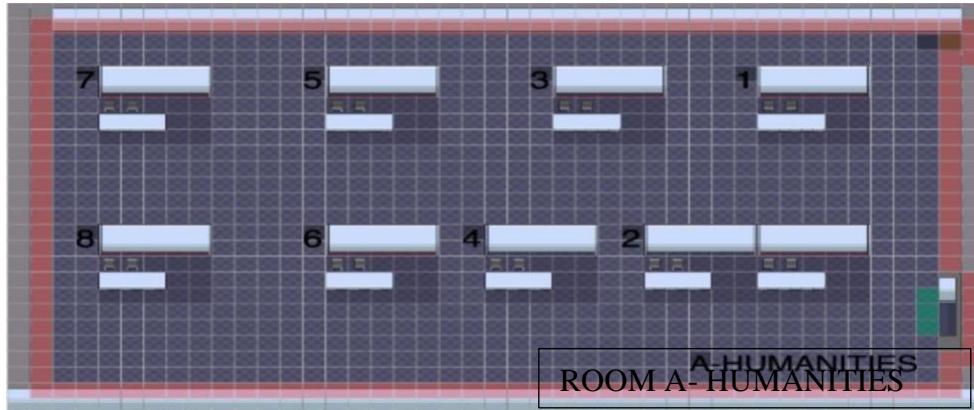
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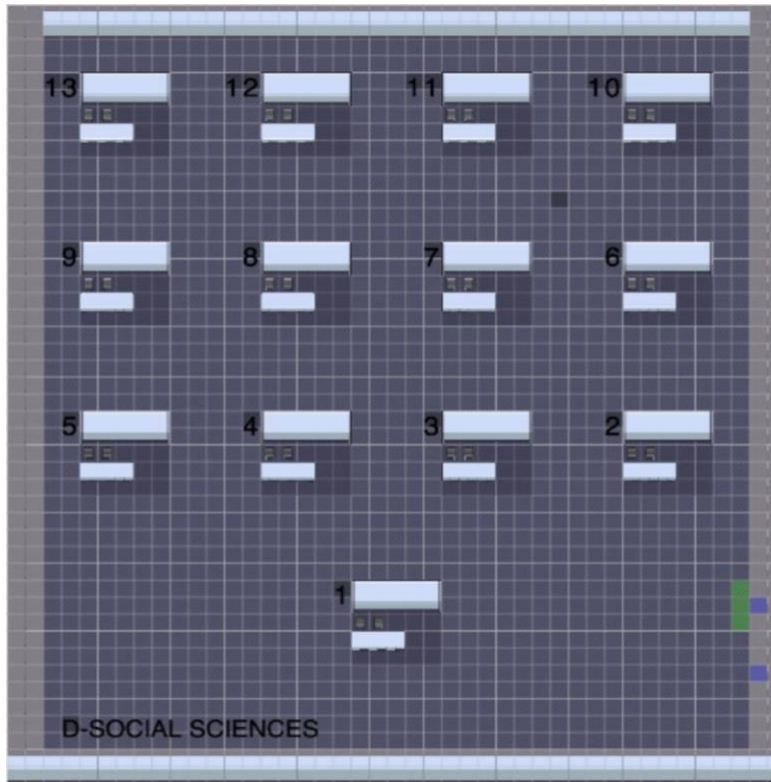
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Room Layout

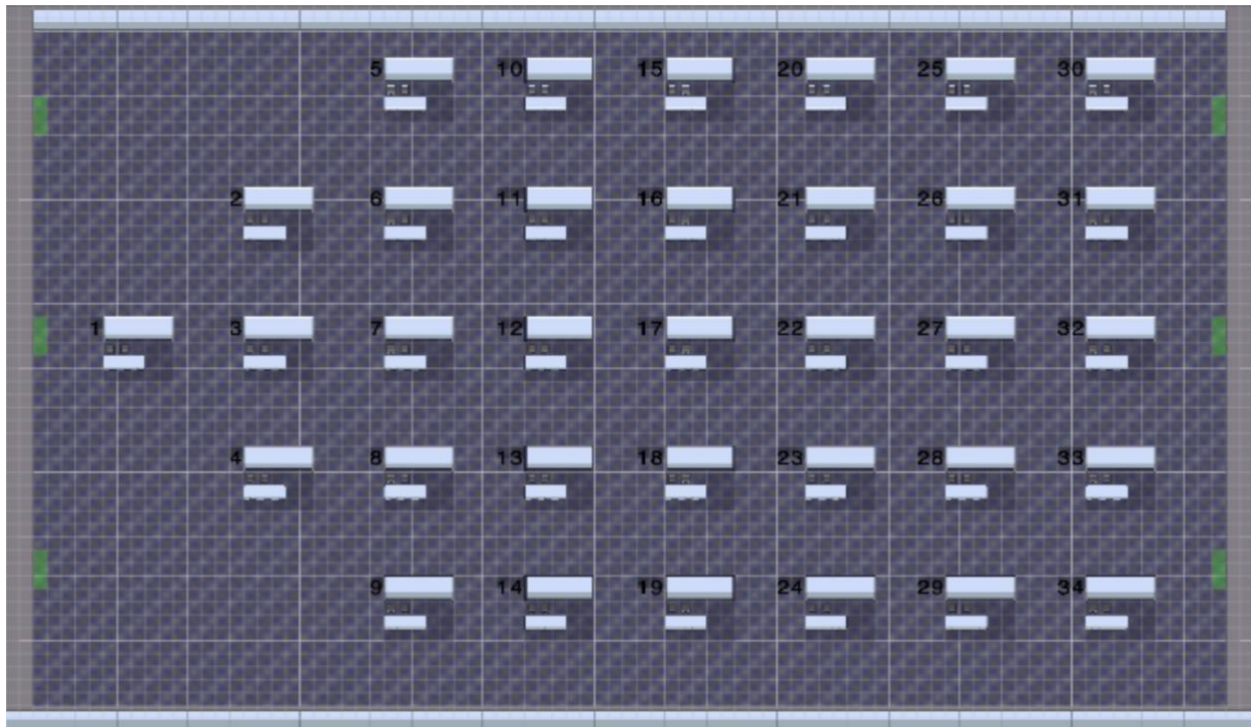


ROOM B - LIFE SCIENCES

Room Layout



ROOM C - PHYSICAL SCIENCES



ROOM D - SOCIAL SCIENCES

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C4- Shreyas Sundara Raman	C24- Xiao (Sean) Zhan	D4- Czenilriene Santander
C5- TZUHWAN SEET	C25- Katie Yetter	D5- Alison Kim
C6- J. Alexander Jacoby	C26- Advay Mansingka	D6- Selene Schiavone
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C15- Isabella Pulzone	C35- Michael Bergar	
C16- Yannie Lam	C36- Kenneth Loi	
C17- Casey Chan	C37- Jason Tsai	
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C19- Keyana Zahiri		
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SUMMER RESEARCH SYMPOSIUM POSTERS

Thursday, August 5

Life Sciences and Humanities Presentations

HUMANITIES PRESENTATIONS

Kaitlan Bui, WendyTran, TobyNgo, Khang Nguyen, Ryan Dang, Anthony Tran, Jenny Tran, Jeanie Nguyen, Amy Truong and Thomas Bui A2

Home Institution: Brown University
Summer Research Program: Royce Fellowship
Faculty Mentor: Mary-Kim Arnold (English) Aoyama Erin (American Studies)

Storytelling as Reclamation: Reshaping Postwar Memory with Young Vietnamese Americans

What does it mean to instill, inhabit, and inherit memory?

My project attempts to answer this question by engaging in sustained conversation with twelve high school students and recent graduates from Orange County, California—the most densely populated Vietnamese community outside of Vietnam itself, and my hometown. Over the summer, I will lead a series of weekly workshops, providing students with a safe space to explore questions of shame and identity, imagination and history, individual remembrances and family narratives. Students will collaboratively piece together knowledge of capital-H History with lowercase-h family history. In this way, our group will construct our own archive of the past. We will orient our discussions via storytelling, mirroring the phenomenon of oral history that has shaped many native, refugee, and immigrant communities. The ultimate goal of this workshop series is to introduce students to modes of equitable, empathetic history, and to encourage intergenerational, intra-generational storytelling in the Vietnamese American community.

I will interview students before and after the workshop series, asking them to articulate their feelings about Vietnameseness and their knowledge of the Vietnam War in relation to their families. I will also propose an activity in which the students interview their relatives about the past, encouraging them to share their findings. Thus, my project consciously promotes engaged scholarship and the co-creation of knowledge.

Kristen Marchetti A3

Home Institution: Brown University
Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA)
Faculty Mentor: Leslie Bostrom (Visual Art) Lincoln Evelyn (History of Art and Architecture)

Color

This summer I collaborated with Professors Leslie Bostrom and Evelyn Lincoln in developing a flexible, thematic framework for “Color,” a Pembroke Research Seminar that will convene during the 2021-2022 academic year. The Pembroke Seminar is a year-long conference that meets weekly, bringing scholars from around the globe to critically examine a relevant topic with Brown faculty, postdoctoral fellows, graduate students, and undergraduates. Professors Bostrom and Lincoln will ask how race, gender, and class are connected to systems of knowledge and power shaped by color. The course incorporates research from the hard sciences and social sciences as well as the arts and humanities, examining how the sensory experience of color has produced historical systems of classification, discrimination, and identity that directly correlate to contemporary issues of race, gender, and class.

As an undergraduate research assistant to Professors Bostrom and Lincoln, my primary task has been to develop a thematic framework for the seminar. I worked with the professors to interrogate existing research and extract essential themes that will guide discussions. It was my responsibility to help find readings for seminar meetings, considering interdisciplinary sources on color from the philosophical treatises of Aristotle to contemporary studies on the psychology behind #thedress that became a viral sensation on social media in 2015. As an art history and visual art concentrator, I have become increasingly aware of the importance of color to our attribution of meaning to the world. By asking productive questions about the ways that color has shaped our cultural, social, and political systems, I worked with Professors Bostrom and Lincoln to create a thematic foundation that encourages deeper acknowledgment of the senses in shaping historical systems of discrimination and work to question how human relations ordered by color can be improved.

Victoria Soto

A4

Home Institution: University of Puerto Rico-Río Piedras

Summer Research Program: Leadership Alliance-Summer Research Early Identification Program (SR-EIP) Faculty

Mentor: Jennifer Lambe (History)

Gendering Criminality: Infanticide in Early Twentieth-Century Puerto Rico

Early twentieth-century Puerto Rico, a new U.S. imperial possession in the aftermath of the Spanish-American War, was subjected to a concoction of eugenic theories, moral reformation, and colonial hygiene measures for the favoring of “progress,” “civilization,” and “modernization.” By selecting and modifying criminological views and theories of sanitation and psychology, elite and colonial agents in Puerto Rico shaped the notions of deviance. At the same time, colonial authorities and European eugenicists regarded Puerto Ricans as “degenerates” and “backward,” while the elite class was trying to prove their virtue in self-governing and policing the popular class. Among these new measures, the Penal Code of Puerto Rico was enacted in 1902. The Penal Code of 1902 represented a shift in the punishment of infanticide. Under the new penal code, infanticide was tried as a homicide, resulting in greater sentences for the women accused. Considering the often contradictory ideas governing Puerto Rican discourse around crime, how were the women charged with infanticide constructed in Puerto Rico during the early twentieth century? Were these women considered criminals, as the Penal Code of 1902 indicates, or was there resistance to this newly imposed legal subjectivity? Using the Penal Codes, newspaper articles, and four infanticide cases as sources, I aim to study the main discourses centered around these women in Puerto Rico during the early twentieth century through a gendered and racial lens. This research project is relevant as the gendered and racialized construction of the female transgressor signified colonial and social hierarchies. The study of the regulation and criminalization of the female body is essential to further understand the nationhood and colonial processes in Puerto Rico.

Tanner Holmes

A5

Home Institution: Spelman College

Summer Research Program: Leadership Alliance-Summer Research Early Identification Program (SR-EIP)

Faculty Mentor: Samantha Anderson (Undergraduate studies advisor) Betts Jennifer (University Archivist)

The History of Black students at Brown University

My project is focused on the history of black students at Brown University. My presentation will cover the integration of black students at Brown, racial climates at the university over the years, and the personal experiences of Brown’s black students.

Home Institution: Brown University
 Summer Research Program: Mellon Mays Undergraduate Fellowship Faculty
 Mentor: Françoise Hamlin (Africana Studies and History)

At the Nexus of Futurity and Liberation: Examining the Black Female Characters Across Nalo Hopkinson's Oeuvre

Since the Afrofuturist tradition was established, it has evolved into a paradigm through which Black people can envision themselves in a liberated future, released from the bonds of oppression and struggle. As the literary genre Black Speculative fiction continues to expand, I am interested in examining how these visions of the future are delineated across the diaspora, particularly among the plethora of Black women and femme authors. I intend on utilizing scholar Susana Morris' Afrofuturist Feminist framework to analyze three of Jamaican-Canadian author Nalo Hopkinson's novels, *Brown Girl in the Ring*, *Midnight Robber*, and *The Salt Roads* to synthesize her depictions of Afro-Caribbean women, namely how they engage with culture as means of informing selfhood and pushing back against hegemonic social structures. I will be grounding my analysis in knowledge on Black Speculative Fiction/Afrofuturism, Black Diasporic Feminisms, Black women's literary traditions, Caribbean Women's writing, and Caribbean religious and cultural practices. This will help to inform my reading not only of the characters but also of the various cruxes that make up the respective societies they live in. My hope from this deep dive into Nalo Hopkinson's work is that the visions of Black women, femmes, and girls, who are often overlooked or silenced altogether, will continue to be uplifted as we individually and collectively imagine what a future that champions liberation looks like.

Home Institution: Brown University
 Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty
 Mentor: Thomas Schestag (German Studies)

Between the Poetic Languages of Matos Paoli and Rita Indiana: The Representation of Madness in *Canto de la Locura* and *La Mucama de Omicunlé*

I study the use of poetic language in two Caribbean artists: 1) a Poet and a pro-independence Political Figure Francisco Matos Paoli (Puerto Rico), and 2) a Singer and Fiction Writer Rita Indiana (Dominican Republic). I look at how the highly symbolic and seemingly universal language of Matos Paoli and the raw and colloquial language of Rita Indiana invoke a similar reading of the Caribbean that exists in the gap between these two forms of writing. I particularly research their interest on the topic of madness and how they both use memory and remembrance as a poetic and narrative tool to delve into this complex subject. I believe that the seemingly personal experiences of these two artists are transformed into insight on political phenomena that span the Caribbean through the use of their respective form of poetic language. My task is to study the political philosophy implicit in the literary and musical work of these two Antillean artists. I am conducting this research through a combination of distinct methodologies. I comparatively analyze poetry by Matos Paoli, a novel and music by Rita Indiana, study work by Hannah Arendt on political philosophy as a theoretical framework and conduct a series of interview with Rita Indiana, who has agreed to participate in the project.

Home Institution: Brown University
Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty
Mentor: Anthony Bogues (AFRI/HIST)

Freedom's World in Boukman's Prayer

In the context of Saint-Domingue's unprecedented 'exterminating war' of master against slave, how do we account for Boukman's perceived importance in the eyes of the black insurgents he led, the white clergy who sympathised (or were suspected of sympathising) with them, as well as their white enemies? This is certainly not a straightforward question to answer for either of these three groups, for as I will argue, Boukman did not formulate his enemy on rigidly racial lines as many of his black compatriots and white enemies did. Rather, the political vision he proffered was a theologically founded one, as outlined in the prayer he delivered at the Bois-Caiman ceremony. The enemy was not the whites as such but their 'god', a false god whose worship permitted the many crimes of slavery. Similarly, the spiritual binding force for the insurgents would not be their respective ethnic lwa —though these were certainly invoked at Bois-Caiman— but rather Bondye —the one, true, and good God — recognised by all Vodouisants and non-Vodouisants, Catholics and non-Catholics alike. Boukman's theo-political vision may then explain his exalted status amongst the insurgents, his protection of white captives who he recognised as 'good' (even as his black subordinates sought to kill them), as well as the intimacy that white soldiers suspected existed between him and Catholic priests such as Abbe Philémon. In this earliest phase of the revolt that he led, Boukman dissociated the status of enemy from the fact of one's whiteness, and so offered even the whites the chance to take vengeance against their god and fight for liberty. Boukman's prayer did not derive its power from his ability to access God's intentions, since direct access to God by practitioners was cut off in both Vodou and Catholicism. Rather, it was based on a mutual trust or belief that liberty could indeed only be guaranteed by God, but that everyone could listen to its voice within them. Thus, Boukman's prayer distinguishes him both from the maroon leader Mackandal before him — who claimed therianthropic and messianic powers — as well as the leaders who appeared after his death: Jean-Francois, Romaine the prophetess, and indeed even Dessalines, all of whom domesticated liberty within their persons by claiming theo-political authority as Kings, Prophets, or Emperors.

LIFE SCIENCES PRESENTATIONS

Aiden Meyer

B1

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Ali Mahta (Neurology and Neurosurgery, Division of Neurocritical Care)

Radiographic Predictors for Ventriculoperitoneal Shunt Placement for Patients with Subarachnoid Hemorrhage

Our project seeks to improve upon medical guidelines used in the treatment of patients suffering from aneurysmal subarachnoid hemorrhages (SAH), a type of brain bleed characterized by bleeding in subarachnoid space between the brain and the tissue that encapsulates it. The most common cause of spontaneous non-traumatic SAH is a ruptured cerebral aneurysm. SAH is frequently complicated by hydrocephalus which refers to a build-up of cerebrospinal fluid (CSF) deep within the brain that consequently increases intracranial pressure to a dangerous level. To resolve this complication, patients are often treated with the placement of a drain called an external ventricular drain (EVD) which works to drain the CSF from the brain to decrease the dangerous pressure levels inside the cranium. However, hydrocephalus does not completely resolve in a subgroup of patients, therefore, they require permanent CSF diversion through a procedure called ventriculoperitoneal (VP) shunt placement. This procedure, which is typically done in an operating room, involves with placement of a catheter into the ventricles to drain CSF into the abdominal cavity instead. Through a retrospective analysis of patient medical records and imaging, we aim to identify clinical and radiographic predictors for refractory hydrocephalus requiring VP shunt placement. These predictors can be used to establish a scoring system which can be incorporated into clinical guidelines to manage EVDs in neurocritical care. EVD management in SAH is quite variable among physicians and institutions in the US without clear consensus. Such guidelines will allow for more efficacious and cost-effective treatment of hydrocephalus in SAH patients.

John Lin

B2

Home Institution: Brown University

Summer Research Program: Summer Research Assistantship in Biomedical Sciences Faculty

Mentor: Paul Greenberg (Surgery (Ophthalmology))

Virtual reality in cataract surgery training: a Cochrane systematic review

Background: Virtual reality (VR) training is often used to introduce ophthalmology trainees to cataract surgery in a learner-centered, risk-free environment. With the increasingly widespread use of VR training, it is important to determine whether cataract surgery skill transfers from the VR simulator to the operating room. This systematic review was performed to evaluate the effectiveness of VR training in cataract surgery for ophthalmology trainees.

Objectives: To assess the effects of VR training for cataract surgery on the operating performance of postgraduate ophthalmology trainees.

Search methods: We searched the following health professions, educational, and computer databases until June 14, 2021: the Cochrane Central Register of Controlled Trials, Ovid MEDLINE, Ovid Embase, PubMed, Latin American and Caribbean Health Sciences Literature Database (LILACS), ClinicalTrials.gov and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP).

Selection criteria: We included randomized controlled trials comparing VR cataract surgery training with any other method of training, including training using another type of simulation, didactics training, or no training.

Data collection and analysis: Two review authors independently assessed the eligibility and methodological quality of trials, and extracted data on the trial characteristics and outcomes. We pooled data for meta-analysis where participant groups were similar, studies assessed the same intervention and comparator, and had similar definitions of outcome measures. We calculated the risk ratio for dichotomous outcomes with 95% confidence intervals (CI). We calculated

mean difference (MD) and standardised mean difference (SMD) with 95% CI for continuous outcomes when studies reported the same or different outcome measures, respectively. We used the Cochrane Risk of Bias Tool to evaluate risk of bias and GRADE to rate the quality of the evidence.

Devin Juros

B3

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Gregorio Valdez (Molecular Biology, Cell Biology and Biochemistry)

The Role of MEGF10 in Regulating the Phagocytic Actions of Perisynaptic Schwann Cells at Neuromuscular Junctions and Muscles

The neuromuscular junction is a tripartite synapse consisting of a motor neuron innervating a muscle cell, and one or more perisynaptic Schwann cells (PSCs), which are specialized nonmyelinating Schwann cells. PSCs regulate the formation, stability, and repair of the neuromuscular junction. Consequently, PSCs and the proteins crucial to their functions are important to study in the context of neuromuscular aging and age-related diseases, such as Amyotrophic Lateral Sclerosis (ALS).

While thus unstudied in PSCs, MEGF10 (multiple EGF-like domains 10), a transmembrane protein, plays crucial functions in other cell types in the brain, retina, and muscle. Based on previously demonstrated roles of MEGF10 in synapse elimination and debris phagocytosis by astrocytes, another glial cell type like PSCs, I investigated possible enrichment of Megf10 in PSCs.

RNAseq, qPCR, western blot, and transgenic reporter mice supported that the RNA and protein products of Megf10 are enriched in PSCs in relation to other cell types near the neuromuscular junction, suggesting that MEGF10 plays a vital functional role in PSCs.

In future work, I will use a Megf10 conditional knockout mouse model to selectively delete Megf10 in PSCs and then assess possible persisting supernumerary motor axons, buildup of axonal debris, and behavioral changes. I will also probe whether MEGF10 deficiency in PSCs contributes to pathology in Early-onset Myopathy, Areflexia, Respiratory Distress, and Dysphagia (EMARDD), a human myopathy caused by mutations in MEGF10.

By demonstrating that Megf10 is enriched in PSCs, this project suggests a vital role for MEGF10 in PSC regulation of the neuromuscular junction. Future studies will discern specific functions of MEGF10 in PSCs, and may uncover mechanisms of EMARDD pathology. Furthermore, a better understanding of the role of MEGF10 in PSCs could instruct research and treatment development for other neuromuscular diseases involving perturbed PSCs, like ALS.

Alp Koksal

B4

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Justin Fallon (Neuroscience)

Promoting Adult Hippocampal Neurogenesis in a Mouse Model in Alzheimer's

In mouse models of Alzheimer's disease, as well as in human patients with Alzheimer's disease, adult hippocampal neurogenesis is diminished. A considerable body of literature demonstrates that augmenting adult neurogenesis results in improved learning and memory in rodents. Therefore in this work, I am seeking to investigate whether restoring neurogenesis in an AD mouse model will mitigate the pathology and manifestation of AD.

In unpublished work, The Fallon Lab has recently discovered that Muscle-Specific Kinase (MuSK), a receptor-enzyme complex involved in synapse formation and maintenance of neuromuscular junctions, is also involved in modulating the Bone Morphogenic Protein (BMP) signaling pathway. Altering this MuSK-BMP pathway in vivo via deletion of the third immunoglobulin domain of MuSK (Ig3) resulted in lower-affinity binding with BMP. In turn, increased neurogenesis in the dentate gyrus of the hippocampus was observed as well as improved cognition, as measured

through the Novel Object Location Task. These results suggest that the MuSK-BMP pathway is crucial for regulating adult hippocampal neurogenesis and that the increased neurogenesis observed in the " Δ Ig3-MuSK" mice leads to cognitive improvement.

For my project, leading to my thesis in the spring, I will initially be scrutinizing whether the constitutive expression of Δ Ig3-MuSK exclusively in neural stem cells of AD mouse models is sufficient to improve adult hippocampal neurogenesis. In the second part of this project, I will examine whether the later onset of Δ Ig3-MuSK expression in AD mouse models might rescue disease phenotype.

We hypothesize that the lower affinity binding of MuSK to BMP in the Δ Ig3-MuSK/5xFAD cross mice will increase neurogenesis and counter the cognitive deficits caused by neurodegeneration in AD. As the main focus of my project, I will be performing the Novel Object Location Task, as well as Contextual Fear Conditioning.

Kai Malcolm

B5

Home Institution: Vanderbilt University

Summer Research Program: Leadership Alliance-Summer Research Early Identification Program (SR-EIP)

Faculty Mentor: Jason Ritt (Carney Institute for Brain Science, Department of Neuroscience, Brown University)

Dynamical Patterns of Neural Models in Hodgkin-Huxley Form

The famous Hodgkin-Huxley (HH) system of differential equations (ODEs) describes electrochemical dynamics of the squid giant axon underlying action potential initiation and propagation. Since their introduction in the 1950's, many generalizations of the ODEs have been used to model a diverse range of neural systems. To facilitate investigation of the essential dynamics of such "HH-type" models, this project seeks to develop a software tool (in python) that procedurally generates networks of HH-type blocks, with configurable parameters and network architecture. Here the focus is not on biological plausibility per se, but the structure of dynamical types imposed by the defining structure of HH-type ODEs. We seek to classify the qualitative behavior of simulated network behaviors, to guide dimensionality reduction algorithms and develop efficient control strategies. An ongoing focus of this project is to determine a way to consistently measure such complexity so that these groupings are informative for inference of unobserved network structures. In future work, we will use this platform to computationally define control schemes based on probe stimuli of the network.

Janet Chang

B6

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Theresa Desrochers (Neuroscience) McKim Theresa (Neuroscience)

A Paradigm for Online Behavioral Research using Amazon Mechanical Turk, Psiturk & JSPsych: With Examples from Studies on Sequential Cognitive Control

The purpose of the project is to implement and collect online behavioral data to compare behavioral markers of sequential cognitive control that have been identified across studies of in-person behavioral data collection. Everyday abstract task sequences, such as studying for an exam, contain goals (reviewing class material) and sub-goals (reviewing a single lecture). Such tasks can be considered hierarchical in that superordinate levels (e.g., goals) affect subordinate level performance (e.g. sub-goals and actions). While much is known about task sequences behaviorally with robust effects, no studies to date of such phenomena have been conducted in an online environment.

Participants will make a series of simple color and shape judgements according to a remembered sequence. Reaction times will be collected for each button press response to the stimulus. We aim to replicate behavioral

effects of sequence tracking, such as differences in reaction time for first-position trials versus non-initial trials, which are indicative of a sequence initiation cost (Schneider & Logan, 2006). We will also measure task switch costs by comparing reaction times on trials when the task repeats to when it switches. Previous studies have demonstrated the presence of initiation costs that far override the effects of task-switching (Desrochers et al., 2015). To emulate previous studies, the online study will closely align the trial-by-trial task setup to measure reaction times to a similar degree of resolution.

Implementing this data collection online will increase the scalability of behavioral studies, in keeping with the trend toward research studies being conducted online. The transition to an online research study format will enable more rapid, robust, and standardized data collection across studies and minimize oversight costs. Finally, this project will help expand existing task paradigms to study variables related to sequence tracking behavior, such as task sequences of different lengths, timing, and interval patterns.

For this poster presentation, we will present an overview of the various aspects of the project and required configuration of Amazon Mechanical Turk, JSPsych, Docker, and other internet-based tools in order to successfully implement an online behavioral study.

Anika Hutton

B7

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA)

Faculty Mentor: Kimberly Mowry (Molecular Biology, Cell Biology and Biochemistry (MCB))

Investigating the role of prion-like low-complexity domains in L-body dynamics and structure

This UTRA project studied RNA localization in *Xenopus laevis* oocytes, which is facilitated by the formation of specific cytoplasmic ribonucleoprotein (RNP) granules termed Localization-bodies (L-bodies). We focused on how proteins with prion-like low-complexity domains (LCDs) function in RNA localization, with an aim to understand how LCD proteins are enriched in L-bodies, the dynamics of LCD proteins in L-bodies, and whether LCD proteins bind to localized RNAs in L-bodies.

For these analyses we have focused on three LCD-containing proteins that are enriched in L-bodies: hnRNPAB, TI B8, and LSM14B. We have generated specific domain constructs to analyze the requirements for partitioning of LCD proteins into L-bodies, we have engineered fluorescently-tagged LCD proteins to analyze protein dynamics by FRAP within L-bodies in vivo, and we will use RNA pull-down experiments to examine RNA binding for the LCD proteins. Ultimately, gaining an understanding of how and why proteins with LCDs partition into and function within L-bodies will be applicable to diseases that are linked to RNP granule dysfunction. L-bodies share notable compositional and behavioral similarities with neuronal transport granules, whose misregulation has been implicated in neurodegenerative diseases, such as ALS and Huntington's. By elucidating the normal function of proteins within a similar structure, like L-bodies, we can understand how these processes can become pathogenic.

Alice Varughese

B8

Home Institution: Rensselaer Polytechnic Institute

Summer Research Program: Leadership Alliance-Summer Research Early Identification Program (SR-EIP) Faculty

Mentor: Thomas Bartnikas (Biology and Medicine / Pathology and Laboratory Medicine)

Investigating Expression of Manganese Transport Genes in Inflammatory Bowel Disease

Solute Carrier Family 30 Member 10 (SLC30BA10) is a manganese transport protein that exports manganese from the liver to the bile. It plays an important role in manganese homeostasis and is dysregulated in genetic disorders leading to a manganese excess in the liver, which causes brain dysfunction, liver failure, and polycythemia. Previous studies have shown SLC30A10 to be downregulated in colorectal cancer (CRC), a common cancer in adults. Inflammatory bowel disease (IBD) is a known risk factor for colorectal cancer. We hypothesized that SLC30A10 is downregulated in IBD colon mucosa compared to normal controls. Datasets from the NIH NCBI GEO database

containing expression profiling by microarray of colons from humans and mice with IBD were analyzed to test if there was a significant absolute change in SLC30A10 expression and if SLC30A10 was among the top genes ranked by absolute change in expression. SLC30A10 was significantly downregulated in studies involving humans, and its change in expression is still being analyzed in mice of different conditions. The results of this study demonstrate that further study can be applied to the development of genetic detection for colorectal cancer, or analysis of pathways for inflammation.

Charissa Chou

B9

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA)

Faculty Mentor: Alper Uzun (Department of Pediatrics) Uzun Ece (Department of Pathology and Laboratory Medicine)

Comparative protein-protein interaction network analysis of urothelial carcinoma subtypes

Cancer, the second leading cause of death in the United States, is a complex disease where multiple genes contribute to the development of the disease. At present, there is a lack of information about the genetic architecture of papillary bladder cancer compared to that of non-papillary bladder cancer. We investigated the existence of a network of genes in the papillary subtype of urothelial carcinoma that differs from a network of genes in non-papillary urothelial carcinoma. Using data from cBioPortal, a database containing genome sequencing and phenotypic data from cancer patients, we compared the transcriptome data from two groups: patients with papillary urothelial carcinoma (n=133) and patients with flat carcinoma or carcinoma in situ (non-papillary, n=273). The dataset contains the mRNA z-score and RNA-seq data from 408 patients. Each patient is a datapoint that contains a list of the most highly expressed genes. To compare the two groups, we employed Protenarium, a multi-sample protein-protein interaction (PPI) tool used to identify clusters of samples with shared networks. This tool can be used to analyze the PPI networks of patients and visualize them in clusters based on their network similarities from high throughput genetic data. We hypothesized that we would observe distinct networks and pathways for the papillary and non-papillary groups, suggesting the presence of different cellular mechanisms that present unique therapeutic targets or genomic screening markers. The resulting PPI networks contained unique genes in each subtype, with genes involved in the MAPK pathway unique to the papillary cancer network and genes involved in the estrogen signaling pathway unique to the non-papillary cancer network. This is a unique approach to investigate these datasets from the network biology perspectives where we take into consideration each patients' exclusive PPI network that reflect the potential consensus networks as in clusters for the disease phenotype.

Muneet Gill

B10

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Anne Hart (Neuroscience)

Investigation of a genetic suppressor of ALS-associated neurodegeneration

Amyotrophic lateral sclerosis (ALS) is a poorly understood neurodegenerative disease that is caused by the loss of cholinergic and glutamatergic neurons. This neurodegeneration often occurs when there are mutations in certain genes, which cause ALS. However, discovering additional genetic mutations that decrease motor neuron degeneration will help reveal the mechanisms underlying ALS. These genes are known as genetic suppressors. In this project, I will examine a recently identified suppressor gene in the nematode *C. elegans*. Thus far, researchers in Dr. Hart's laboratory have created single-copy models of ALS in *C. elegans*—including a patient allele, G85R, found in the SOD1 gene in ALS patients. They carried out a forward genetic screen for suppressors of glutamatergic neuron degeneration in the sod-1G85R model. This screen identified a gene whose loss of function suppressed glutamatergic and cholinergic neuron degeneration, called geneX herein. However, we are unsure if geneX loss of function (geneX(lf)) suppresses

cholinergic neuron degeneration in other sod-1 models. The A4V mutation is a common SOD1 mutation causing ALS. The *C. elegans* sod-1A4V model shows cholinergic neuron degeneration. I will create a double mutant strain by crossing geneX(lf) onto the A4V background and will make the corresponding wild-type control. By creating this double mutant strain, I will be able to explore and potentially answer my research question: “Does geneX(lf) suppress cholinergic neuron degeneration in the sod-1A4V model?” Since geneX(lf) suppresses cholinergic neuron degeneration in the sod-1G85R model, I hypothesize the same suppression will be observed in the sod-1A4V model. Ultimately, identifying a genetic suppressor that decreases cholinergic neuron degeneration will help researchers better understand the mechanisms behind ALS spinal motor neuron degeneration and opens up opportunities to explore potential treatments for this disease.

Lang Liang

B11

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Kate O'Connor-Giles (Neuroscience)

Structural and functional analysis of TRAPP complexes in the *Drosophila* larval central nervous system and neuromuscular junction

Communication in the nervous system is the basis for behaviors such as movement and cognitive functions including learning and memory. Synapses are the sites of this communication between neurons. In presynaptic neurons, neurotransmitter filled synaptic vesicles are docked near calcium channels for efficient neurotransmission upon arrival of an action potential. Yet, little is known about how synaptic vesicles are recruited and positioned at the presynaptic membrane to achieve this organization. Ultrastructural analysis of synapses across species shows the presence of protein tethers linking synaptic vesicles to other vesicles and to active zone membranes. However, the composition of these tethers remains unknown.

The Transport Protein Particle (TRAPP) is a multi-subunit protein complex that has been identified to tether endoplasmic reticulum-derived vesicles to vesicular tubular clusters. Mutations in TRAPP subunits have been implicated in motor dysfunction, intellectual disability, and developmental delay. However, a potential role for TRAPP in tethering synaptic vesicles at synapses remains unexplored. We find that core TRAPP subunits are expressed in the *Drosophila* larval ventral nerve cord and at the neuromuscular junction, where we observe colocalization with synaptic vesicles. Functionally, we find that knocking down some, but not all, TRAPP subunits leads to decreased levels of synaptic vesicle proteins as well as components of the active zone cytomatrix, a conserved complex of proteins implicated in the organization of synaptic vesicles at synapses. We propose that TRAPP complexes play an important role in synaptic vesicle recruitment and neurotransmission, and that studying their function will provide new insights into long-standing questions about synaptic vesicle trafficking.

Denise Danielle Tamesis

B12

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA)

Faculty Mentor: Alfred Ayala (Division of Surgical Research) Hensler Emily (Division of Surgical Research / Department of Surgery)

The role of VISTA in the neonatal model of sepsis

Sepsis is the leading cause of death in neonates, occurring in 1-10 of 1000 live births globally, with U.S. per-patient expenses that can triple those of adults — yet, the field offers no approved immunomodulators, nor even a consensus definition, for neonatal sepsis. Exploring the roles of various immune checkpoint proteins (including PD1, PD-L1, and VISTA) in neonates may not only contribute to our knowledge on innate immunity but may also lead to development of therapeutics for this vulnerable population. Our project aims to examine the role of VISTA, a

relatively recent discovery among checkpoint inhibitors, in the murine model of neonatal sepsis. To do this, sepsis is induced in 5-to-7-day-old wildtype (WT) or VISTA knockout (-/-) mice via the cecal slurry (CS) model, involving intraperitoneal injection of stool derived from donor mice.

Our multi-part experimental plan investigates the effect of VISTA on mortality (7-day survival) and morbidity (histological and chemical analyses of organ injury) in CS vs Sham WT and VISTA -/- mice. Preliminary data is trending toward decreased survival in VISTA -/- vs WT neonates following CS (35% vs 50%, $p=0.3165$), as opposed to the previous finding of increased survival in PD-1 -/- neonates. Ongoing flow cytometry analysis also reveals tissue-specific differences in the neonatal septic response: neutrophils in WT lungs upregulate VISTA, PD-1, and PD-L1 after CS, whereas splenic neutrophils show no such change. Thymic CD4+CD8+ T-cells in WT neonates also decrease following CS.

Moving forward, we will explore the mechanism by which VISTA impacts mortality. We will isolate T-cells, neutrophils, and macrophages from the spleen, lung, thymus, liver, and peritoneal lavage, analyzing cell counts and degree of checkpoint protein expression. Additionally, we will examine histological changes to the lung, liver, kidney, thymus, and spleen and measure lung edema using wet-to-dry weight ratios. AST, ALT, and bilirubin will be used as serum markers for liver damage, as well as creatinine and BUN for kidney damage. Lastly, proinflammatory cytokine profiling using the LEGENDplex Multiplex Assay will quantify the overall inflammatory response. Ultimately, our overarching goal is to elucidate the role of VISTA in the neonatal septic response.

John Maragakis

B13

Home Institution: Brown University

Summer Research Program: Summer Research Assistantship in Biomedical Sciences Faculty

Mentor: Anne Hart (Neuroscience)

Identifying Suppressors of Motor Neuron Degeneration in *Caenorhabditis elegans* ALS-mutants

Amyotrophic Lateral Sclerosis (ALS) is a neurodegenerative disease that is characterized by motor neuron degeneration resulting in loss of strength in voluntary movement, and eventually death by respiratory failure. While a large proportion of ALS cases appear to be sporadic, a number of genes have been causally linked to the disease. Of these genes, a G4C2 hexanucleotide repeat expansion (HRE) in C9orf72 is responsible for approximately 40% of the observed cases of familial ALS. In an effort to uncover potential genetic modifiers that might be relevant to patients with the C9orf72 HRE, we utilized a *C.elegans* model containing a 30x G4C2 construct to reproduce the neurodegenerative phenotype of ALS. Notably, these worms display significant neuronal death in the phasmid tail neurons, which are easily dye-filled and counted as a quantifiable marker of degeneration. The goal of this project is to identify modifier genes whose perturbation suppresses neurodegeneration in the HRE model. To undertake this, we expose these worms to EMS (ethyl methanesulfonate) mutagenesis, examine them for potential rescue of the neurodegenerative phenotype, and identify and isolate the causal mutation via whole-genome sequencing. Preliminary results have identified numerous mutant lines that show quantifiable rescue of neurons, and whole-genome sequencing is currently underway to identify the underlying modifier genes accounting for this neuroprotection. This identification of novel neurodegeneration suppressors has potential to uncover new therapeutic targets that could one day improve the outcomes for people with ALS and other neurodegenerative diseases.

Anna Kim

B14

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Jonghwan Lee (Biomedical Engineering)

Vascular Changes in a Non-Invasively Induced Model of Migraine

Migraine is a debilitating neurological disorder characterized by moderate or severe recurrent headaches with accompanying reversible neurological and systemic symptoms. Though the pathophysiology of migraine pain accompanied with aura is largely unknown, cortical spreading depression (CSD) is widely accepted as the neural correlate of migraine aura. CSD is a slow-spreading wave of neuronal depolarization associated with an initial phase of cerebral hyperperfusion followed by prolonged hypoperfusion. CSD has been shown to be associated with migraine with aura, both in animal models and humans, although the association does not necessarily support any cause-effect relationship. Migraine aura commonly occurs without headache, and most migraine attacks do not include aura, indicating that the aura is not necessary or sufficient for headache. The robustness of the theory of CSD as a potential trigger for migraine pain is limited by the fact that all the studies used to analyze migraine pain or the role of CSD use an invasive trigger of migraine. Because of the invasive nature of these protocols, studies in humans have resorted to instructing patients to come as soon as possible to the lab at the onset of a headache leading to delays with very little evidence of what happens at the onset of a headache. This study aims to find a noninvasive trigger of migraine, which would allow for more applicable research. A more ethical and clinically relevant migraine trigger may be a combination of invoked stress and sensory stimuli. For both the group of FHM1 mice and WT mice, we make a cranial window on the cortex and then measure the mice's blinking and shuddering behavior for one week. While recording mouse facial features and after initiating OCT imaging, we simulate acute stress by placing mice in a restrainer tube inside an empty cage illuminated by two separate light sources. The light stimulus is shone at a range of frequencies with different wavelengths of light.

Josephine Chen

B15

Home Institution: Brown University

Summer Research Program: Undergraduate Research Assistant

Faculty Mentor: Reshma Munbodh (Radiation Oncology) Patrick John (Radiation Oncology)

Evaluating methods of dose computation on head-and-neck cancer patients using Adaptive Radiation Therapy (ART)

In conventional radiation therapy, patient treatment plans are created from the information acquired at the time of computed tomography (CT) simulation. Such plans are utilized throughout the course of treatment, which is administered daily over several weeks. However, a patient's anatomy and physiology can change from the time of simulation due to tumor shrinkage, weight loss, etc. This can cause radiation dosage inaccuracies, as the plans disregard the geometric deformation in the area around the target site for therapy. Adaptive radiation therapy (ART) is a rapidly emerging process that seeks to resolve the disadvantages of conventional radiation therapy. ART considers patient-specific anatomical and physiological changes over time through consistent dose tracking and plan corrections to improve the treatment's accuracy. In this study, we evaluated the accuracy of three different dose calculation methods that can be implemented into ART to treat head-and-neck cancer patients: computing dose on segmented cone-beam computed tomography (CBCT), deforming dose onto the CBCT, and computing dose on deformed CT with CBCT geometry. Using the treatment planning system RayStation, the three dose calculation methods were performed on a patient. Through this study, we were able to determine the strengths and limitations for each of the three methods of dose evaluation. Based on this preliminary evaluation, computing dose on deformed CT provided the most accurate and practical dose calculation. In addition, we found that dose tracking and real-time adaptive planning are feasible for clinical implementation with the current tools we have. However, further research into automating several components of the workflow on a larger patient cohort is needed for seamless application of ART in a clinical environment.

Jacqueline Cho

B16

Home Institution: Brown University

Summer Research Program: Undergraduate Research Assistant

Faculty Mentor: Anne Hart (Neuroscience)

Swimming exercise and fatigue in ALS SOD1 models

Amyotrophic Lateral Sclerosis (ALS) is a fatal disorder characterized by cholinergic and glutamatergic neuron degeneration. Fatigue is a common symptom of multiple neurodegenerative disorders, including ALS, however it continues to be poorly understood in this context. Professional athletes who engage in excessive physical activity throughout their career have increased risk of developing ALS, suggesting a correlation between exercise and ALS. Prolonged *C. elegans* swimming activity demonstrates key shared features of mammalian exercise including postexercise locomotory fatigue and increased muscle mitochondrial oxidative stress. *C. elegans* also cycle between active and inactive bouts after prolonged swimming; these inactive quiescent bouts may act as a recovery state like fatigue. *C. elegans* ALS SOD1 models show increased swimming activity when exposed to paraquat, an oxidative stressor. Since exercise is stressful, investigation of locomotion quiescence in *C. elegans* ALS SOD1 models during prolonged swimming activity may allow us to better understand the pathways involved in fatigue, specifically in ALS and neurodegenerative disorders.

Phoebe Lokwee

B17

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Reshma Munbodh (Radiation Oncology, Alpert Medical School)

Radiation Toxicity in the Use of Gamma Knife Radiosurgery for Refractory Trigeminal Neuralgia

Trigeminal Neuralgia (TG) is a debilitating illness that causes facial pain in patients making it difficult to perform daily tasks, such as washing one's face. It mainly occurs when a blood vessel presses down on the root of the trigeminal nerve. There are several treatment options available including, pharmacological options, invasive and non-invasive surgeries. Our research focuses on Gamma Knife Radiosurgery (GKR). GKR is a non-invasive surgical method that applies radiation to the root of the trigeminal nerve. We study how spatial dose distribution on the nerve, follow-up time, and other comorbidities contribute to radiation toxicity in patients. The data is from 99 patients treated with Trigeminal Neuralgia using GKR in the Tufts Medical Center between 1999 and 2016. We use python to acquire necessary data from patient DICOM (Digital Imaging and Communications in Medicine) images consisting of MRI scans and dose plans. We use PyDICOM to read patient images and acquire relevant metadata. Numpy and Scipy are then used to analyze and manipulate all matrix information. Dicompyler is used to calculate dose-volume metrics, such as the maximum, minimum, and mean radiation dose applied to the nerve. In the future, we aim to perform statistical analysis using Sklearn to determine the relationship between these dose metrics and the radiation toxicity experienced by patients. We, therefore, aim to find ways to improve patient outcomes by establishing the demographic and spatial factors that would minimize radiation toxicity among patients treated with Trigeminal Neuralgia using Gamma Knife Radiosurgery.

Hossam Zaki

B18

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Rithambhara Singh (Computational Biology)

Predicting Cell Type using Single Cell Expression Data and Gene Regulatory Networks

Single-cell RNA sequencing (scRNA-seq) is a powerful tool for identifying cell types and understanding the transcriptional basis of cellular identity. However, the biological interpretation of scRNA-seq data is often challenging due to the complexity of the gene regulatory networks that underlie cell type differentiation and the interdependence of the different cell types within a tissue. We present a novel approach to this problem by combining single-cell gene expression data and gene regulatory networks to predict cell type from a graphical neural network. Our approach uses a graph-based artificial neural network with gene expression values as inputs and a gene regulatory network as the

graph. A classification of any cell type can be represented by a subgraph on the graph. We have found that this method can be used to accurately predict cell types by utilizing the known gene regulatory networks or using a computational approach for determining them. Overall, the model performs as well as the state-of-the-art models that have been developed. However, our model will enable us to conduct further analyses of gene regulatory networks as well as allow for easy interpretability to learn cell-specific genes. Such insights would be especially useful in studies of cellular differentiation, to infer through which regulatory mechanisms a cell differentiates into one type from another, or in studies of finding potential therapeutic perturbation targets in heterogeneous diseases.

Melih Ozsoy

B19

Home Institution: N/A

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA)

Faculty Mentor: Jennifer Ribeiro (Obstetrics and Gynecology) James Nicole (Obstetrics and Gynecology)

Immunologic Signatures of Treatment Efficacy in High Grade Serous Ovarian Cancer

Epithelial ovarian cancer is the most lethal gynecologic cancer, globally accounting for 152,000 deaths annually. However, our understanding of the factors contributing to chemotherapy resistance and the factors that predict clinical outcomes is still limited. Our project aims to analyze the effect of different standard of care therapies, namely Carboplatin, Paclitaxel, Olaparib, and Bevacuzimab, on tissue based immunologic profiles in high grade serous ovarian cancer (HGSOC), with a specific focus on the immune ligands ICOS-L and PVRL2. Our preliminary data showed that the T cell co-receptor ICOS is associated with improved HGSOC patient outcomes, while PVRL2 was the most highly expressed ligand in HGSOC tissue. We believe that this analysis can better our understanding of how chemotherapy and targeted therapies affect the tumor immune microenvironment, which may aid in tailoring treatment approaches and uncovering opportunities for novel treatments. We hypothesize that immunologic signatures may predict chemotherapy response in HGSOC and that the patterns of expression for these signatures will vary with different therapeutic approaches and different resistance profiles. Our experimental results so far indicate that ovarian cancer therapeutics differentially modulate levels of the immune ligands ICOS-L and PVRL2 in tumor cells, and that HGSOC cells with different chemotherapy resistance profiles also display alternative cytokine signatures.

Chloe Wray and Emma Whittemore

B20

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Micheal Barresi (Biological Sciences and Neuroscience)

Manipulating connexins to explore the role of bioelectrics during early development in *Danio rerio*

Our overarching goal is to understand how gradients of membrane potentials, which generate bioelectric signals, play a role in establishing an organism's body plan. In order to achieve this we have focused on determining the role of connexins and other ion channels in mediating early axis formation. Using zebrafish as the model, preliminary studies from the Barresi Lab at Smith College suggest that distinct bioelectric patterns may exist prior to the determination of cell fates along the zebrafish axes. To dissect whether bioelectrics may play a superimposing role on the inductive effects of morphogens, we set out to test whether Connexin-mediated bioelectric signaling is essential for early axis determination. We established a heat shocking technique that allowed us to activate the transcription of connexin modulating genes and induce a heat shock promoter within the zebrafish embryos of heat shock line Tg(hsp70: miR133sp) and heat shock line Tg(hsp70: miR-133 B22), also known as "pre". In doing so, we were able to both upregulate and down regulate connexin43 signaling, a gap junction protein that suppresses joint formation, showing that connexin-mediated bioelectrics is required for proper anterior brain and posterior tail development.

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Ian Wong (Engineering)

Collective and Individual Invasion from Multicellular Spheroids in 3D Collagen Matrix

Epithelial tissues and tumors exhibit both collective (group) and individual invasion based on instructive and permissive cues from the surrounding extracellular matrix (ECM). For instance, malignant tumors display multicellular strands with leader cells, while individual cells can also break away with propulsive amoeboid or adhesive mesenchymal phenotypes. Multicellular spheroids embedded in reconstituted collagen-1 hydrogels provide a physiologically-relevant, 3D platform for investigating tumor invasion. In this project, we investigate how collective and individual cell migration are governed by collagen microstructure. We systematically tuned the collagen biopolymer's microstructural properties such as fiber length, density, and spacing in order to promote cellular migration by adjustment of the gel's collagen concentration, gelation temperature, and salt concentration. Next, breast cancer cells with varying vimentin intermediate filament expression, including MDA-MB-231 malignant epithelial cells, non-malignant epithelial MCF-10A cells, and MCF-7 luminal epithelial cells, were embedded in the gels in order to elucidate which collagen conditions permit collective cellular migration. Our engineered gels had microstructures ranging from optically clear with many short, thin fibrils to turbid with long, thick fibrils. We observed that MDA-MB-231 cells capable of secreting MMPs invaded individually in all gel conditions. Non-MMP expressing MCF-7 cells showed the highest degree of collective invasion in gels with large fibers pore size. Our results indicate that the appropriate collagen conditions are able to mimic physiological conditions in promoting collective cellular migration for a variety of breast cancer cells, demonstrating potential as a 3D biomimetic model for investigating collective invasion and metastasis in vitro. In future work, we will investigate the functional role of vimentin intermediate filaments in mediating cellular deformability and adhesion.

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA)

Faculty Mentor: Qian Chen (Department of Orthopaedics) Liu Yajun (Department of Orthopaedics)

Determining the efficacy of NRTI Lamivudine for OA intervention

Osteoarthritis (OA) is a leading cause of age-related disability with no current FDA-approved disease-modifying osteoarthritis drug. OA involves the gradual degeneration of joints due to cartilage deterioration, chronic inflammation, and bone remodeling. Cell senescence, a critical component of OA pathogenesis, may be prevented by manipulation of LINE-1 (L1). L1 is a human retrotransposon occupying 17% of the human genome and capable of autonomous retrotransposition. L1 is responsible for insertional mutagenesis and overall DNA damage and genome instability in somatic cells. In the case of OA, L1 expression has been shown to promote miRNA-365, a key inflammatory mediator of OA. L1 retrotransposition can be inhibited by nucleoside reverse transcriptase inhibitors (NRTIs), a class of antiviral drugs approved by the FDA. The main objective of this project is to determine if NRTIs can be used to treat OA by L1 inhibition in the joint. If successful, NRTIs, which are safe and readily available, can be re-purposed to treat human OA. In this study, the NRTI Lamivudine (3TC) will be used in a mouse model to treat OA caused by a destabilized medial meniscus (DMM) injury. To determine the time window for intervention in injury-induced OA, two intervention windows will be tested: early intervention immediately following the injury, and delayed intervention following the disease onset and structural changes in the joint. The mouse model Col2A1CreERT2;miR-365 will be used, which is susceptible to both injury and aging-induced OA. Following treatment, histology and micro-CT will be performed to quantify cartilage degeneration and bone morphology. RNA and proteins will be collected to quantify SASP expression and other OA markers. Gait analysis will be utilized to identify changes in movement in the mice. This

project will establish the efficacy and ideal timeframe of NRTI intervention for OA, laying the framework for the first FDA-approved disease-modifying osteoarthritis drug.
Morgan Woolridge

B23

Home Institution: University of Missouri-Columbia
Summer Research Program: Leadership Alliance-Summer Research Early Identification Program (SR-EIP)
Faculty Mentor: Lalit Beura (Department of Molecular Microbiology and Immunology) Hasan Mohammad (Department of Molecular Microbiology and Immunology)

Analysis of Intrinsic and Extrinsic Factors that Control CD8 Resident Memory T Cell Differentiation

Resident memory CD8 T cells (TRM) are critical defenders against intracellular infections and cancers in barrier organs. Because of their critical anti-pathogenic function it is important to understand how these cells are established in barrier organs. The various cell- intrinsic and -extrinsic factors that make an effector T cell permanently reside in tissue and become a TRM is an intense area of investigation. However, the identification of factors that play a deterministic role in TRM differentiation is in its infancy. To analyze which factors influence TRM localization at the site of pathogen encounter, primary literatures were collated and their findings were summarized. These findings and the relevant context of the experiments were discussed. Findings indicate that the expression of markers CD127 and KLRG1 identifies a pool of precursor cells that gives rise to TRM. It was also found that the strength of the interaction between the T cell receptor (TCR) and the antigen-presenting cell (APC) significantly impacted T cell differentiation into TRM. Transcription factors such as Blimp1, Runx3, Eomes, and T-bet also play a significant role in TRM differentiation. The findings of this literature review will help in guiding future questions and experimentation related to TRM differentiation and ultimately aid in the development of future vaccines and therapeutics.

Gio Guanuna

B24

Home Institution: Brigham Young University
Summer Research Program: Leadership Alliance-Summer Research Early Identification Program (SR-EIP)
Faculty Mentor: Michael Frank (Cognitive, Linguistic, and Psychological Sciences) Hitchcock Peter (Cognitive, Linguistic, and Psychological Sciences)

Rumination Impairs Learning

Rumination can be detrimental to mental health and other brain functions as it involves repetitive negative reflection on past events and their future implications. Past studies have shown that rumination impairs learning mechanisms such as working memory (a limited amount of information temporarily stored for immediate use which is thought to guide rapid adjustment during learning) and reinforcement learning (a more long-term mechanism based on the idea that learning occurs when expectations conflict with perceived outcomes), but how it does is not fully understood. In a future test phase of our investigation this question will be fully analyzed while in this acquisition phase we will be utilizing computational methods in a pilot simulation task that compares sample data reflecting ruminative and neutral conditions. We hypothesize that by varying our data inputs we will see ruminative conditions leading to slower learning during this acquisition phase of our investigation. The validity of this hypothesis could help us to know better the effects of rumination on choice and learning and what can be done to prevent this unfavorable tendency which may lead to improvements in how to treat mental illness.

Leona Hariharan

B25

Home Institution: Brown University
Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty Mentor: Kate O'Connor Giles (Neuroscience)

Investigating the role of PDZD8 in behavior and aging

Membrane contact sites (MCS) are the sites at which cellular organelles connect to facilitate intracellular signalling, lipid metabolism, and organelle dynamics and biogenesis in eukaryotic cells. The endoplasmic reticulum (ER) forms an extensive and dynamic network of MCSs with almost all organelles. MCSs between ER, endosomes, and mitochondria are particularly abundant, suggesting important physiological roles. MCSs are made possible through the use of contact site proteins. The functional relevance of MCSs in neurons is a matter of active research.

PDZD8 is a synaptotagmin-like mitochondrial-lipid-binding domain (SMP) containing protein. It is an intrinsic endoplasmic reticulum (ER) transmembrane protein reported to be localized at membrane contact sites between ERmitochondria and ER-late endosomes. We identified PDZD8 in a screen for uncharacterized conserved synaptic genes in *Drosophila*. We have shown that PDZD8 is neuronally enriched and promotes synaptic growth. However, little is known about its effect on behavior and maturation of the nervous system. Based on its expression, I have hypothesized that PDZD8 may play a crucial role in age-dependent regulation of behavior. In order to test this, I used several behavior paradigms to study age-dependent changes in activity in loss of function mutants in dPDZD8. Preliminary analysis suggests that PDZD8 mutants perform worse than wild type flies in motor behavior assays and this difference is exacerbated by age. These findings suggest a critical role for ER MCSs in the nervous system that may increase with age.

Christina Hung

B26

Home Institution: Smith College

Summer Research Program: Leadership Alliance-Summer Research Early Identification Program (SR-EIP) Faculty

Mentor: Jason Ritt (Neuroscience)

Full-Body Coordination in Mice During Tactile Exploration

Active sensing is the process by which organisms selectively extract information from their environment through actions such as eye motions, sniffing, or body motions like finger scanning. This project explored full-body coordination in mice during whisker-based tactile exploration, a key example of active sensing. Videos of mice searching for randomly located water rewards were analyzed using DeepLabCut (DLC), an open-source machine learning application for pose estimation. In ongoing analysis, we are investigating if detection of tactile contacts, or changes in head and body trajectories, are influenced by the timing of foot placement. Better understanding of motor coordination during tactile exploration could inform future treatments for sensory impairments and the development of technologies such as haptic interfaces.

Claire Brown

B27

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Peter Belenky (Molecular Microbiology & Immunology)

Streptozotocin-induced Host Hyperglycemia as a Determinant of Susceptibility to *Salmonella enterica* Infection

The gut microbiome is the amalgam of microorganisms inhabiting the gastrointestinal tract. In a healthy state, these microbes aid in digestion and pathogen resistance. Disruption of microbiota function—through antibiotics, dietary changes, or host metabolism changes—can affect host susceptibility to opportunistic pathogens such as *Salmonella enterica*. Despite our understanding of microbiome damage from these perturbations individually, the combinatory damage of aberrant host metabolism and antibiotic exposure remains understudied. This project aims to characterize how microbiome damage from streptozotocin (STZ)-induced hyperglycemia and amoxicillin (AMX) treatment impacts the susceptibility of mice towards *S. enterica* infection.

To accomplish this, four experimental groups were established: (1) normoglycemic mice without AMX treatment, (2) normoglycemic mice treated with AMX, (3) STZ-treated mice without AMX treatment, and (4) STZ-treated mice treated with AMX. Sustained hyperglycemia was induced using STZ injection; we confirmed this phenotype's duration in the first phase of this project. We established the four treatment groups, then challenged mice with *S. enterica* Typhimurium. Throughout infection, we monitored pathogen burden and animal welfare, finding the combination of STZ/AMX treatment to greatly worsen infection burden. Additionally, we found that STZ/AMX cotreated mice had greater outgrowth of an unidentified colony. Using traditional microbiological techniques we confirmed this to be *Klebsiella oxytoca*. It is possible that differences in microbiome function between experimental groups impacts the trajectory of changes in microbiome taxonomy during infection, prompting us to assess the microbiome's taxonomic composition before and during infection using 16S rRNA sequencing. We found that STZ and control mouse microbiomes are similar before antibiotic treatment but differ afterwards, likely driving differential susceptibility to *S. enterica* infection.

Jonathan Ge

B28

Home Institution: Brown University
Summer Research Program: PLME-SRA
Faculty Mentor: Qian Chen (Orthopedics)

Matrilin-2 within a Lysine Enhanced Chitosan Scaffold Enhances Schwann Cell Migration and Axonal Outgrowth during Peripheral Nerve Regeneration

The purpose of these experiments is establishing a biomimetic scaffold of Matrilin-2 (MATN2) in a lysine enhanced chitosan conduit. We hypothesize that this scaffold enhances Schwann cell (SC) migration and adhesion as well as axonal outgrowth during peripheral nerve regeneration. An agarose drop migration assay evaluates change in SC migration in MATN2 compared to water. After culturing SCs atop tissue culture dishes coated with MATN2, an adhesion assay will be performed and compared to water dishes. Testing the percent weight of Chitosan and the MATN2 concentration forms the initial scaffold constructs. A MATN2/Chitosan solution is placed into collagen conduit, and SC migration will be tested in conduits with and without scaffold in a capillary migration assay. A three-dimensional organotypic assay is performed utilizing dorsal root ganglions (DRG) placed atop empty versus scaffold filled conduits. The conduits are fixed, cryosectioned, and stained against neurofilaments under immunofluorescence protocol to determine axonal outgrowth. Greater SC migration and adhesion was found with MATN2 compared to water. The SCs are able to migrate against gravity up the scaffolded conduit compared to no migration within the empty conduit. Three-dimensional organotypic assay demonstrated that scaffolds with chitosan augmented by lysine and MATN2 supported greater DRG adhesion and subsequent axonal outgrowth.

MATN2 interacts with SCs to permit greater migration and adhesion within their environment. To exploit this in three-dimensional structures to improve nerve repair, MATN2 was combined with chitosan forming a porous scaffold within a collagen conduit, demonstrating improved SC interaction and activity. Addition of Lysine to the chitosan-MATN2 complex demonstrated greater adherence of the DRG complex, permitting axonal outgrowth.

Shakson Isaac

B29

Home Institution: Brown University
Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty
Mentor: Mamiko Yajima (Molecular Biology, Cell Biology & Biochemistry)

Reverse-Engineering the Sea Urchin: Uncovering Network Mechanisms of Differentiation through Single-Cell Transcriptomics

Reverse engineering is described as extracting complexities without a-priori knowledge. Biological organisms are complex and contain many regulatory elements that control defined processes such as the cell cycle, morphogenesis, and cellular differentiation. Temporal and spatial regulation of gene expression is important to describe potential

models for the differentiated cell lineages. Through a reverse engineering approach, this project aims to construct gene regulatory networks depicting important cellular differentiation events in sea urchin embryogenesis through scRNAseq data.

Available scRNA-seq data of the sea urchin embryo from Foster et al., 2020 was used to develop gene regulatory networks driving differentiation of important cell lineages such as pigment vs blastocoel cells, primary mesenchyme vs secondary mesenchyme cells, etc. The scRNA-seq data covered eight time points in sea urchin embryogenesis, 8cell to late gastrula stage. scRNA-seq data was clustered into cell lineages through semi-supervised algorithms using marker gene expression and neighboring non-marker gene expression levels. Trajectory inference was performed on sets of cell lineages to depict the start, decision, and endpoints of a particular topology (linear, bifurcation, tree, etc.). Differentially expressed genes along multiple lineages were characterized by their pattern of expression and potential to be a driver of differentiation. Network analysis was performed on the differentially expressed set of genes to detail networks specific to each cell lineage and find possible subnetworks that describe decision points in differentiation.

Through this process, gene regulatory networks were constructed describing both the differentiation of cell lineages and cell lineage-specific regulation. These constructed networks can be used to assess perturbations that can lead to failure to differentiate, developmental delays, gastrulation failure, etc. Through these computational results, experimental tests involving the knockdown of genes and validation of localization of genes through whole-mount insitu hybridization can be performed.

Selin Baydar

B30

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Amitai Shenhav (Cognitive, Linguistic & Psychological Sciences)

The Role of Performance Efficacy and Penalty in Cognitive Effort Allocation

People have the remarkable ability to flexibly adjust how much mental effort they invest in a task. This ability, called cognitive control, allows us to adjust how we process information and allows us to successfully reach our goals. Previous research has shown that people allocate more cognitive control in situations in which they expect that this will translate into better outcomes (either as gaining reward or avoiding punishment). While the value of expected outcomes determines how much control is worth, another crucial component of motivation determines whether the effort is worthwhile. Namely, how much control people allocate also depends on performance efficacy – the probability that people will reach the desired outcome given their performance. Specifically, people allocate more cognitive control when they expect that outcomes will depend on their performance, rather than on random chance. In this study we will test how expected negative outcomes interact with performance efficacy to determine control allocation. We will run a web-based behavioral experiment in which people will have the opportunity to earn rewards and avoid penalties while performing a cognitively demanding task that requires cognitive control. Before each run of the task, they will receive information telling them whether (a) they are in a high penalty or low penalty condition and whether (b) outcomes (monetary rewards or losses) will be based on their performance (high performance efficacy) or determined by random chance (low performance efficacy). This design will enable us to investigate the effects of expected performance efficacy and expected penalty on cognitive control allocation. Specifically, we will test how the impact of negative outcomes on cognitive control differs depending on whether the penalties depend on task performance or random chance.

Leya Groysman

B31

Home Institution: Macaulay Honors College at Hunter College

Summer Research Program: Leadership Alliance-Summer Research Early Identification Program (SR-EIP)

Faculty Mentor: Wafik El-Deiry (Pathology and Laboratory Medicine) Carlsen Lindsey (Pathology and Laboratory Medicine)

Evaluating the Effects of Chemotherapy on p53 Targets and Cytokines in Breast and Colorectal Cancer

Chemotherapy is a widely used form of treatment for cancer but the mechanisms by which these drugs mediate efficacy and toxicity in patients are not fully known. Drugs, such as cisplatin, are used to treat multiple cancers yet there is heterogeneity in the response of the TP53 gene across tissue types. The p53 protein is widely known as the “guardian of the genome” and plays a critical role in cancer prevention by either inducing DNA repair, cell cycle arrest, or apoptosis. In response to chemotherapy, cancer cells can induce cytokine production which can promote proliferation, metastasis, and drug resistance. In addition, chemotherapy drugs often have efficacy despite p53 mutation and so our knowledge of exactly how the drugs work or don't work for some patients is limited. By evaluating the effects of oxaliplatin, cisplatin, 5-fluorouracil (5-FU), doxorubicin, paclitaxel, docetaxel, and carboplatin on p53 targets and cytokine induction in the MCF7 breast cancer cell line and in the HCT116 colorectal cancer cell line, a preliminary understanding of how these drugs function may begin to be discerned. While clearly much work remains to improve treatments for patients with cancer, the long-term goal of these efforts may contribute to improved patient outcomes in the future by advancing the development of targeted therapies and novel drug combinations.

Emma Whall

B32

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Ruth Colwill (CLPS)

Revision of an Online Laboratory Course (CLPS1191)

Online learning is the way of the future. In response to the COVID-19 pandemic, CLPS1191 (Animal Behavior Laboratory), while traditionally taught in a 14 week in-person semester, has been shifted to an online virtual lab course taught during Wintersession 2022. When taught in person, CLPS1191 drew from visits to the Roger Williams Zoo, where students would conduct assignments pertaining to animal behavior observation and exhibit resources. Currently, the course has been modified to have materials available to all students in place of the zoo visits. The new resources are available to all students no matter location on the globe to allow for more diversity and equity across the student population in caliber of online learning. While transitioning the course to be able to run fully remotely, new grading rubrics and assignment details have been designed, as well the course schedule have been modified to encapsulate a semester long course to a 28-day Wintersession lab course.

Johnson Renita

B33

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Craig Lefort (Department of Surgery)

Investigating Genes that Regulate ROS Generation in Neutrophils

Neutrophils, the most abundant leukocyte in circulation, are critical for maintaining host defenses against infection. These cells traffic quickly to sites of infection and carry out effector functions such as phagocytosis and subsequent intracellular killing using reactive oxygen species (ROS). Neutrophils' ability to generate ROS is dependent on the NOX2 complex. Disruption of NOX2 can lead to impaired ROS generation and systemic immunodeficiency as seen in Chronic Granulomatous Disease (CGD). Conversely, overproduction of ROS and its aberrant release can also be harmful and may result in collateral tissue damage at sites of inflammation. Given the central role ROS production plays in modulating the immune response, understanding how specific genes influence ROS production is important. Previous research has identified that Rnf145, a ubiquitin cycling gene, regulates the NOX2 complex in monocytes. Rnf145 however, has yet to be studied in neutrophils. Through our research we hope to elucidate the role of Rnf145 in neutrophils and in doing so further expand our understanding of ROS regulation. In addition, we will investigate

how neutrophil elastase as well as cathepsin C and G contribute to non-oxidative killing (NOX2-independent) and the impact of their disruption on ROS generation. These studies will provide insight into ROS regulation, and this may in turn inform development of interventions against drug-resistant microorganisms.

Lindsay Marmor and Kenneth Bradley

B34

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: David Rand (Ecology and Evolutionary Biology)

Genetic Analyses of Sex-Specific Mitonuclear Interactions and their Phenotypic Consequences in *Drosophila*

Mitochondria play important roles in determining the fitness or disease states of individuals based on how the 37 genes in mtDNA interact with the ~1000 genes in the nuclear genome that are expressed inside mitochondria. Each individual has a unique mito-nuclear genotype due to the mutations that can occur in our two genomes. These gene x gene interactions (GxG) and the interactions of mito-nuclear genomes with the environment (GxE) will cause different phenotypic consequences in different individuals. We sought to determine how these mito-nuclear interactions affect phenotypes through the use of two different assays that place demands on central metabolism: starvation resistance time and climbing speed in *Drosophila*. It has been proposed that mitochondrial diseases may be more pronounced in males than in females due to the maternal inheritance of mtDNA which imposes stronger natural selection on female-based mitochondrial phenotypes. This 'Mother's Curse' hypothesis predicts that phenotypic variation should be greater among males than among females due to the relaxed selection on males. We tested this hypothesis by measuring starvation and climbing in both male and female *Drosophila* among several distinct mito-nuclear genotypes: 5 different mtDNAs from 3 different species each placed on three different nuclear genetic backgrounds. Our starvation assays reveal that female *Drosophila* are more starvation resistant than male *Drosophila*, however female *Drosophila* vary more than males across mtDNA genotypes. We also found that male *Drosophila* are faster climbers than female *Drosophila*, however female *Drosophila* showed higher levels of mito-nuclear interactions compared to males which showed very little. Overall, there was limited support for the Mother's Curse predictions. These studies will be used to determine if it is specifically the mtDNA which is affecting these phenotypes or specific nuclear genes that are responsible for these complex mito-nuclear interactions.

Kathleen Meininger

B35

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Alexander Jaworski (Neuroscience)

The Role of Transient Axonal Glycoprotein Type-1 in Neuron Cell Body Anchoring and Motor Axon Guidance

Axonal wiring during nervous system development requires the presence of molecular guidance cues, which steer the axon as it projects from the cell body towards its target synapse. The cell surface protein Transient Axonal Glycoprotein Type-1 (TAG-1) plays several important roles in motor neuron (MN) wiring in mice, including anchoring cell bodies within the spinal cord and maintaining fasciculation of axons during their projection from the neural tube. Our previous work demonstrated that, in mice lacking TAG-1, MN cell bodies become unanchored and ectopically migrate out of the spinal cord; further we found that non-MN cells of unknown identity also aberrantly exit the spinal cord. For the first part of my project, I used immunohistochemistry to characterize these non-MN ectopic cells and identified several populations of neurons that require TAG-1 to remain within the spinal cord. Previous research had also shown that loss of TAG-1 causes limb-innervating motor axons to misproject into the dorsal root ganglia (DRG), leading to reduced axon extension into the limb buds. This effect is stronger in mice with global loss of TAG-1 than in mice lacking TAG-1 in MNs only, suggesting that DRG-derived TAG-1 might also play a role in MN axon guidance. However, this idea remains to be tested directly. Further, it is unknown whether impaired motor axon growth into the limbs caused by loss of TAG-1 ultimately results in reduced synapse formation. Hence, for the

second part of my project I tested the hypothesis that MN- and DRG-derived TAG-1 cooperate during axon guidance by deleting TAG-1 from the DRGs and comparing motor axon projections to those in global TAG-1 knockouts, as well as wild-type mice. I also used immunohistochemical methods to investigate whether neuromuscular synapse formation in forelimb muscles of TAG-1 mutant mice is reduced compared to wild type. My results provide novel insights into TAG-1's role in neuronal cell body anchoring and guidance.

Calvin Perkins

B36

Home Institution: Brown University

Summer Research Program: NSF Research Experience for Undergraduates

Faculty Mentor: Mark Johnson (MCB) Ponvert Nahtaniel (MCB)

Is There a Rapid Block to Polyspermy in Plants?

Polyspermy is an event in which a female gamete is fertilized by multiple sperm cells resulting in an inviable zygote or dramatic changes in genomic content. It is important to understand the mechanism driving the prevention of polyspermy events across all species as it increases viability by ensuring the next generation will inherit the correct amount of DNA. In flowering plants, reproduction occurs when a pollen grain containing two sperm cells lands on the stigma of a flower. The sperm cells travel inside a pollen tube, a cellular extension of the pollen grain, from the stigma to the female ovules where they burst into an area between the two female gametes: the egg and the central cell. Each sperm cell pairs with either the egg or central cell; two sperm cells almost never fuse with one female gamete. Gamete pairing is essential for the success of plant species and is key to understanding how they bypass fatal polyspermy events each time sperm are delivered. Some animal species possess a rapid block to polyspermy in which the egg plasma membrane depolarizes after fusion with one sperm preventing all other sperm from fertilizing the egg. We hypothesize that in flowering plants, there is a rapid block to polyspermy on the egg cell preventing multiple sperm from fusing. To address this hypothesis we are taking two approaches. The first approach involves utilizing genetically encoded fluorescent voltage sensors to test the plasma membrane of the egg and central cells for voltage potential changes at the moment of gamete fusion. The second approach is to analyze TMEM16A, a conserved chloride ion channel implicated in the block to polyspermy in animals, and to determine the role it plays during gamete pairing in *Arabidopsis thaliana*. The importance of determining the highly effective mechanism that drives the block to polyspermy is crucial in understanding how every sexually reproducing species is able to pass on a viable amount of genetic information.

Jared Zhang

B37

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Thomas Bartnikas (Department of Pathology and Laboratory Medicine)

Decreasing liver manganese via dietary treatment corrects manganese excess, erythropoietin excess, and polycythemia in Slc30A10-deficient mice

Manganese is an essential nutrient to the human body and is required for proper function. However, an excess of manganese can be toxic. The regulation of manganese levels in the body is transporter-dependent, with the Slc30A130 metal transporter responsible for excretion of manganese from liver hepatocytes into the bile. Mutations in the Slc30A10 gene resulting in Slc30A10 deficiency cause severe manganese excess. Our lab previously generated mutant mice with Slc30A10 deficiency which developed manganese excess due to impaired manganese excretion. These mice also developed polycythemia, a condition of abnormally high levels of red blood cells, and an excess of erythropoietin (Epo), a hormone normally produced in the kidneys that stimulates synthesis of red blood cells. Mutant mice had increased liver Epo RNA levels but decreased kidney Epo RNA levels, suggesting that the liver is the site of Epo production in mutant mice. To determine if liver manganese excess causes liver Epo excess and polycythemia in Slc30A10-deficient mice, wild-type and Slc30A10-deficient mice were raised on manganese-sufficient and -deficient

diets and analyzed for liver manganese levels, liver Epo RNA levels, and red blood cell counts. In mutant mice, the manganese-deficient diet resulted in lower liver manganese levels, liver Epo RNA levels, and red blood cell counts. This suggests that decreasing liver manganese via dietary treatment corrected the manganese excess, Epo excess, and polycythemia in mutant mice. Overall, the results provide evidence that manganese excess causes liver Epo RNA excess and polycythemia in Slc30A10-deficient mice.

Marko Milić

B38

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Gerard Nau (Infectious Diseases RI Hospital)

COVID-19 Pathogenesis: Anti-Cytokine Antibodies in Convalescent Plasma

COVID-19 infections manifest in a variety of different clinical phenotypes underpinned and characterized by a misdirected host immune response. Compared to uninfected individuals, COVID-19 patients have been found to have high levels of autoantibody activity against immunomodulatory proteins. Antibodies against cytokines and chemokine may disrupt regulated immune functioning. Convalescent plasma therapy infused to patients may provide them neutralizing antibodies against COVID-19, but the potential significance of extraneous autoantibodies remains less clear. We developed an ELISA assay and tested 150 samples of convalescent plasma infused to patients. Our analysis finds detection of autoantibodies against proteins IFN-alpha, IFN-omega, IL-15, IL-31, and CCL3.

Thomas Usherwood

B39

Home Institution: Brown University

Summer Research Program: Working over the summer in a biomedical engineering lab at Brown Faculty

Mentor: Anubhav Tripathi (Engineering)

An Electrokinetic Microfluidic Platform for Solid-Phase Cell Free DNA Extraction from Plasma for NonInvasive Prenatal Testing

Non-invasive prenatal testing (NIPT) is a screening technique that can be used to gather genetic information about a growing fetus. In particular, NIPT is an important tool for aneuploidy testing due to the fact that it only requires a maternal blood sample. An important analyte for many NIPT workflows is cell-free DNA (cfDNA), which consists of small (~150 bp) fragments of DNA released by the placenta into the bloodstream. However, cfDNA is in very low concentration in blood plasma, and the fraction useful for NIPT is lower still, so high-yield procedures for cfDNA extraction from plasma are crucial. We present a high-yield, high-purity, and simple extraction method for cfDNA extraction. Using commercial buffers, an extraction workflow was formulated to include two wash steps on a polydimethylsiloxane microfluidic chip to ensure optimal removal of impurities. cfDNA was bound to magnetic beads through a binding buffer off-chip, and the beads were dragged through microfluidic chips pre-filled with wash buffer to remove contaminants from the blood plasma or previous buffers. In order to improve purification, electric fields were applied across the microfluidic chip from inlet to outlet wells to induce electroosmotic flow inside the microchannels. COMSOL Multiphysics simulations were performed to optimize the microfluidic chip design and understand the fluid mechanic and electrical properties of the wash buffers within the microfluidic chip. Applying both wash buffers on-chip was found to have a significantly higher cfDNA yield than when both washes were performed off-chip, outperforming most commercial protocols. In addition, applying the first wash buffer on-chip greatly increased the purity of the extracted cfDNA, measured by a A260/230 value. This indicates the increased removal of guanidinium thiocyanate (GTC) salts from the eluate, which is critical because GTC reduces the effectiveness of downstream NIPT quantification methods, due to the fact that it is a PCR inhibitor. An increased electric field applied inside the microfluidic chips further increased the removal of these impurities.

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Jennifer Sanders (Pathology and Laboratory Medicine)

Liver Normothermic Machine Perfusion Decreases Reperfusion Injury and Improves Viability

In the United States the number of patients on the waitlist for a liver transplant far exceeds the availability of viable liver donors. In fact less than 30% of patients on the national waitlist receive transplants. One of the major reasons for this phenomenon is a shortage of viable livers that can withstand hepatic ischemia-reperfusion (IR) injury during transplantation. IR injury occurs when a donor liver experiences prolonged periods of ischemia (insufficient or zero blood flow) followed by reperfusion treatment (a medical technique which restores blood flow). It is evident that there is a urgent and critical need for pharmaceutical therapies and nonpharmaceutical interventions to promote graft survival and increase the number of livers able to withstand IR injury. Normothermic machine perfusion (NMP) is one such therapy that may rehabilitate discarded steatotic (fatty) livers. This study aims to better understand transcriptomic changes associated with NMP in livers and examine the efficacy of inhibiting apoptosis. Hopefully, this increased understanding will reveal key DNA, RNA, protein, cytokine, and neutrophil targets to assist in the creation of more effective treatments. Six viable and five non-viable human livers that were discarded by local transplantation centers were obtained and underwent NMP with oxygenated blood. Serial tissue biopsies and plasma samples were obtained from the livers after they underwent 0 (pre-), 3 hours, 6 hours, and 12 hours of perfusion. Five other human livers underwent the same methods with the addition of an irreversible pan-caspase inhibitor, emricasan, at a dose of 5mg/kg liver. It was found that nonviable livers demonstrated significantly higher markers of apoptosis (for example cleaved cytokeratin 18, caspase-3/7 activity) than viable livers during NMP. Furthermore, the addition of emricasan significantly decreased apoptosis and IR injury.

Jason Tsai

B41

Home Institution: Brown University

Summer Research Program: project for NEUR 1970 (summer research independent study class) Faculty

Mentor: Anne Hart (Neuroscience) Yanagi Katherine (Neuroscience)

Examining shared suppressors of ALS-associated phenotypes in multiple SOD1 ALS C. elegans models

Amyotrophic lateral sclerosis (ALS) is a fatal, incurable disease characterized by degeneration of spinal cholinergic and cortical glutamatergic motor neurons. Mutations in superoxide dismutase 1 (SOD1), which encodes for the SOD1 enzyme protecting neurons from oxidative stress, cause ALS. However, mutations of other functionally diverse genes, such as C9ORF72, have also been associated with ALS, suggesting other genetic factors also contribute to its pathogenesis.

Additionally, other genetic factors known as modifiers may affect how ALS progresses given a certain causal mutation, such as SOD1. These modifiers could explain some of the clinical heterogeneity present in ALS patients populations, including those with SOD1 gene mutations, and may provide insights into disease-associated pathways. Some modifiers are suppressors, genes that, when mutated, ameliorate ALS-associated phenotypes despite the presence of the SOD1 mutation. This project aims to find shared suppressors of ALS-associated phenotypes across multiple SOD1 ALS C. elegans models.

This project investigates the sod-1G85R single-copy/knock-in and SOD1G93A overexpression models, both of which display ALS-associated phenotypes, for shared suppressors. The Hart lab has completed a classical forward genetic screen in single-copy/knock-in sod-1G85R C. elegans models, generating candidate suppressors of glutamatergic neurodegeneration. Additionally, Silva et al. (2011) performed an RNA interference (RNAi) genetic screen to identify suppressors of mutant SOD1G93A-YFP aggregation in a SOD1G93A overexpression C. elegans model. These two lists were compared to generate a list of common candidate suppressor genes of ALS-associated phenotypes.

Of the list, I am investigating if four of these genes suppress glutamatergic neurodegeneration in the sod-1G85R knock-in model. If suppression occurs, that could suggest common genetic factors underlie ALS-associated phenotypes in both the overexpression and the single-copy/knock-in ALS model. Shared suppressors could provide insight into the shared biochemical pathways underlying multiple forms of SOD1 ALS. Moreover, orthologs of these genes could be examined as potential targets for treatment for SOD1 ALS.

Sunny Lee

B42

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Alfred Ayala (Department of Surgery)

The Role of Gene Expression in a Murine Model of Hemorrhagic Shock-Induced Priming

Authors: Sunny Lee^{1,2}, Brandon Armstead^{1,2}, Sean Monaghan M.D.^{1,2} and Alfred Ayala Ph.D.^{1,2} Institutions: Brown University¹, Rhode Island Hospital²

Introduction:

Acute Respiratory Distress Syndrome (ARDS) and Indirect Acute Lung Injury (iALI) are potentially life-threatening conditions often resultant from traumatic injury followed by blood loss and/or infection. Through a fixed pressure hemorrhage model, pathology related to clinical shock can be represented in murine hosts. Infectious insults following hemorrhage (ie. sepsis), can trigger the primed microenvironment that is associated with an influx of inflammatory cytokines dispersed systemically. This study addresses gene expression in post-shock lung priming as it contributes to the pathogenesis of ARDS/iALI that develops after subsequent infectious challenge.

Methods:

A model of shock was implemented on C57BL/6 mice, which were hemorrhaged and kept at a fixed blood pressure of ~40 mmHg for 90-minutes. They were resuscitated with a lactated ringer's solution, and 24 hours later were sacrificed. Lungs were dissociated into single-cell suspensions. Samples from 2 mice per condition (sham or hemorrhage) were pooled. Libraries were prepared and sequenced by a contractor. Partek software was used to analyze single-cell RNA sequencing data, focusing on a subset of clinically relevant cytokines.

Results: IL-1 β gene expression trended downward in all cell types post-shock, except for neutrophils and eosinophils. The two phenotypes that didn't exhibit a decrease in IL-1 β expression conversely showed an increase in IL-1 α expression. IL2 in macrophages, T-cells, and CD209 +CD11B + dendritic cells displayed an increasing trend.

Conclusion:

Somewhat unexpectedly, there was a marked decrease in several mediators, including IL-1 β , in most cell types. However, an increase in IL-1 α expression was seen in only two phenotypes. Increasing and/or decreasing trends for other cytokines implicated in clinical shock, such as TNF- α , IL-6, MCP-1, IL-23 and IFN- γ , were detected in some phenotypes but not all, suggesting a dysregulated inflammatory response concurrent with clinical shock.

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA)

Faculty Mentor: Matt Nassar (Neuroscience Department) Yu Linda (Neuroscience Department)

How learning, memory and decision-making change with age in healthy adults

My research project aims to explore age-related changes in learning, memory, and decision making in healthy adults. The study emphasizes the presence of latent states, which are defined as a set of unobserved variables that must be inferred from observations and help to focus primarily only on relevant and important stimuli for learning and reinforcement. The goal of my project is thus to test a computational behavioral task oriented towards latent states in healthy adults and compare obtained data in younger and older adults.

The study consists of two parts: a behavioral & cognitive session and a fMRI session. Additionally, we conducted cognitive measures, such as WASI (fluid & crystallized intelligence), RBANS (cognitive functioning), ADMC (decision-making capacity). Overall, 25 younger adults and 6 old adults took part in both study sessions.

Collecting data from both younger and older adults will help us to analyze how learning and memory change with age. Since two different age-groups are present in our study, we hope to produce quantitative predictors on how different their learning and decision-making processes are and whether they undergo significant changes with increasing age. Additionally, we want to look if there is any relationship between a participant's behavior on the task and his or her cognitive measures, and whether the participant's performance on the task can be explained by variables like age and cognitive factors.

It was interesting to find that young adults learn at a faster rate and improve their performance with more blocks unlike older adults whose performance in the task does not significantly improve with more practice. Furthermore, performances of both young and old adults were influenced by several factors, such as prediction error (how close a response of a participant was to the location of the bomb in each trial), state return accuracy (how well a participant learn the correct location of the color for each of the two states), and state return response (how close a participant's response was to the last time he or she was in the same state).

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Mark Johnson (Molecular Biology, Cell Biology & Biochemistry)

Genetics Fall 2021: Preparing for what comes next

BIOL 470 is a popular introductory genetics course boasting an enrollment of well over 100 students each fall semester in recent years. Following a semester of completely remote teaching and lab components in Fall 2020, future iterations of Genetics will aim to combine and improve upon the most effective elements of virtual and in-person classroom models. The Fall 2021 design will feature a return to course material delivered through traditional classroom lectures supplemented by modular, pre-recorded videos highlighting auxiliary topics. The online videos allow in-class time to focus on discussion and problem solving approaches. Fall 2021 homework will be problem set based following a Gradescope analysis of Fall 2020 problem set submissions that quantifies pooled student performance on a question by question basis. The analysis yielded question-specific pitfalls typical among all submissions that were individually revised for clarity, difficulty, and narrowness. Fall 2021 problem sets and lab sessions will feature an integration of expanded bioethics units introduced in Fall 2020 that require group discussion of, and short writing responses to, readings covering ethical issues that have emerged in classical and modern genetics; these include eugenics, genomic databases used in criminal cases, gene drives, and personalized medicine via gene therapy. Foreseeing a return to inperson Clinic hours, undergraduate TAs will adopt the SignMeUp system first used in Fall 2020 to automatically order student questions based on submission time. New course material to be covered in Fall 2021 includes units on genetic model organisms, further exploration of epigenetics, and a reintroduction of population genetics topics trimmed from Fall 2020 material due to a shortened semester.

Home Institution: Brown University
Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty
Mentor: Mark Johnson (MCB)

Differential calibration of a cellular thermometer across tomato cultivars

As rising temperatures due to climate change threaten the yield of staple crops such as tomatoes, it has become increasingly important that we find a way to promote plant reproduction under these conditions. Of particular interest is the pollen tube, which is sensitive to heat and likely to burst under stress, thereby inhibiting the proper fertilization of an ovule. In order to investigate the molecular mechanisms behind thermotolerant crop varieties' ability to reproduce at higher temperatures, we are using the unfolded protein response (UPR) as our cellular thermometer. In the UPR, IRE1, an ER transmembrane sensor, detects local, denatured proteins resulting from heat stress, thereby activating its splicing activity, resulting in a cytosolic splicing event of bZIP60 mRNA. When spliced by IRE1, bZIP60 makes a transcription factor that activates UPR genes that allow the cell to respond appropriately to heat stress. By testing thermosensitive and thermotolerant tomato cultivars, we are able to compare each cultivar's sensitivity to temperature by monitoring the amount of IRE1-dependent splicing of bZIP60 mRNA. Our experimental setup is based on previous heat stress work in *A. thaliana* seedlings established by Deng et al. (2011) and consists of applying a heat stress of 37°C to pollen tubes, seedlings, and mature pollen grains for 1 hour. Though our primary goal is to understand the UPR in pollen tubes, testing seedlings and pollen grains will allow us to elucidate the specificity of the unfolded protein response with regards to plant material. Our hypothesis is that thermotolerant cultivars are primed to respond to heat stress and will exhibit more bZIP60 splicing under heat stress than those from thermosensitive cultivars. Our early results with seedlings are really interesting and suggest that the dynamics of the UPR are different between thermotolerant and thermosensitive cultivars in a way that is consistent with the priming hypothesis. We look forward to extending these experiments to pollen and other reproductive tissues to determine if the UPR can explain differences in fruit production under heat stress between thermotolerant and thermosensitive varieties of tomato.

Home Institution: Brown University
Summer Research Program: Summer Research Assistantship in Biomedical Sciences Faculty
Mentor: Kyle Martin (Division of Global Emergency Medicine)

Stop the Bleed: Hemorrhage Control for Traumatic Injury in Rwanda

Background: Traumatic injury is a major cause of morbidity and mortality in Rwanda. Road traffic accidents are a significant source of traumatic injury in the pre-hospital setting. For this reason, it is important to strengthen the prehospital response to trauma in Rwanda. Stop the Bleed (STB) is a standardized course on bleeding control basics and tourniquet application, designed by the American College of Surgeons. The course aims to empower laypersons to intervene quickly in traumatic emergencies while awaiting EMS arrival.

Objective: The objective of this study was to determine the impact of STB training on participant knowledge, attitudes and practices regarding bleeding control.

Methods: A total of 64 participants from two community organizations (Healthy People Rwanda and the Rwandan Emergency Care Association) were provided with training in STB. The course included a didactic presentation and a skills session where participants could practice wound packing and tourniquet application. A KAP (Knowledge, Attitudes, Practices) survey was provided to participants before and immediately after the STB training session. Additional follow-up surveys will be sent to participants at 3 months and 6 months post-training.

Results: Participant knowledge of techniques for bleeding control improved across 5 of 7 questions. Following STB training, more participants could correctly identify tourniquet placement (98% vs. 85%) and identify the correct order

of steps to take when treating bleeding (63% vs. 9%). There was also a significant increase in post-training confidence across six measures: identifying life-threatening bleeding, applying a tourniquet, applying direct pressure, wound packing, treating severe active bleeding, and teaching bleeding control techniques to others ($p < 0.001$). Finally, participants reported an increase in willingness ($p < 0.05$) and preparedness ($p < 0.001$) to apply bleeding control techniques in real-life situations.

Conclusions: This study found that STB training increased participant knowledge of bleeding control techniques and confidence in performing techniques for bleeding control.

Diana Milk-Batista

B47

Home Institution: Columbia University

Summer Research Program: Leadership Alliance-Summer Research Early Identification Program (SR-EIP) Faculty

Mentor: Joseph Braun (Epidemiology)

A cross-sectional study of hair cortisol concentration and cardiometabolic risk among 12 year-olds in HOME study

Background: Psychosocial stressors may negatively impact cardiometabolic health outcomes. High levels of cortisol, a hormone released in response to psychosocial stress, have been associated with negative cardiometabolic health outcomes in adults. However, less is known about the role of cortisol in the etiology of cardiometabolic health in children.

Aims: We examined the associations between hair cortisol concentrations and cardiometabolic risk markers among adolescents aged 12 years.

Methods: Using data from the Health Outcomes and Measures of the Environment Study (HOME), we estimated child hair cortisol concentrations (HCC) via hair samples and calculated cardiometabolic risk scores using the summation of standardized z-scores for glucose, insulin, triglycerides, high-density lipoprotein (HDL), the mean of systolic blood pressure and diastolic blood pressure, and waist circumference. Using multivariable linear regression, we estimated the difference in cardiometabolic risk summary scores and individual components with increasing hair cortisol concentrations.

Results: We expect that higher HCC to be associated with greater cardiometabolic risk summary scores at age 12.

Conclusion: Identifying the association between cortisol and cardiometabolic risk in children could contribute to improved methods for early detection of poor cardiometabolic health outcomes. This would allow for the implementation of health interventions in childhood to prevent negative cardiometabolic health outcomes, like cardiovascular disease, in adults. This would also provide some biological basis for prior associations observed between psychosocial stress and cardiometabolic risk.

Camilo Ramirez

B48

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Mark Johnson (Biology)

Can differences in reproductive success under temperature stress be explained by properties intrinsic to pollen performance?

In an era when the Earth's climate is rapidly changing, it has become increasingly important to develop an understanding of how to improve agricultural output and crop productivity. By exploring how heat stress affects model

organisms like *Arabidopsis thaliana*, it becomes possible to understand the connection between reproductive success and temperature. When pollen germinates in *Arabidopsis*, pollen tubes carrying two sperm cells each, form and grow into the pistil of the flower to fertilize ovules. Earlier works have shown that different ecotypes of *Arabidopsis* are affected differently by heat stress. For example, Col-0 was better able to produce seeds than Hi-0. Moreover, the few Hi-0 seeds produced under heat stress were located closer to the stigma, the site of pollen tube germination, indicating that pollen tubes were smaller in Hi-0 than in Col-0. Our goal is to determine whether heat stress affects an intrinsic property of pollen tubes or if prior experimental results were due to more complex cellular interactions between pollen and the stigma/style. By growing Col-0 and Hi-0 pollen in vitro for 3 hours at 20C and 30C, where 20C is considered optimal, we explored the effects heat stress has solely on pollen. Unexpectedly, we found that Col-0 and Hi-0 had higher pollen germination rates at 30C compared to 20C. Interestingly, Hi-0 pollen tubes were longer when grown at 30C compared to 20C; while Col-0 exhibited a decrease in average tube length from 20C to 30C. We analyzed pollen tube integrity by measuring the fraction of pollen tubes that burst during our experiment. We found more Col-0 pollen tubes burst at 30C compared with Hi-0. Since many of our trials exhibited variability amongst results, which is expected, it is imperative more trials be conducted to make strong conclusions. However, our preliminary experiments suggest that differences observed between Col-0 and Hi-0 reproductive success under heat stress are not due to differences in intrinsic pollen performance as measured in vitro. Future experiments should focus on pollen tube growth in vivo while under heat stress as they could help discover a more complex mechanism within the pistil impacting pollen growth.

Zinab Eisa

B49

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA)

Faculty Mentor: Amanda Jamieson (Molecular Microbiology and Immunology) Crane Meredith

The Role of NLRP3 Inflammasomes in Wound Healing

Under any circumstance, wound healing is a critical part of recovery. The innate immune system provides early inflammatory mediators in the wound area that facilitate immune cell infiltration and initiation of microbial clearance, promoting wound healing behaviors. As such, the innate immune response comprised by such inflammatory mediators - such as inflammasomes - is among the initial defenses against pathogen invasion and tissue damage. Inflammasomes are systolic protein complexes that are activated in response to these stressors and their activation mediates a number of downstream inflammatory responses. It is established that the inflammasome pathway facilitates recruitment of inflammatory cells to wound sites, but the kinetics of such activation is not as properly characterized. NLRP3 encodes for the protein cryopyrin, which is involved in the formation of inflammasomes. Utilizing NLRP3 knockout mice, it becomes possible to assess how the immune response promotes wound healing via the inflammasome pathway. As such, what happens in the wound in the absence of a properly working inflammasome can be more clearly understood. When the pathway is removed, NLRP3 models indicated fewer cells in the wound that correspond to immune cell populations such as neutrophils and inflammatory monocytes - cells that are important in early wound healing stages. As such, looking at the role of inflammasomes through the lens of cytokines and cell populations in the presence and absence of inflammatory cell signaling indicates a downstream defect in wound healing. Better understanding of this pathway and its role in wound healing responses is necessary for advancing wound care. However, further investigation into the specific kinetics of the various cell types found in the wound and among different kinds of wounds is required to map a clearer picture of this pathway.

Home Institution: University of Maryland Baltimore County
Summer Research Program: Leadership Alliance-Summer Research Early Identification Program (SR-EIP) Faculty
Mentor: Jessica Plavicki (Pathology and Laboratory Medicine)

Effects of Dioxin Exposure on Nervous System Development in Zebrafish

Dioxins are a group of toxic chemical compounds that share a planar chemical structure and a common mechanism of toxic action. 2,3,7,8-tetrachlorodibenzo-p-dioxin (dioxin, TCDD) is the most potent congener in this class of chemicals. Dioxin can be released into the environment through natural processes such as volcanic eruptions and forest fires. However, the majority of dioxin contamination is the result of industrial activities such as the burning of medical waste and herbicide production, which can pollute our air, water, soil, and food supply. Once released into the environment, dioxin is highly persistent and bioaccumulates due to its lipophilic nature. Dioxin has shown to adversely affect a number of health endpoints, including changes in sex ratios, disruptions in cardiovascular development, and cancer. Although epidemiology such dioxin exposure can produce peripheral neuropathy in humans, laboratory models have not been systematically used to understand how dioxin affects the development and function of the peripheral nervous system. We are using the zebrafish model to study how embryonic exposure of TCDD alters the formation of the peripheral nervous system development. We are using the zebrafish model because it is a rapidly developing vertebrate that is optically transparent and accessible during embryogenesis. To determine the effects of the TCDD exposure on neurological development and function, TCDD exposed and controlled embryos were collected at specific developmental stages, fixed, and fluorescent immunohistochemistry was performed against acetylated alpha-tubulin. We used confocal microscopy to image acetylated alpha-tubulin expression in the embryonic nervous system and performed morphometric analysis using Image J. These studies provide a critical foundation for understanding how pollution impacts neural development and contributes to diseases of the nervous system.

Zachary Levin

B51

Home Institution: Brown University
Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty
Mentor: Alexander Fleischmann (Department of Neuroscience)

Discovering Biomarkers for Neurodegeneration Using New Machine Learning Tools and Next-Generation RNA Sequencing

Normal Pressure Hydrocephalus (NPH) is a neurodegenerative disease characterized by an accumulation of cerebrospinal fluid (CSF) in the brain's ventricles. Patients with NPH present with cognitive, motor, and urinary symptoms, but accurate diagnosis of NPH remains a challenge due to its similarity to other neurodegenerative diseases like Alzheimer's and Parkinson's disease. Diagnosis of NPH relies on expensive neuroimaging, patient histories, and clinical expertise, which all lack objective quantitative measures. Unlike other neurodegenerative diseases, NPH can be effectively treated with shunt surgery to drain excess CSF. Nevertheless, shunt surgery only results in symptom alleviation for up to 50% of the patients who receive it, making accurate, early diagnosis of NPH and prediction of shunt surgery success a critical challenge.

To identify predictive biomarker candidates, we are using a combination of next-generation RNA sequencing (RNA-seq), liquid-chromatography mass spectroscopy (LC-MS), and immunoassays to characterize the CSF of NPH patients. Integrating these datasets using dimensionality reduction techniques, pathway analysis tools, and machine learning classifiers will allow for a comprehensive understanding of the NPH disease state.

I have analyzed the transcriptomic profiles of extracellular vesicles in the CSF of 9 patients undergoing shunt surgery for NPH at Rhode Island Hospital. Pathway analysis identified candidate pathways that correlate with NPH symptoms. For example, genes involved in beta-alanine metabolism were found to be downregulated in patients presenting with pre-operative memory impairment (normalized enrichment score (NES) = -1.45, FDR = .20); genes involved in glycerophospholipid metabolism are upregulated in patients who show gait symptom improvement after shunt surgery

(NES = 1.64, FDR = .47). This initial dataset and analysis establishes an innovative approach to identify new biomarkers for neurodegenerative disease.

Justice Owah

B52

Home Institution: Stanford University

Summer Research Program: Leadership Alliance-Summer Research Early Identification Program (SR-EIP)

Faculty Mentor: Samuel Parker (Brown School of Engineering) Borton David (Brown School of Engineering)

Speed Racers: Estimating spinal neuron population characteristics through rostrocaudal and mediolateral analysis of ECAP conduction velocity & pulse width

Following a traumatic spinal cord injury, there is a period of high volatility in the affected neuronal fibers. While there may be some spontaneous recovery and neuronal regeneration, there may also be significant inflammation or hemorrhagic necrosis, leading to further neuronal death. Therefore, there is clinical interest in methods to assess the functionality of spared neurons after a spinal cord injury. To test this functionality, we are researching the conduction velocity of evoked compound action potentials in healthy sheep's spinal cord. Then, analyze the data gathered and apply it to injured spinal cords. We are making a tool to map varying types of neurons affected in spinal cord injury allowing us to achieve targeted stimulation and regrow communication across the lesion more effectively. Knowledge of residual ascending and descending pathways across the lesion can guide applications of both existing spinal cord stimulation treatments (such as those reliant on the Gate Control theory of pain modulation) and novel spinal cord stimulation methods, such as those designed to restore sensorimotor function in people living with a spinal cord injury.

Gabriela Rivera

B53

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Nicole McLaughlin (Psychiatry and Human Behavior, Neuropsychiatry)

An Analysis of Online Chat Forums and discussions on the impact of the COVID-19 pandemic on individuals with Obsessive-Compulsive Disorder

Little is known about the impact of the novel coronavirus disease (COVID-19) pandemic on individuals living with Obsessive-Compulsive Disorder (OCD). Emerging literature has been mixed, consisting primarily of survey studies that suggest OCD-related anxiety or distress may worsen due to various factors associated with the pandemic. Online chat forums where posters describe their experiences with mental illness, in particular, have been shown to elucidate novel phenomena and themes of patient experiences. Despite increasing involvement of individuals on online communities during quarantine, no studies to our knowledge have attempted to assess the impact of the COVID-19 pandemic on communication among various OCD-centered online communities.

We conducted systematic searches of publicly available online chat forums including Reddit and Quora. Specific search terms including "COVID-19," "Coronavirus", and "COVID pandemic" yielded 210 individual posts, posted between April-August 2020 that met inclusion criteria. Using applied thematic analysis, 4 independent qualitative raters developed a coding scheme after reading through the posts to characterize emerging themes in the data. NVivo (QSR International) qualitative coding software was used by 4 independent raters to code posts related to patient experiences with OCD, COVID-19, and various aspects of the pandemic.

In our sample, 84 individual posts out of 210 explicitly discussed topics relating to COVID-19.

The aspect of COVID-19 most frequently discussed centered around "transmission" (53/84, 63.1%). Common themes in these conversations included worries about hygiene and hygienic routines. Posters discussed their strategies for "sanitizing," including practices of proper hand washing, removal of clothing worn outdoors, washing only certain exposed bodily areas, and being "careful about what you touch."

Due to the ongoing nature of the COVID-19 pandemic and its unpredictability, we believe that future studies examining the evolution of perspectives and experiences of mental illness, and of OCD in particular, could be of tremendous value. Our findings seem to suggest that the lived-experiences of individuals with OCD during the COVID-19 pandemic may continue to evolve and impact clinical care for years to come. Nevertheless, online communities may prove a fruitful resource for qualitative analysis of the experiences and conversations shared by many who experience OCD.

Anna Rezk

B54

Home Institution: Brown University
Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty
Mentor: Sunil Shaw (Pediatrics)

Colonization and invasion mechanisms of *Candida parapsilosis* yeast

Candida parapsilosis is a common cause of systemic fungal infections in immunocompromised individuals. The yeast's adhesion to host surfaces is a critical factor in its pathogenesis and host invasion. The Shaw lab has previously identified several genes (e.g. ALS7, PHR1) associated with *C. parapsilosis* yeast adhesion. Yeast deficient in the Als7 gene show reduced adhesion, suggesting that this gene plays a critical role in adhesion. Here I report the methods used to create an Als7 revertant from Als7 mutants using CRISPR/Cas9 technology. This technique involves utilizing homology directed repair and inserting a designed repair template into the yeast genome. This inserted repair template is identical to the wild-type Als7 genome, except for three silent mutations. Electroporated yeast are screened for the presence of the repair template using a PCR primer specific for the designed repair template, including its silent mutations. 54% of electroporated JMB49 Δ Als7.01 were positive for the repair template while 70% of electroporated JMB77 Δ Als7.06 were positive for the repair template. Future studies observing the adhesion properties of these revertants may provide insight into the role of this gene in *C. parapsilosis* adhesion and potential therapeutic targets for this pathogen.

Stefan Atanasov

B55

Home Institution: Brown University
Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA)
Faculty Mentor: Elena Oancea (Biology/Neuroscience) Cho Eunyoung (Biology/Dermatology)

Genotyping of OPN3 in Knockout & Wild-Type Mice

Over the course of the summer, I have been looking into several different genotyping protocols that will allow me and the lab to genotype mice for the OPN3 gene. The lab has been producing mice with either a Knockout gene (KO), a Wild-Type gene (WT), or both (heterozygous). My job this summer has been to ultimately contribute to genotyping all of the mice in the lab. However, the protocol that has been used in this lab prior to my arrival has recently stopped working, so I have been spending the summer figuring out what needs to be fixed/replaced and what materials/supplies to use. I have tested several different genotyping kits and protocols, and I am close to finding out what works best for this lab. If I do not have time to help genotype the mice, I hope to contribute by finding the best protocol and kit so that the lab can use this method in the future.

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Christopher Moore (Neuroscience) Bath Kevin (CLPS)

Early life care leads to different reward seeking and decision making across the lifespan

Stable early life care is a crucial element of childhood development that can impact long-term mental health stability. Research has shown that unpredictable early life care resulting from environmental stressors can dramatically alter brain development and lead to deleterious mental health outcomes in adulthood, such as depression and substance abuse disorders. One possible explanation is that poor early life care causes structural changes to reward circuitry in the brain, which may lead to maladaptive reward-seeking behaviors in the future. Here, we used home cage recordings to characterize early life care in the presence or absence of an environmental scarcity. We tested the long term effects of the quality of early life maternal care on reward seeking behaviors with a Probabilistic Bandit Task at adulthood. In ongoing analysis, we are exploring the relationship between aberrant maternal care and maladaptive mechanisms of reward behavior.

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA)

Faculty Mentor: George Lisi (Molecular Biology, Cell Biology and Biochemistry) East Kyle (Molecular Biology, Cell Biology and Biochemistry)

Computational Characterization of Residue Communities in the REC2 Domain of CRISPR-Cas9

The REC2 domain is a previously unexplored region of the recognition lobe of the Cas9 protein which accommodates the single guide RNA-target DNA duplex. It undergoes remarkable structural remodeling as the catalytic domain, HNH, approaches the DNA cleavage site. This UTRA focused on performing an initial investigation into the REC2 domain using computational methods to identify significant residues and networks within REC2 that may be later explored in a wet-lab setting. These residues were identified using the High Throughput Stability Indexer (HTSI), a tool developed by the Lisi Lab in order to identify integral residues in the primary amino acid sequence of a protein. Here, we used this tool to first identify these residues and then extrapolate that data onto the 3D structure of the protein. Residues with significant HTSI values were identified and communities of residues were constructed by developing networks of those amino acids that are within a chemically significant radius (7 Å). These networks were then mapped onto the 3D structure of CRISPR-Cas9. With the 3D structure, amino-acid mutations of residues within the networks that may result in higher fidelity mutants of CRISPR-Cas9 were identified and models of these mutants were made using the Phyre2 web portal for protein modeling, prediction, and analysis. This method was also used to study regions of the CRISPR domain for which known high fidelity mutants have been found. This method of analyzing protein communities can also be applied to larger domains in the future. The next step forward will be to apply this work in a laboratory setting to analyze the mutants that were identified

Home Institution: University of Puerto Rico - Arecibo

Summer Research Program: Leadership Alliance-Summer Research Early Identification Program (SR-EIP) Faculty

Mentor: Jonathan Kurtis (Pathology and Laboratory Medicine)

Malaria Vaccine Development

High average mortality in children occurs annually in endemic areas of Africa, due to malaria. The poor and inefficient public health services are responsible for the increasing spread of the *Plasmodium falciparum* parasite, which has a complicated life cycle. Unfortunately, the RTS, S vaccine candidate, despite decades of study, only manages to protect children by 16%. In effect, a new vaccine is proposed against PfGARP, a protein on the surface of infected red blood cells that generates a high natural antibody response. We identified PfGARP as a target of antibodies that induce the parasite programmed cell death. Therefore, in case of infection, anti-pfGARP IgG causes a lower density of parasites in the blood, thus reducing the risks of infection. In the current study, our approach was carried out through a literature review and statistical analysis, measuring anti- PfGARP IgG antibody levels and parasitemia from a cohort of n=400 children, ages 2-7 years living in western Kenya. These analyzes were performed using the bead-based ELISA antibody test method and comparing them with the parasitemia data recorded in each child. The results demonstrate that higher anti-PfGARP IgG levels were significantly related to lower parasitemia, thus PfGARP antibody levels protect against parasitemia in young children. Consequently, many children at high risk for malaria will be able to ensure their health and well-being through an accessible and viable vaccine.

Annie Huang

B59

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Erica Larschan (Department of Molecular and Cell Biology)

Biomolecular condensates and their role in co-transcriptional regulation and RNA processing

Biomolecular condensates are membrane-less functional entities formed by biophysical phenomena of liquid-phase transition mainly through RNA-protein interactions. Understanding functions of these condensates is constantly enriching our understanding of cellular processes and their regulation. It is thus essential that we constantly study new components of biomolecular condensates and their interactions with each other. With several transcription factor proteins being reported to be part of such condensates, it is interesting to study the possibility that some of the known RNA-proteins complexes could actually be functioning via phase transition, forming/dissolving condensates. In the present study, we have explored the potential of DNA binding transcription factor protein CLAMP (Chromatin Linked Adaptor for MSL Proteins) with IDR (Intrinsically Disordered region) domain in *Drosophila Melanogaster* as a protein that can form bio-condensates. CLAMP recruits the Male Specific Lethal Complex (MSL), RNA-protein complex consisting of non-coding RNA rox1 and 2 along with five other proteins to the male X-chromosome resulting in its transcriptional upregulation, also known as dosage compensation. Therefore in this project, we studied the interaction between CLAMP and rox2 RNA to test the hypothesis that these two components might drive the process of dosage compensation via phase separation. Also, CLAMP regulates sex-specific splicing, a process regulated by ribonucleoprotein complexes called spliceosomes, co-ordinating co-transcriptional RNA processing via mechanism of alternative splicing. In flies as well as mammals many RNA-binding proteins are part of alternative splicing spliceosome alongwith non-coding RNA components. In *Drosophila*, CLAMP binds to several of such RNA binding proteins which in turn are reported to be interacting with another non-coding RNA hsr ω -n. Thus, we also explored CLAMP binding with hsr ω RNA to test CLAMP's potential as a legitimate player of phase transitioning biomolecular splicing condensates. Using electron mobility shift assays (EMSA) we found that CLAMP protein and the CLAMP domain that contains the IDR physically binds to both rox2 and hsr ω -n non-coding RNAs, reinforcing our hypothesis that CLAMP is a bifunctional protein with DNA/RNA binding capacity and potential of regulating transcription and co-transcriptional RNA processing via manipulating bio-physical properties of RNA-protein complexes.

Home Institution: Brown University

Summer Research Program: Summer Research Assistantship in Biological Sciences

Faculty Mentor: Alison DeLong (Department of Molecular Biology, Cell Biology and Biochemistry)

Characterizing Leaf Cell Size: Getting a Clearer View

Leaf size, a vital agronomic trait in plants, is determined by the regulated processes of cell division and cell expansion, which yield the characteristic profiles of cell numbers and cell sizes in mature leaves. Work in the DeLong laboratory focuses on analyzing growth regulatory mechanisms controlled by the conserved eukaryotic protein phosphatase 2A (PP2A). Recent work with plants carrying mutations in genes that encode PP2A regulatory B subunits identified a novel large leaf phenotype. The goal of this project is to determine whether this phenotype is a result of increased cell size and/or cell number. Answering this question can provide insight into the molecular pathways and processes that produce the large leaf phenotype, and will direct future investigation of how PP2A controls leaf size. To examine cell size and number, I developed a method for fixing and clearing *Arabidopsis thaliana* leaves by adapting previously published protocols. I am developing methods for imaging mesophyll cells and quantifying their sizes at specific positions along the leaf blade. In addition, I carried out an analysis of root length and seed yield to determine whether these PP2A regulatory subunits also control development of the root system and seeds. These assays will direct and inform future molecular and genetic examinations of PP2A's role in leaf development and crop yield.

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Matthew Nassar (Neuroscience)

Noise Correlations Facilitate Learning

Neurons in our brains are noisy, and noise refers to the trial-to-trial variation of the neurons' firing rates while the same stimulus is presented. This noise in our brains is typically correlated across neurons - particularly neurons that encode similar features. One disadvantage of such correlations is that they limit theoretical encoding potential. But a potential advantage of noise correlations is that they might simplify a learning task by constraining learning to task-relevant dimensions. Recent work from Nassar lab has demonstrated this possibility, but it was achieved by assigning correlation structures artificially. Aside from directly assigning correlations to the neurons directly, we propose that some mechanisms, such as passing information from the decision neurons back to the input layer, could induce noise correlations and potentially enhance learning performance. We tested this possibility by implementing this information-passing idea: weak but distinguishable noise correlations have been observed. After training, neurons with similar tuning curves become positively correlated in general, while those with dissimilar tuning curves become negatively correlated. However, the enhanced performance as the number of back-and-forth passing increases was caused by the new input signals rather than noise correlations. Some future directions include (i) learning decision tasks without an optimal solution (ii) learning in a context with a dynamic noise correlation pattern.

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA)

Faculty Mentor: Wen-I Chang (Pediatrics (Hematology-Oncology)) Honeyman Joshua (Pediatric Surgery)

Imipridones as novel therapy for pediatric neuroblastoma

Neuroblastoma is a childhood neuroendocrine tumor that accounts for 15% of all pediatric cancer-related deaths, with an under 50% survival rate for high-risk patients. Neuroblastoma tumors with the MYCN amplification display more aggressive features at diagnosis and progress more quickly during treatment. Patients with MYCN-amplified tumors have lower chances of survival after relapse/progression and are therefore especially difficult to treat. Treatments remain limited for advanced disease, calling for the development of novel therapies. Our research investigates the anti-tumor effect of a promising new class of small molecules, imipridones ONC201, ONC206, and ONC212, in neuroblastoma. Imipridones are potent anticancer drugs that have previously demonstrated effectiveness as both single agents and in synergy with other therapies for a variety of solid tumors. Imipridones induce tumor cell apoptosis by targeting mitochondrial protease ClpP. Binding to ClpP activates mitochondrial proteolysis, leading to cancer cell death. Using standard cell culture techniques, we chose the MYCN-amplified neuroblastoma cell line SK-N-BE(2) for experiments. We performed cell viability assays using CellTiter-Glo to determine dose response curves and IC50s. Imipridones ONC201, ONC206, and ONC212 all demonstrated single-agent killing in the SK-N-BE(2) cells. We also extracted cell lysates for further protein quantification studies. Western blotting confirmed markers of apoptosis and cell death, and protein studies provided insight into the mechanisms of action of imipridones on neuroblastoma cells. Further investigation is needed to determine synergy and mechanisms of synergy when imipridones are used in novel combinations with histone deacetylase (HDAC) inhibitors such as Vorinostat and Panobinostat. HDACs play a role in controlling MYCN function, and both HDAC activity and MYCN are upregulated in chemotherapy-resistant neuroblastoma. HDAC inhibitors promote cell cycle arrest and apoptosis, and have been shown to restore cell susceptibility to cytotoxic chemotherapeutic agents. Cell viability assays with Vorinostat and Panobinostat demonstrated single-agent efficacy and synergistic effects in combination with imipridones on the SK-N-BE(2) cell line. Our data reveals promise in imipridone therapy, and future studies are proposed to explore the mechanism of action of cell killing in synergistic combinations with imipridone therapy.

Julienne Chaqour

B63

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Kathryn Grive (Department of Obstetrics and Gynecology)

Effects of Maternal Docetaxel Therapy on the Ovarian Reserve and Fertility Potential

Increasing maternal age leads to increasing rates of maternal malignancies, the majority of which are breast or gynecological cancers. While some chemotherapeutics are accepted as “safe” in the second and third trimester, these conclusions are based on short-term fetal studies, without an understanding of long-term toxicity. Critically, exposure to chemotherapeutics in all postnatal age groups is known to cause Primary Ovarian Insufficiency (POI), a condition resulting in premature depletion of the ovarian reserve, a finite and non-renewable oocyte population representing a female’s entire reproductive capacity. POI can also cause heart attacks, cognitive decline, and a significantly shortened lifespan. To assess whether the ovarian reserve of the child exposed in utero will be impacted by chemotherapeutic exposure to the mother, we conducted an in vivo study using Docetaxel, a common chemotherapeutic for breast cancer. Mice matings were timed so that either the control (saline, n=8) or Docetaxel (n=7) was administered to pregnant mice once during late-gestation, just prior to primordial follicle formation in the developing fetal ovary. At postnatal day 14, the ovaries of the daughters were collected, dissected, sectioned, and stained using immunofluorescence or hematoxylin and eosin. While in our previous in vitro organ culture studies, Docetaxel left immature oocytes in neonatal ovaries relatively unaffected, the in vivo model demonstrated an increase in atretic follicles (7.565% in saline

vs 38.23% in Docetaxel; $p=0.0002$), and the appearance of several multi-oocyte follicles in juvenile ovaries, potentially suggesting an increase in granulosa cell apoptosis and follicular anomalies. In addition, while there was a non-significant reduction in oocyte abundance overall, we found a significant reduction in the average follicles per follicle stage in Docetaxel-exposed daughters (primordial: $p=0.0169$, primary: $p=0.805$, secondary: $p=0.0002$). As predominantly secondary follicles exhibited degenerative effects, these findings provide insight on the timeline needed for Docetaxel's toxic effects to be established in utero. In future studies, the daughters of these pregnant mice will be bred to determine fertility, and other maternal chemotherapeutic options will be tested to ascertain which therapies are least detrimental to the long-term fertility of the fetus.

Jonah Boardman, Vikas Rana and Helen Zhou

B64

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA)

Faculty Mentor: Kristi Wharton (Department of Molecular Biology, Cell Biology & Biochemistry) Bartoletti Mathieu (Department of Molecular Biology, Cell Biology & Biochemistry)

A Genetic Screen to Identify Modifiers of Neurodegeneration in a *Drosophila* GGGGCC Model of ALS

The expansion of GGGGCC hexanucleotide repeats found in the first intron of C9orf72 is the most common cause of familial amyotrophic lateral sclerosis (ALS) and has also been associated with sporadic ALS. Extended GGGGCC repeats undergo repeat associated non-AUG (RAN) translation which forms dipeptide repeat protein products that form harmful aggregates, leading to neurodegeneration. Using a *Drosophila* model we expressed 49 repeats of GGGGCC, (G4C2)_{49x}, in motor neurons using OK371-Gal4. The Gal4 protein binds to an upstream activating sequence (UAS) located 5' of (G4C2)_{49x} and induces expression of the repeats. tub-Gal80ts, a ubiquitously expressed transcriptional repressor, was also employed to achieve temporal control of (G4C2)_{49x} expression. Below 29°C tubGal80ts blocks expression of (G4C2)_{49x} by binding to Gal4 at the UAS. At 29°C the tub-Gal80ts protein undergoes a conformational change that inactivates it, allowing for expression of UAS-(G4C2)_{49x} by OK371-Gal4. When OK371-Gal4, tub-Gal80ts/+; UAS-(G4C2)_{49x}/+ embryos are placed at 29°C, the larvae will pupate, but die as pharates (adults) immediately prior to eclosion from the pupal case. When raised at 25°C OK371-Gal4, tub-Gal80ts/+; UAS-(G4C2)_{49x}/+ adult flies will emerge from the pupal case. When shifted to 29°C immediately following eclosion they will die prematurely within 8-10 days. We used that lifespan defect in a genetic screen to identify dominant suppressors of this ALS model using chromosomal deficiency lines covering the majority of the *Drosophila* genome on the X, 2nd, and 3rd chromosomes. To date, we have screened over 350 lines and identified at least 30 deficiencies that produce an extension of lifespan of at least 3 days (suppressors). By comparing overlapping deficiencies, the locations of genes responsible for lifespan extension have been narrowed. Located in these regions are genes that have previously been identified as suppressors of ALS such as *lilli*, *Droj2*, and *bel*, as well as genes that have been previously associated with neurodegeneration. We have also identified suppressing chromosomal regions that appear to contain only novel genes. In order to establish the genes and cellular pathways responsible for suppression we will test smaller deficiencies, null alleles, and RNAis.

Samra Beyene

B65

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA)

Faculty Mentor: Erica Larschan (Molecular Biology, Cell Biology & Biochemistry (MCB)) Ray Mukulika (Molecular Biology, Cell Biology & Biochemistry (MCB))

Role of zinc-finger transcription factor protein CLAMP in the regulation of *Drosophila* Fragile-X syndrome protein function in the brain

One of the most common genetic causes of intellectual disability in human males is Fragile Male X syndrome. This disease is caused by a mutation in Fragile Male Retardation Protein (FMRP), a protein expressed abundantly in the

brain that helps with mRNA translation and transportation. The typical mutation causing this syndrome is a CGG expansion; however, recent studies identified mutations in different domains of FMRP that affect its shuttling between the nucleus and cytoplasm. These mutations also induced the stereotypical presentation of Fragile Male X Syndrome. Little is known about how other proteins affect FMRP's localization via interaction with these domains. In particular, this project focuses on how deletions of the C-Terminus (CT) and the Nuclear Localization Sequence (NLS) affect FMRP's interaction with CLAMP, a maternally deposited transcription factor that is abundant in the brain and binds to multiple RNA binding proteins including FMRP. We expressed in *Drosophila melanogaster* neurons the dFMRP protein with either the CT or NLS regions deleted. We also depleted CLAMP in these mutants to assess whether these two proteins genetically interact with each other in the brain. Using western blotting, the expression of mutant dFMRP protein and their localization between the nucleus and cytoplasm was confirmed. Adult and third instar larval brains were imaged to determine if the combination of these mutations led to normal or increased axonal branching (a synthetic effect) or if it caused axonal collapse (suppression of mutant phenotype).

Christine Schremp

B66

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Linda Carpenter (Psychiatry and Human Behavior)

Psychotropic Medication Changes and Motor Cortex Excitability in Patients with Major Depressive Disorder

Repetitive transcranial magnetic stimulation (rTMS) is a treatment for Major Depressive Disorder (MDD) in which magnetic pulses are repeatedly delivered to the brain. Stimulation intensity is determined using a patient's motor threshold (MT), or the amount of stimulation over the motor cortex required to elicit a twitch in the contralateral hand. If a patient's rTMS stimulation intensity is too high, they are at risk of seizure, but if the stimulation intensity is too low, then treatment will be sub-therapeutic.

Motor threshold is a measure of cortical excitability. Based on TMS studies in healthy controls, single doses of psychotropic medications can alter cortical excitability. For example, voltage-gated sodium channel blockers, including many anticonvulsant medications, increase MT, indicating that a higher level of stimulation is needed to achieve the same motor response. Other classes of psychotropic medications do not affect MT but alter other measures of cortical excitability that are not routinely checked during clinical rTMS, such as short-interval cortical inhibition (SICI) and intracortical facilitation (ICF). For example, benzodiazepines increase SICI and decrease ICF through positive modulation of GABA receptors. The majority of patients receiving rTMS therapy for MDD are concurrently taking multiple psychotropic medications. Therefore, it is essential to understand the impact of medication changes on cortical excitability to ensure optimal treatment intensity.

I investigated the effect of psychotropic medication changes on MT in patients receiving a 6-week course of rTMS for MDD. Through a retrospective chart review, I coded medication changes based on medication class and direction of dosage change, and quantified the change in MT following these changes. Further studies of cortical excitability metrics beyond MT are needed in populations with psychiatric disorders and chronic psychotropic medication usage to potentially optimize rTMS in the future.

Alexandra Trouilloud

B67

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA)

Faculty Mentor: Elena Oancea (Department of Molecular Pharmacology, Physiology and Biotechnology)

Assessing UVA-induced DNA damage in melanocytes with high vs. low melanin content

The UV portion of sunlight incident on human skin is composed of 95% long wavelength UVA, which can deeply penetrate to the skin's basal layer to reach melanin-producing melanocytes and induce a pigmentation response. This natural defense mechanism protects skin cells from oxidative DNA damage such as double strand breaks (DSBs)

caused by UVA-generated reactive oxygen species (ROS). The photoprotective brown-black eumelanin pigment synthesized in melanocytes absorbs UV wavelengths and prevents UV-induced DNA damage, while the photounstable yellow-red pheomelanin pigment has been shown to contribute to cellular ROS levels. Previously, our lab showed that these ROS could also act as signaling molecules involved in a UVA-activated Gαq/11 coupled pathway to trigger an increase in melanin synthesis and prevent further oxidative DNA damage. Here, we explore the complex role of melanin on UVA-induced ROS as both signaling molecules in early melanogenesis and a source of oxidative DNA damage. Via western blot analysis, we assessed levels of phosphorylated Histone H2AX (γH2AX), a DSB marker, in immortalized human epidermal melanocytes with differing eumelanin and pheomelanin amounts immediately after exposure to a physiological dose of UVA. Our results indicated higher levels of γH2AX in cells with low eumelanin compared to cells with high eumelanin, suggesting that UVA induces greater oxidative DNA damage in cells with lower melanin and thus higher ROS levels. This finding is critical in understanding the balance between ROS involved in melanogenic signaling vs. damage-inducing high cellular ROS levels that accumulate in less pigmented cells exposed to UVA. The mechanisms of UV-induced DNA damage in populations with varying skin pigmentation phenotypes are key to understand and prevent resulting Inflammation, skin photoaging, and highly lethal skin cancers like melanoma.

Lauren Jacoby

B68

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Joseph Bliss (Pediatrics) Shaw Sunil (Pediatrics)

Expression of Candidate Genes in Adhesion and Colonization in *Candida parapsilosis*

C. parapsilosis frequently colonizes the gastrointestinal tract in healthy humans, but can lead to serious yeast bloodstream infections in immunocompromised populations, such as premature infants, as well as people with neutropenia or implanted medical devices. The long-term goal of my mentor's laboratory is to gain a better understanding of the mechanisms of yeast adhesion and virulence involved in pathogenesis in order to contribute to the development of new strategies to treat or prevent such infections. The goal of this project is to study the interactions between the yeast and gastrointestinal tract so as to better understand the mechanisms involved in adhesion of yeast that lead to infection and allow for the yeast to escape the bloodstream and spread to organs in the host. Previous work has identified a number of candidate genes and regulatory pathways that are likely to have a role in these processes, and targeted mutations in genes of interest have been constructed to allow closer analysis of their functions. Specifically, my project uses quantitative PCR to explore the role of the transcription factor Rim101 and explore pH-dependent, Rim101-mediated-pathways in *C. parapsilosis*. Using Rim101 knockouts, we analyzed specific candidate genes of interest involved in cell wall formation and adhesion, namely Phr1, Phr2, and Als7. We looked at the expression of these genes in response to different host stimuli, including pH in two different adhesive *C. parapsilosis* strains as well as in *C. albicans*, for which the Rim101 pathway has been more thoroughly researched. Our results show that Rim101 is itself upregulated in alkaline conditions, and in turn upregulates Phr1 and downregulates Phr2 in both *C. parapsilosis* and *C. albicans*. While Als7 in *C. parapsilosis* is homologous to the *C. albicans* cell-surface protein Als3, which has been shown to be a Rim101-dependent gene, Als7 in *C. parapsilosis* was not found to be Rim101-dependent. Our results show that Rim101 is an important regulator for *C. parapsilosis* to respond to alkaline conditions, and may be necessary for gut colonization. Ultimately, this analysis will allow us to better understand the genes involved in adhesion and the genetic pathways that helps *C. parapsilosis* act as an effective pathogen.

Home Institution: Brown University

Summer Research Program: Undergraduate Summer Research Assistant

Faculty Mentor: Mamiko Yajima (Molecular Biology, Cell Biology and Biochemistry)

The Role of the Metabolism in Early Sea Urchin Embryonic Development

It has been considered that embryos are largely dependent on Warburg Effect, a glycolysis-dependent metabolism for energy. Yet, recent studies in vertebrate embryos have found that specific metabolites and metabolic enzymes involved in glycolysis are asymmetrically enriched in the posterior part of the embryo, which is critical for presomitic mesoderm patterning. Recently, the host lab has identified a similar phenomenon in the sea urchin embryo: enrichment of glycolytic metabolites in the vegetal cells – known as micromeres – which are formed through asymmetric cell division at the 16-cell stage of embryonic development. Micromeres are known as major signaling centers in early development, inducing endomesoderm specification in adjacent cells; however, the exact mechanism of this signaling is still unknown. In this study, we hypothesize that this metabolic asymmetry contributes to the signaling mechanism of micromeres and embryonic patterning. To test this hypothesis, we tested and identified that key metabolic pathways, such as glycolysis and fatty acid synthesis, are indeed critical for early embryonic patterning. We will also show ongoing efforts to determine a functional mechanism of the micromere signaling and metabolism.

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA)

Faculty Mentor: Amanda Jamieson (Department of Molecular Microbiology and Immunology)

The Effects of *S. Pneumoniae* Coinfection on the Differential Expression of the Influenza A Virus Transcriptome

Influenza A Virus (IAV) infection can cause significant cell death and mortality. Patients with IAV are more susceptible to secondary pneumonia (Rudd et al., 2016), leading to extreme morbidity. By targeting Beas2B human bronchial epithelial cells, with IAV/bacterial coinfection, we collect RNA samples of the cells for further analysis. Using RNA sequencing technologies and bioinformatic techniques, we have identified pathways relevant to the differential expression of IAV transcripts during coinfection. We have applied overrepresentation analysis of differentially expressed host genes to identify differentially expressed gene patterns in the host, which may explain observed changes in the IAV transcriptome. We hypothesized that concurrent *S. pneumoniae* infection modulates the host response to IAV, through ubiquitination of host proteins, suppression of intrinsic antiviral immunity, and disruption of pattern recognition. Dysregulation of these pathways could cause IAV transcripts to be differentially regulated during coinfection. We show that aggravated pathogenesis of IAV/bacterial coinfection reflects the expected lethal synergistic effects on human bronchial epithelial cells. The identification of host-pathogen interactions and host gene regulatory networks provide a means to begin establishing therapeutics for host resilience during coinfection. By regulating host resilience mechanisms and pathways involved in IAV/bacterial coinfection, host resilience can be significantly improved to tolerate the effects of coinfection.

Home Institution: Brown University

Summer Research Program: Summer Undergraduate Research Assistantship

Faculty Mentor: Matthew Nassar (Department of Neuroscience) Li Tiantian (Department of Neuroscience)

Investigating Midfrontal Theta Signal and Learning

Authors: Tiantian Li, Meera Singh, Rasmus Bruckner, Michael J. Frank, Matthew Nassar. An increase in midfrontal theta signal (4-7 Hz) in the brain has been previously observed in surprising situations requiring learning, leading to the proposal that theta may be a learning signal. Conversely, theta could also relate to latent states, which inform the brain about the current context and help us make decisions accordingly. To determine whether theta relates to learning or latent state representation, we re-analyzed data from a predictive inference task requiring participants to block cannonballs on a computer screen by predicting where the cannonball would strike. The task contained two blocks with differing statistical contexts that helped inform predictions. One context (“changepoint”) featured persistent changes in cannonball location, i.e. cannonballs would strike in one location for some time, then switch to a new location for some time, and so on. Thus, a change in cannonball location should prompt subjects to update their predictions. The other context (“oddball”) featured transient changes in cannonball location; the cannonball would generally strike in the same area, with an occasional cannonball strike in a different location. Here, changes in cannonball location should not prompt prediction updates. We used time-frequency decomposition to extract theta frequency from EEG data collected during the task. We then performed two regressions, one to analyze theta signal strength during surprising trials (trials with a change in cannonball location), and one to analyze the relationship between theta strength and learning (prediction updates). We found that theta signal strength increases during surprising trials compared to regular trials for both statistical contexts. Additionally, during changepoint blocks, a larger theta signal corresponded to an increase in learning, while during oddball blocks, a larger theta signal corresponded with a decrease in learning. These results suggest that theta is not a direct learning signal as previously speculated, but rather may play a role in modulating latent state representation. Our most recent analysis shows that these basic relations between theta and learning are not exclusive to theta, but extend across other frequency bands such as delta, which we are currently investigating.

Amber Parson

B72

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Audrey Tyrka (Psychiatry and Human Behavior)

Investigating COVID-19 as a stressor in adults with early life stress

While some studies have begun to explore the effects of COVID-19 as a stressor with various impacts on health and psychological outcomes, few have examined the role of early life stress (ELS), a common and important risk factor for numerous psychiatric and other health conditions. In this study, COVID-19 will be observed as a population-wide stressor to allow for comparison of participants with and without ELS on the effects of stress on health behaviors (i.e., sleep, physical activity, outdoor time, substance use) and emotions/worries related to anxiety and depression.

The LIFE Study consisted of healthy men and women ages 18-40 years old (N = 95, 76% female) without any medical comorbidities or medications other than hormonal contraceptives and took a comprehensive measure of assessments related to early-life stress. Participants who completed the LIFE Study were offered a modified version of the CRISIS Survey, a self-report questionnaire developed in the wake of COVID-19 to assess the experience of participants in the month of April 2020 and retrospectively in the three months prior to the pandemic. Participants with ELS (N=57) and those without ELS (N=38) were assessed regarding demographics, adversity, psychiatric diagnoses, life conditions during COVID-19, health behaviors, and emotions/worries. Bivariate relationships were analyzed using chi-square

tests and t-tests. Repeated measures linear models, controlling for relevant covariates, were used to assess the effect of time (i.e., at three months prior to and during the COVID-19 pandemic) and differences between groups.

In the sample as a whole, increases in anxiety ($p < .001$) and depression ($p < .001$), and decreases in time spent outdoors ($p = .046$) were reported in the pandemic. The ELS and control group did not differ significantly with respect to age, sex, and race/ethnicity, but participants in the ELS group had a significantly lower socioeconomic status (p 's $< .01$) and were more likely to have higher resting heart rates ($p = .02$). We did find that early life stress significantly affected several measures for the following effects: greater anxiety ($p = .014$) and depression ($p < .001$), higher levels of sleep or sedative/hypnotic medication usage ($p = .047$), but lower levels of alcohol usage ($p = .007$). There was no potential confounding from the presence of medical comorbidities or medication due to the health of the participants. Implications and next steps will be discussed.

Matthew Solomon

B73

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Rami Kantor (Division of Infectious Diseases)

HIV Transmitted Antiretroviral Resistance and Transmission Networks in the Dominican Republic

Background: Since the 1980s, antiretroviral therapy (ART) availability for Human Immunodeficiency Virus-1 (HIV1) has increased drastically and spread globally. However, as ART becomes more widely used, evolving resistance has led to the ubiquity of treatment failure. ART resistance can be transmitted from individuals on ART to those not on ART. Such transmitted drug resistance (TDR) is particularly damaging in resource-limited countries because (i) there are limited alternative treatments and (ii) there are limited costs and infrastructure for drug resistance testing. Sequence data derived from drug resistance testing can also be used to infer molecular transmission networks, characterize a local HIV epidemic, and disrupt transmission. ART coverage has more than doubled in the Dominican Republic since 2010, yet both TDR evaluation and transmission networks research are limited in the country. The goals of this study were to investigate the extent of TDR and its demographic and clinical associations in the Dominican Republic and explore transmission networks.

Methods: Participants were enrolled in a regional hospital in Santiago, Dominican Republic if they were (i) 18 years or older and (ii) ART-naïve via self-report. Samples were shipped to the Kantor lab at Brown University for HIV-1 pol drug resistance testing using next generation sequencing (Illumina). TDR was then characterized based on ART class using the Stanford University HIV Drug Resistance Database along with the World Health Organization's (WHO) list of surveillance drug resistance mutations (SDRMs). Transmission networks were also determined by the maximum likelihood phylogenetic method using Molecular Evolutionary Genetics Analysis (MEGA) software. Analyses of TDR associations are ongoing.

Results: Of the planned 100 participants, we present preliminary data for 53 participants. TDR prevalence was 11%, all to one ART class (non-nucleoside reverse transcriptase inhibitors=NNRTI). Of the 53, 17% were in transmission clusters.

Discussion: Preliminary data from the Dominican Republic demonstrate TDR levels higher than the WHO-defined 10% threshold and the existence of transmission networks. This information can help public health officials implement targeted approaches towards regimen design and controlling the spread of HIV.

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Craig Lefort (Department of Surgery, Division of Surgical Research)

The potential of OLFM4 deletion as a treatment for patients with chronic granulomatous disease

Neutrophils are a vital component of the immune system due to their role as one of the primary groups of cells to be recruited in an immune response. Through oxidative and non-oxidative mechanisms, neutrophils have the ability to engage in fungal and bacterial killing. However, in patients with Chronic granulomatous disease (CGD), neutrophils cannot effectively clear out microbes which results in recurrent and serious infections that can be life-threatening. Olfactomedin 4 (OLFM4) is a gene that negatively regulates neutrophil bactericidal activity and has been a large topic of study. Furthermore, neutrophils in OLFM4^{-/-} mice have shown increased intracellular killing compared with CGD mice against *S. aureus*. Thus, the objective of this study is to explore the potential use of OLFM4 as a target for gene knock-out in CGD patients in order to increase host defense bacterial clearance. We aim to achieve this by deriving mature human neutrophils from progenitors and inducing CYBB and OLFM4 knock-outs in order to replicate the findings previously reported. By analyzing neutrophil activity against *S. aureus* and *S. pneumoniae*, we can determine if OLFM4 deletion in humans could be used as a viable treatment for patients with CGD.

Home Institution: Hunter College CUNY

Summer Research Program: Leadership Alliance-Summer Research Early Identification Program (SR-EIP) Faculty

Mentor: David Sheinberg (Neuroscience)

Impact of familiar vs similar scene on eye saccade

Eye saccade is an unconscious eye movement. Under rapid eye movement, eyes will shift to focus on an image. Through studying the saccade movement, we can understand cognitive neural works. Under clinical settings, early detection methods of neurodegenerative diseases such as Alzheimer's are still under research. Eye saccades have the potential to be a new biomarker for neurodegenerative disease detection and tracking. This research can also provide valuable data for criminal interrogation. In our research, we are interested in the impact of familiar and similar scene on primates. Previous research about face recognition indicate human take less reaction time (RT) and conduct less saccade rate under familiar face recognition. Humans make eye saccade to observe an unfamiliar environment. We would expect less eye saccade under familiar scene recognition. Compare eye saccade of human to primates, human saccades take longer than primates, which is due to humans make more selection than primates. We predict similar scenes are going to cause more distraction, take longer RT and make more eye saccades. Patients with early stage of Alzheimer trend to reject their symptoms. During clinical setting, current available test for early Alzheimer detection can be "cheat" by patients. To decrease patient's consciousness without impact their awareness, we put an optokinetic nystagmus (OKN) video prior to each test.

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Elana Oancea (MPPB)

Opsin 3 and its role regulating melanocortin receptor and potassium channel signaling

Opsin 3 (OPN3) belongs to a family of light sensitive G-Protein Coupled Receptors best known for their ability to integrate light activity into further intracellular signalling. Unlike other opsins, largely expressed in the retina, OPN3

is expressed deep in the brain. Previous research by the Oancea Lab has explored the light-independent regulatory effects of OPN3 on the melanocortin 1 receptor (MC1R) on pigmentation in human epidermal melanocytes. This project is exploring if a similar regulatory link exists between OPN3 and a related protein expressed in the paraventricular nucleus of the hypothalamus, the melanocortin 4 receptor (MC4R). MC4R is known to have a role in maintaining energy homeostasis, and the Oancea Lab has preliminary data that an OPN3 knockout alters the metabolism of mice. This possible relationship between OPN3 and energy homeostasis is being further investigated this summer through a feeding experiment I am conducting comparing the weight gain of OPN3 wild type and knockout mice over the course of 12 weeks. Mechanistically, MC4R is known to have a role in closing an inwardrectifying potassium channel (Kir7.1). Because of this, another component of my summer project is to investigate whether the three proteins (OPN3, MC4R and Kir7.1) form a complex via co-immunoprecipitation and western blot.

Micah Selengut.

B77

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Allison Delong (MCB)

Leaf Area

Leaf area is an important agronomic trait regulated by complex, and not fully understood, molecular pathways. B16 and B17 genes (At5g28850 and At5g28900) in the model plant *Arabidopsis thaliana* encode a pair of nearly identical subunits of one potential regulatory player, the Protein Phosphatase 2A (PP2A) enzyme family. Previously isolated mutants that carry partial loss of function mutations in these genes showed a distinct large leaf phenotype, which motivated a CRISPR-based strategy to create a full knockout of these tightly linked genes. After preliminary observations showed similarly increased leaf area in these plants (designated 'b16Δb17Δ' because the CRISPR-induced mutations are deletions that introduce premature termination codons), my work has been to give more developmental depth to this leaf expansion phenotype over time. By tracking leaf area over ~30 days of development, my analysis indicates that b16Δb17Δ plants show larger areas on multiple leaves throughout rosette development. Unfortunately, the transgene construct that programmed the mutations, Cas9 and its guide RNA sequences, still remain in the b16Δb17Δ plants and may result in off-target mutations if not cleared from the genome. Thus, a parallel goal of my work has been to create b16Δb17Δ plants without Cas9, by crossing the b16Δb17Δ plants with the wild-type parent and allowing the transgene to segregate away from the b16Δb17Δ mutations. By using a drug resistance marker linked to Cas9 along with PCR-based assays for the b16b17 alleles, I have been able to screen for Cas9-free b16Δb17Δ plants. Isolating these clean deletion plants will hopefully create a stock of strong loss of function alleles desirable for future genetic and molecular experiments to understand PP2A's role in regulating leaf expansion.

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Kaitlyn Wong and Miriam Marlink

A1

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Kyle Denison (Biomed)

Patient Characteristics and Care Provided as Part of a Community Health Worker Program for Management of Hypertension in Rural Haiti

Introduction: Chronic diseases, such as diabetes and hypertension, are a growing concern in global health. Community Health Worker (CHW) programs have been effective at managing chronic diseases across many settings, including rural and impoverished communities. From 2010-2018, a CHW program operated in a remote area of southeast Haiti with a focus on chronic disease management. As part of the program, CHWs screened for hypertension and provided

medications under the supervision of a qualified healthcare provider. This study examines the demographics of the patient population enrolled in the program and the services provided, including medications and education.

Methods: This is a retrospective cross-sectional study of medical records from a CHW program in rural Haiti. As part of the program, staff are required to document each patient encounter. This documentation contains information on patient demographics and services provided, including medical care and health education. A randomly selected sample of documentation from patient encounters was chosen for input and analysis.

Results: A total of 307 patient encounters were examined. Of these encounters, the majority of patients were female (75%) with a mean age of 51 years. Approximately 84% of patients met WHO criteria for hypertension (Systolic Blood Pressure ≥ 140 or Diastolic Blood Pressure ≥ 90), with a mean blood pressure of 157/100. Patients receiving treatment for hypertension were most frequently provided Nifedipine (69%) and Hydrochlorothiazide (25%). About 5% of patients were given multiple medications for blood pressure control. All patients knew how to take their medications as directed and were provided with education on lifestyle changes to improve blood pressure. Aside from medications for hypertension, patients were most frequently provided with low-dose aspirin (35% of total patient encounters), albendazole (19%) and paracetamol (18%).

Conclusions: This retrospective study of a CHW program in rural Haiti provides useful information as to the prevalence and severity of hypertension in the region. Future studies aim to longitudinally follow a small subset of patients receiving treatment to determine the effectiveness of care.

SUMMER RESEARCH SYMPOSIUM POSTERS

Friday, August 6

Physical Sciences and Social Sciences Presentations

PHYSICAL SCIENCES PRESENTATIONS

Liam Storan

C1

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Derek Stein (Physics)

Extracting Parameters from the Motion of Particles in a Viscosity Gradient

We model a microscopic particle's path in a viscosity gradient utilizing a discretized version of a stochastic differential equation, for both one and two dimensions, using the Ito, Stratonovich, and isothermal formalisms. Then, by projecting various dynamics of a particle's path onto some complete basis, say the polynomials, we can extract important information, like diffusion coefficients or drift. Since we manufactured the particle's path, we know the true value of the parameters, and can then cross check these estimations to make sure the method is working correctly. This step of verification is important for when we apply this scheme to real world data.

J. Alexander Jacoby

C2

Home Institution: Brown University

Summer Research Program: Experimental Program to Stimulate Competitive Research (EPSCoR-NSF) Faculty

Mentor: Brad Marston (Physics)

Entanglement in SU(4) Quantum Spin Chains

We explore the ground state entanglement entropy of a general SU(4) invariant spin model in one dimension and constrain the dynamics that may arise on top of this state. Beginning at the exactly solvable, C-breaking xVBS point, we calculate the entanglement entropy analytically, confirming our results with both ED and DMRG numerical methods. Then we extend the same numerical techniques beyond the exactly solvable point. Finally, we make use of some representation theoretic and field theoretic techniques to constrain possible parent Hamiltonians.

Jacob Polatty

C3

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Ugur Cetintemel (Computer Science)

Supporting Accuracy vs Performance Tradeoffs in Deep Learning for Real-time Inference

The overall focus of the project has been analyzing real-time deep learning models in an effort to develop comprehensive optimization methods for improving both inference accuracy and runtime. This area of study is of major importance to the field of sensory data processing for applications including autonomous robotics and selfdriving vehicles, in which attaining the maximum precision in predictions is crucial to ensuring that a robot can

navigate terrain successfully or that a vehicle can safely transport its passengers. The primary programmatic challenge in this field is the selection of the best classification model or combination of models to provide maximal inference accuracy based upon visual data. While in practice this data would typically be obtained in real time from a camera input feed, this project has relied on the MNIST and CIFAR image classification datasets to provide consistent baselines and a wide range of example models for analysis.

A key challenge at the heart of this optimization problem is developing automated techniques for the quantification of the accuracy/time tradeoff involved in running any inference model or combining the outputs of two or more models to produce a more informed prediction. This numerical analysis can allow for the solution of separate optimization problems in terms of both accuracy and runtime, with the user providing constraints on one parameter and allowing our platform to identify the best combination of models that will yield the peak accuracy or minimal runtime within the specified constraints. The final product of this work is a Python library that automatically executes this optimization step for multiple deep learning and deep reinforcement learning architectures, providing a range of options for accuracy and runtime improvements based upon the user-provided parameters.

Joseph Hall

C4

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Brad Marston (Brown Theoretical Physics Center)

Are Gaseous Plasmon Polaritons Topologically Protected?

Topological Band theory has garnered much attention in the solid state and condensed matter physics community in recent years. However, recent work has shown the potential of identifying topological behavior in gaseous media, namely in plasmas. In a cold, cylindrical plasma column under an external magnetic field, we expect to find a topologically-protected edge mode analogous to that in the integer Quantum Hall effect, known as a Gaseous Plasmon Polariton (GPP). In order to support ongoing research in this area, we devised a computational model of a cylindrical plasma column, focusing on a 2-dimensional domain at fixed z . Using the Dedalus spectral code, we solved for the plasma's spectrum and identified the topological surface wave. By integrating this problem, we can visualize the wave traveling unidirectionally around the plasma-vacuum interface, and observe that it exhibits topological protection when encountering surface perturbations. We discuss considerations when extending this to the fully three-dimensional domain, and outline further computational and experimental possibilities aimed at studying the properties of topological phenomena in plasma.

Phum Siriviboon

C5

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Jia Li (Physics)

Antiferromagnetism and Magic-angle Twisted Trilayer Graphene

By overlaying identical layers of two-dimensional material with relative angle, periodic pattern known as the Moire pattern emerges. As the band structure of the material is altered by the extra periodicity, the moire pattern introduces a new method of material engineering. It has been found that an extreme flat energy band appears at a "magic" twist angle of 1.05 degree. In this scenario, the kinetic energy of electrons is suppressed and Coulomb interaction dominates. As a result, a series of quantum phenomena associated with correlated physics are stabilized, such as correlation-driven insulators and superconductivity. [1]. Moreover, by adding another layer of graphene, the magic-angled twisted trilayers graphene is found to increase the robustness of the superconductivity and the tunability of the system [2]. In this work, we will explore the electrical property of the interface between the magic angle twisted-trilayer graphene with the NiPS₃. Being an anti-ferromagnetic van der Waals material, NiPS₃ allows us to introduce the antiferromagnetism to the system while retaining the two-dimensional nature of the device.

References:

- Bistritzer, R., & MacDonald, A. H. (2011). Moiré bands in twisted double-layer graphene. *Proceedings of the National Academy of Sciences*, 108(30), 12233-12237.
- Park, J. M., Cao, Y., Watanabe, K., Taniguchi, T., & Jarillo-Herrero, P. (2021). Tunable strongly coupled superconductivity in magic-angle twisted trilayer graphene. *Nature*, 590(7845), 249-255.

Anvita Bhagavathula

C6

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Jia Li (Physics)

Atomic Force Microscopy in the Assembly of Twisted Multilayer Graphene Devices

The fabrication of devices made from twisted layers of single-atom-thick graphene is a multistep process involving procedures such as exfoliation, scanning, and stacking. These procedures enable us to isolate monolayer graphene, cut it, and shape it into the device we want. The Atomic Force Microscope (AFM), a high-resolution scanning microscope, plays a key role in this process. In this poster, we will discuss what the AFM is, how it works, and how it is relevant to the innovative fabrication process at our lab. The AFM contains some fundamental components that allow it to image at a nanoscale precision; these include: a cantilever that is affected by changing Van Der Waals forces that bends towards or away from a sample surface, a scanning tip, and a photodiode sensor that senses cantilever movement via a laser and maps the topology of the surface. We will discuss in depth the range of protocols available for use within the AFM. For example, we will outline the difference between contact mode and non-contact mode. More significantly, we will explore the ways in which the lab is innovatively employing the AFM in two distinct processes: scanning and lithography. Currently, the scanning mode on the AFM is a crucial part of the fabrication of twisted multilayer graphene devices as it allows us to qualify the homogeneity of the surfaces we intend to use. Additionally, the AFM is frequently used to slice samples into smaller components in order to build feasible devices. To conclude our discussion of the AFM, we will ultimately outline how the lab plans on using AFM lithography in the near future for nanopatterning on substrates: specifically, to build twisted trilayer graphene quantum dots which are also known as qubits.

Phillip Schmitt

C7

Home Institution: Brown University

Summer Research Program: Neal Mitchell Systems Thinking Project Award - School of Engineering Faculty

Mentor: Kareen Coulombe (Engineering)

Wet-spun Polycaprolactone Scaffolds Provide Customizable Anisotropic Support of Cardiac Tissues

Myocardial infarction is a leading cause of death worldwide and has severe consequences including ischemic damage to the myocardium which can lead to heart failure. A main focus of cardiac tissue engineering research is reengineering the infarcted myocardium using tissues made from human-induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs) to regenerate heart muscle and restore contractile function via an implantable epicardial patch. Current limitations of this technology include both biomanufacturing challenges in maintaining tissue integrity during implantation and biological challenges in inducing cell alignment, maturation, and integration of engineered tissues into the host. Polymer scaffolds serve to mechanically reinforce tissues and enhance tissue morphology. Here, we introduce a novel biodegradable, anisotropic scaffold composed of wet-spun polycaprolactone (PCL) microfibers to strengthen engineered tissues and provide a controlled mechanical environment to promote hiPSC-CM function. A wet-spinning process has been optimized to produce consistent fibers, which are then collected on an automated mandrel that allows the intersection of fibers to be precisely controlled at any angle between 0° and 90° to alter tissue anisotropy and provide cues for cellular alignment. Scaffolds are embedded in a collagen hydrogel, seeded with hiPSC-CMs, and cultured. Preliminary results show mechanical behavior of single fibers that is consistent with the literature,

as well as precise control over whole-scaffold mechanics via fiber angle manipulation. Additionally, we show CMs to proliferate and compact into tissues on our scaffolds. Ongoing work focuses on assessing the alignment of CMs as well as the contractility of engineered tissues. This study demonstrates the facile production of anisotropic biodegradable scaffolds that promote CM proliferation and allow for simple control over tissue mechanics. The anisotropic support achieved in these scaffolds has significant impacts on the development of hiPSC-CMs into contractile tissues that promote regeneration of the infarcted myocardium and have great potential for clinical adoption.

Stacey Xiang

C8

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Bjorn Sandstede (Applied Mathematics)

Bifurcations of LDEs on Random Graphs

In this project, we study equilibrium patterned states of bistable lattice dynamical systems on random graphs. We focus on patterns and bifurcation diagrams emerging from single differentiated nodes (SDNs) in the regime of small coupling strength. We find that the bifurcation diagrams take on two distinct forms: snaking and figure-8 isolas. We show that the form of the bifurcation diagram depends on the relative degree of the SDN and its neighbors in the random graph. We also develop a method to predict the way patterns evolve based on graph structure.

Vivian Yuen

C9

Home Institution: Brown University

Summer Research Program: NSF Summer Research Program

Faculty Mentor: Ming Xian (Chemistry)

Synthesis of a Dual-Donor Template for Controlled Release of HNO and H₂S

Nitric oxide, or NO, is a broadly researched biological gasotransmitter. In particular, nitric oxide is known for its important physiological properties, such as vasodilation, neurotransmission, and metabolism. While nitric oxide and nitrosyl complexes have been well studied, nitric oxide's redox partner, nitroxyl (HNO), has been less studied. HNO is the one electron reduced form of NO, and while there are preliminary studies of HNO's physiological properties, HNO has shown therapeutic value, especially with cardiac disease treatment. Another important biological gasotransmitter is H₂S. While it is often believed to be a toxic gas, H₂S plays an important biological role through mediating beneficial activities such as vasodilation, antioxidant and antiapoptotic pathway activation, and antiinflammatory activities.

Controlled release of such therapeutic gasotransmitters is an important area of chemical biology research. While there have been donors reported to release HNO, H₂S, or NO, many of them exhibit short half-lives. Additionally, there are not many donor compounds that can release more than one biologically relevant gasotransmitter, limiting the therapeutic applicability of the compound. We are currently investigating a dual HNO and H₂S donor that mediates the controlled release of HNO and H₂S. We have reported the use of Diels-Alder adducts to spontaneously release HNO at 37°C and H₂S in the presence of carbonic anhydrase. The use of these dual-donor Diels-Alder adducts to control the release of these biologically important gasotransmitters (HNO and H₂S) is significant due to 1) their ability to release two gasotransmitters in a controlled fashion and 2) their relatively long half-lives compared to other reported HNO donors. Preliminary experiments demonstrate the impact of para-substitution on the decomposition rates of donor analogues.

Home Institution: Michigan State University

Summer Research Program: Leadership Alliance-Summer Research Early Identification Program (SR-EIP) Faculty

Mentor: Eva Golos (Department of Earth, Environmental, and Planetary Sciences) Fischer Karen (Department of Earth, Environmental, and Planetary Sciences)

Imaging the Boundaries in the Crust and Mantle of the Southwestern U.S. From Seismic Waves

The study of seismic waves has helped us discover Earth's interior and composition. In particular, converted seismic waves provide information about boundary layers within the Earth. We generated receiver functions from converted waves observed at seismograph stations in southwestern U.S. starting with initial stations in Arizona. During the analysis, S to P converted body waves are measured by their velocity gradients and depth. Our initial results show us the crust-mantle boundary (Moho) at a depth of about 50 km and the lithosphere-asthenosphere boundary (LAB) is about 75 km. Further research will explore different regions and continents as well as looking at the effects of bandpass filters. These results will help us understand deformation of plate boundaries, lithospheric properties, and how continents are formed.

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Meredith Hastings (DEEPS) Walters Wendell (DEEPS)

Analysis of Isotopic Concentrations of Sulfuric Acid Utilizing Barium Chloride Precipitation

Sulfur dioxide is an important trace gas of the atmosphere that has important implications for air quality, acid deposition, and climate. Over the last several decades, sulfur dioxide emissions from power plants and vehicles have dramatically declined due to effective regulations.

However, atmospheric deposition of sulfur remains a large terrestrial stressor having important implications for land and water quality and important interacting effects with climate and air pollution. This project will investigate why acid deposition has not improved as much as expected in New England. Sulfuric acid will be extracted from atmospheric filter samples collected in Rhode Island over the past 15 years and analyzed for concentrations and isotopic composition. The data in this project will be analyzed using atmospheric emission data, air mass transport calculations, and advanced geospatial statistical packages to investigate changes in atmospheric chemistry and longrange transport to near-surface sulfate trends.

Current progress has been made on the development of a working procedure to precipitate sulfate out of sample solutions using barium chloride; repeated control tests were developed on the basis of previous experiments and results of iterative testing.

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Ming Xian (Chemistry)

Evaluation of Novel Hydrogen Sulfide Scavengers

Not only is Hydrogen Sulfide (H₂S) an important signaling molecule in the body, it is linked to many pathological processes not limited to cancer, inflammation, tissue repair, and hypertension. Despite Hydrogen Sulfide's apparent role in a plethora of diseases harming the body, there is a lack of effective H₂S down-regulators because it is

challenging to develop potent and specific inhibitors for H₂S-producing enzymes. However, if a chemical regulator of H₂S were to be found, it would be both an important research tool and a potential therapeutic agent for many.

Previous research has shown that selenium compounds are good scavengers of H₂S. However, previous research has not used these selenium compounds for physiological implications. In this project, I tested one specific Selenium based H₂S scavenger and its ability to scavenge H₂S using UV visible spectroscopy, Methylene Blue Assay in situ, fluorometer, and electrode. The results of my project indicated that my Selenium based H₂S compound is an effective scavenger of H₂S and works the most efficiently when reacted with Hydrogen Peroxide, a common compound in the body. Future steps of my project include testing more Selenium compounds and testing the current Selenium compound in biological systems like mice.

Casey Chan

C13

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Jerome Robinson (Chemistry)

Progress Towards Incorporating Conjugatable Linkers in a Novel Azamacrocycle Designed to Chelate ⁶⁴Cu

Detection of carcinogenic cells is essential for the successful treatment of cancer. For cancers such as breast, melanoma, and prostate, early detection (during stage one) informs crucial intervention. When prostate cancer is detected in stage one, survival is around 100%. This number drops to 47.7% if it is detected at stage 4. Positron Emission Tomography (PET) has established itself as a leading method of detection for these cancers. Copper-64 is a radioactive isotope with decay characteristics ($t_{1/2} = 12.7$ h, $\beta^+ = 653$ keV) that make it suitable for PET scans and targeted radiotherapy. Organic chelates can form inert metal complexes with copper-64, enabling in vivo application. To be successful for early cancer detection, these complexes must be conjugated to specific cell targeting agents while demonstrating appreciable stability. While the well-studied DOTA system is a stable chelate framework, its stability in vivo is not favorable. We recently reported a new class of chelators derived from cyclen that contain a spirocyclic ring (DO3ACXHY). These chelators form thermodynamically stable complexes with copper-64 that have high fidelity in blood plasma. Herein we begin establishing the synthetic steps necessary to conjugate these complexes to DUPA, a targeting agent for the prostate specific membrane antigen (PSMA) overexpressed in prostate cancer. Synthetic methodology, characterization, and coordination of the copper-64 DO3A complex to a small molecule linker will be discussed. This work provides an effective means to evaluate the viability of CuDO3ACXHY based structures as radiotherapeutics.

Adrian Rogel

C14

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: James Valles (Physics)

Paramecia in Solution & Gravity Detection

My research looks at Paramecium Caudatum swimming in solution in various tubing sizes in order to determine how Paramecia detect gravity when swimming and in order to confirm that they do indeed detect gravity in solution.

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA)

Faculty Mentor: Kareen Coulombe (Center for Biomedical Engineering, School of Engineering and Division of Biology & Medicine, Brown University)

Automated Analysis of Angiogenesis for Ischemic Tissue Repair and Cardiovascular Regeneration

Development of effectively perfused vascular networks is essential to engineering functional human cardiac tissue for regenerative medicine applications. Previous studies have demonstrated the significance of angiogenic growth factors in vascular development as they activate quiescent endothelial cells to migrate away from parent vessels and recruit smooth muscle cells and/or pericytes to stabilize newly formed vessel networks. Growth factors are released in a tightly controlled cascade to direct angiogenesis, but the interactions between growth factors and cytokines involved in this process are not well understood. This study aimed to develop an unsupervised image analysis program in MATLAB to automate processing, visualization, and analysis of fluorescently stained images of vascular networks in tissue samples in order to quantify angiogenesis in response to the different growth factors in vivo. Inputted images were binarized, corrected for autofluorescence, and thresholded, yielding an output image denoting automatically detected luminal structures and calculations for vascular area, number of vessels, lumen size, percent area, and vessel density. Evaluation of automated measurements from the code compared to manually analyzed metrics revealed successful performance within an acceptable range of variation. This code was further adapted to give users the option of whole image analysis or analysis of a region of interest (ROI) via a manual selection tool. The consistent and unbiased image processing performed by this program can streamline analysis of histological images and reduce subjectivity of human error from manual analysis in studies evaluating vascular development in response to various biochemical or physical stimuli in vivo. This program will aid in future research efforts in objectively quantifying angiogenesis and ultimately identify the stimuli important for formation of functional vasculature, advancing research efforts towards tissue and heart regeneration.

Momoka Kobayashi and Stephen Pyon

C16

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Kareen Coulombe (School of Engineering)

Implementation and Evaluation of in vitro Prevascularization on Engineered Cardiac Tissue

Engineering three-dimensional tissue constructs composed of human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs) is a promising approach for regenerating damaged heart tissue. Despite the many advances in the field, the limited size of engineered heart tissues remains an obstacle for clinical use. The high metabolic demand of cardiac cells gives rise to a need for a constant flow of oxygen and nutrients, which proves more difficult to achieve in large, dense tissues. One of the main goals of cardiac tissue engineering is to design efficient vascularization systems that maintain viability and functionality of implanted tissues while also allowing rapid integration with host vessels upon implantation.

Here, we present an innovative in vitro method of prevascularization involving the creation of a dynamic perfusion network inside of an engineered cardiac tissue (ECT). Gelatin-alginate fibers were used as sacrificial structures for the construction of arteriole sized channels (~600 μm). The outer surface of the fibers were coated with a solution composed of gelatin, alginate, collagen, and human umbilical vein endothelial cells (HUVECs). Cardiomyocytes were then seeded around these fibers and the alginate was uncrosslinked to establish ECTs with patent, perfusable channels. Finally, the tissues were perfused in vitro prior to implantation in a rat model of ischemia reperfusion myocardial infarct (MI) for immunohistochemical evaluation and microCT based vascular reconstruction.

We determined that a 0.5%/0.25%/1mg/mL solution of gelatin, alginate, and collagen respectively coated the fibers most effectively while allowing for HUVECs to be seeded at a density of 20M cells/mL. Prior to implantation, the tissues were perfused in vitro and compaction ratios, fiber diameters, and beating were evaluated.

Furthermore, immunohistochemical staining of explanted tissue showed the engraftment of fabricated tissue and the development of vasculature. Coronary vasculature was reconstructed to quantify vessel development.

In conclusion, we present a novel method for prevascularization and evaluation of vasculature by imaging and reconstruction techniques for dynamically perfused ECTs.

Megan Fay

C17

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Ian Wong (Engineering)

Synthesis of Graphene Oxide and Silk Fibroin Composite Aerogels with Programmable Oil / Water Adsorption

Aerogels are ultra-porous, air-filled materials with extraordinary surface area that can be used for environmental remediation, energy storage materials, and sensing. In particular, ice-templating offers a facile and economical process to create ultra-porous cryogels with extraordinary surface area. I investigated freeze-casting of biologically-inspired composites that incorporate graphene oxide (GO) and silk fibroin, a naturally-occurring polypeptide. In mesoporous structures, natural polymers like silk fibroin often exhibit limited mechanical strength and aqueous stability. However, silk fibroin is capable of forming crystalline β -sheets as a result of hydrogen bonding between repetitive subunits. I hypothesized that silk fibroin could be reinforced by leveraging the inherent structural stiffness and surface functionalization of GO, a nanomaterial that would readily form hydrogen bonds between silk subunits. By studying the physical, chemical and mechanical properties, I was able to gain insight into the nature of self-assembly of this composite meso-structure.

My work optimized the freeze-casting process by tuning the pH and freezing direction which resulted in porous microstructures. Next, I varied the ratio of GO to silk content by weight. I found alterations to the micro-porous structure, mechanical stiffness and uptake of both water and oil with the addition of GO. I treated the cryogels with methanol vapor to induce β -sheet formation in silk unbound to GO. Moreover, with increasing β -sheet content, there is an improvement of chemical and mechanical stability in water, ionic solutions, and oil over relatively long periods of time. Using analytical techniques including FTIR-ATR, SEM, contact angle, compression and other mechanical tests, I was able to deduce structural information and interactions of GO with silk sub-units. Overall, these self-assembled mesoporous materials exhibit outstanding physicochemical properties with potential for extreme mechanics, environmental remediation, and energy storage.

Anthony Barisano

C18

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Leigh Hochberg (Engineering)

Data processing of hdEEG dynamics during movement intention of healthy controls

Each year, 795,000 Americans experience a first-time stroke. Stroke is a leading cause of long-term disability in adults, and approximately 80% result in upper extremity paresis. Despite that only one-third of patients fully recover, therapeutic options remain limited. Previous studies demonstrated that electroencephalogram brain-computer interfaces (EEG-BCIs) may be a solution. Achieving reliable control is a challenge to implementing EEG-BCIs as a standard of care. For EEG-BCIs, the participant's "sensorimotor rhythms" must be decoded with 70% accuracy for control of an external device. These sensorimotor signals are distorted following stroke and cannot be interpreted by current techniques. Measures of connectivity are independent of band power modulation and offer a new approach to achieve EEG-BCI control. The goal of this study is to develop a neural decoding strategy to improve reliability and

control of a high-density EEG-BCI (hdEEG-BCI) in real time. EEG is easily contaminated with noise during movements, another hurdle to decoding movement intention. These unwanted signals create non-neural, physiologic signals, or artifacts, in the data. These artifacts range from eye movements and blinks, to heartbeats, to other muscle movements. Such signals interfere with neural information and can hinder reliable decoding of the neural data. The primary purpose of this project was to identify and standardize methods of removing these movement induced artifacts to improve the signal to noise ratio of signals for further analysis. To do so, a multistep process was developed which relied on visual inspection of the data. In addition to removing transient artifacts, interpolating bad channels, and removing line noise, this process implemented a combination of Principal Component Analysis and Independent Component Analysis to precisely identify and remove artifactual components. The result of my work is standardizing this process to precisely remove those components yet retain meaningful neural data that can be used for further analysis. This project supports the development of a decoding strategy to improve control of rehabilitative hdEEGBCI for patients with stroke.

Samantha Magpantay

C19

Home Institution: Brown University
Summer Research Program: Advisor grant
Faculty Mentor: Jerome Robinson (Chemistry)

Chemical and Electrochemical Studies on Peroxide-Selective Oxygen Reduction with Eu(OTf)₃

Metal-oxygen binding is central to many natural and industrial processes, and improved understanding of these events can further facilitate applications in catalysis, biology, and energy storage. Recently, strong Lewis acidic rare-earth metals have been shown to enhance the rate of oxygen binding and reduction during catalytic oxygen reduction reactions. However, little is known regarding the structure and reactivity of rare-earth metal-oxygen species. Previous work in our group found that redox-inactive trivalent rare-earth metals facilitate oxygen reduction in the presence of an outer-sphere reductant, decamethylferrocene (Fc*). Use of a redox-active RE(III), Eu(III), leads to dramatically enhanced rates of O₂ reduction. In this study, we report the chemical and electrochemical peroxide-selective oxygen reduction reaction with Eu(III) and Fc* in MeOH and MeCN. We demonstrate high peroxide selectivity with excess Brønsted acid and sub-stoichiometric Eu(III), which has encouraging implications for electrochemical generation of H₂O₂ using catalytic amounts of RE. Chemical and electrochemical reactivity studies followed by UV-Vis spectroscopy and cyclic voltammetry will be discussed.

Adam Furman

C20

Home Institution: Brown University
Summer Research Program: Space Grant/NASA, NASA Student Airborne Research Program
Faculty Mentor: Raphael Kudela (Ocean Sciences Department, University of Southern California)

Modeling CDOM Spectra from Satellite Measurements

Colored Dissolved Organic Matter (CDOM) is an important environmental marker in ocean water. The concentration (absorption) and spectral slope provide information about the source of the water. Consisting of organic dissolved material from various sources, it strongly absorbs light at blue and ultraviolet wavelengths, thereby influencing the energy available for phytoplankton, as well as overlapping with chlorophyll absorption spectra. This study models CDOM spectra based on satellite measurements of downwelling irradiance and water-leaving radiance. Samples measured in a laboratory setting are used to construct linear models that map ratios of radiance and irradiance values to CDOM absorption values. By fitting these extrapolated values to known mathematical models of CDOM spectra, an algorithm is developed for finding the CDOM spectral slope and reference absorption based on available remotesensing quantities alone. Error bounds for the algorithm are determined by evaluating the root mean squared distance between the modeled and the reference samples. Using a second dataset linking spectral slope and absorption values to different CDOM types, a classification method is established to categorize a given unknown value from the

remote sensing algorithm. The categorization method is then applied to Sentinel-3 and Landsat imagery, resulting in geospatial data extrapolating CDOM type from radiance values for each pixel of the image. The model results are compared to ground-truth data collected at sites located within the satellite image.

Xiao (Sean) Zhan

C21

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Daniel Ritchie (Computer Science)

Learning Structure-Aware Generative Models of 3D Characters

Recent advances in deep learning have enabled new generative models for 3D objects, in particular manufactured shapes (e.g. chairs, tables, airplanes, cars, ...). The most state-of-the-art methods in this space are "structure-aware": they take into account the parts of which the object is made and how those parts are assembled. However, there has been relatively little progress in generating 3D characters: people, animals, and other such 'living agents.' Generative models of characters would be useful for content creation in animation, visual effects, and games; they would also find application in 3D reconstruction applications (for example, marker-less tracking and reconstruction of animals). Character modeling presents unique challenges not shared by manufactured shapes: characters can vary widely in body structure, shape, and pose, and they typically do not decompose into assemblies of parts (since they are mostly organic). How can we design structure-aware generative models of 3D characters and learn them from data?

This project seeks to answer this question. Our hypothesis is that a good representation for a character's structure is its skeleton. This may not be a physically-based skeleton, but instead the kind of abstract skeleton (or "rig") used to control characters in 3D animation. Our goals are then twofold: (1) learn a generative model of character skeletons; (2) learn a generative model of character body geometry given a skeleton.

Katie Yetter

C22

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Mascha van't Wout - Frank (Psychiatry and Human Behavior)

tDCS and Mindfulness: Combating Psychopathology after Trauma

Most individuals show remarkable resilience in the face of trauma. Yet, the high levels of arousal and activation of stress hormones in response to trauma will, in a minority of cases, result in emotional dysregulation that increases the risk for mental health problems. This is particularly relevant for first responders who experience recurrent occupationspecific traumatic stress exposure, and report higher than average rates of post-traumatic stress disorder, depression, and substance use. The prevention of these negative mental health sequelae is highly desirable. Yet, current prevention approaches after trauma exposure rely on adapting interventions intended to treat posttraumatic stress disorder and is thus often limited to individuals already experiencing prodromal symptoms. Here I will outline the rationale for a novel intervention approach that combines transcranial direct current stimulation (tDCS), a non-invasive neuromodulation technique, with mindfulness. This is based on the theory that increasing medial prefrontal activity using tDCS while decreasing amygdala reactivity using mindfulness supports the flexible use of emotion regulation and thus, decreases the development of psychopathology after trauma.

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Roberto Zenit (School of Engineering)

Champagne Problems: Investigating Bubble Growth in Carbonated Fluids

Our study investigates the effect that solutes have on the gas evolution rate in a carbonated aqueous solution. The experiments used various carbon dioxide partial pressures, ranging from 3.0 bars to 4.0 bars. Samples were prepared using varying concentrations and mixtures of sucrose, citric acid, ethanol, and SDS surfactant. Each carbonated fluid sample was placed in a petri dish and observed via a camera for one hour. The videos were processed to extract data showing the growth of the bubbles as a function of time. Comparing the datasets to the Epstein-Plesset equations allowed us to model the rate at which CO₂ gas evolved from the liquid sample. We found that some solutes significantly impact the decarbonation rate and the frequency of bubble formation. The modelling allowed us to predict the degassing behaviours of commercially available carbonated fluids, and our results were tested against Sprite, Ginger Ale, and Beer in order to verify the predictions.

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA)

Faculty Mentor: Omid Amili (Department of Mechanical, Industrial, and Manufacturing Engineering, the University of Toledo)

Particle Tracking in a 3D-Printed Stenosis Model for Medical Applications

Physical changes by hemodynamics are considered a major factor for diseases such as atherosclerosis, stenosis, and aneurysm. Findings from *ex vivo*, *in vitro*, and computational fluid dynamics studies, suggest fundamental relationships exist between fluid mechanic pathways for mechanical platelet activation and the mechanisms governing their transport. The goal of this *in vitro* study is to quantify the complex flow pattern in an idealized canonical stenosis geometry yet clinically relevant. This study has a wide range of applications from understanding the drug delivery mechanisms to the embolization process. A stenotic tube with barbed fittings at both ends was designed in Solidworks and exported to a Stereolithography (STL) format to be 3D printed. The model is then placed in an in-house developed flow loop where physiologically accurate steady-state and pulsatile flows can be imposed. Green florescent particles acted as tracers were injected via a syringe pump into the flow stream downstream of the stenosis tube. A high-speed camera in conjunction with pulsed LED light sources were used to record the fluid motion through the stenosis tube. A flow rate of 61 mL/min was imposed to match the Reynolds number of $Re = 142$. PIVview was used for the crosscorrelation of the recorded image sequence to analyze the local velocity field. MATLAB was used for data processing and generating both a streamline and vector field plots. The streamlines, which depicts the path traced out by the particle field where at every point along the path the velocity is tangent to it. The velocity appears to be higher in the stenotic region and gradually decrease as the particles exit the model. The high-resolution velocity vector field depicted similar behavior. The 3D-printed tube with a symmetric stenosis was successfully fabricated for the purpose of optical imaging. A steady state flow rate was imposed to its inflow and the flow pattern was measured using particle tracking velocimetry (PTV). The measured flow map shows the local hemodynamics as the flow goes through the stenotic region. Understanding fluid flow behavior within blood vessels will aid in better developing medical procedures and techniques.

Home Institution: University of Pittsburgh

Summer Research Program: Leadership Alliance-Summer Research Early Identification Program (SR-EIP) Faculty

Mentor: Ritambhara Singh (Computer Science)

Investigating the Performance of Deep Learning Methods for Hi-C Resolution Improvement

DNA, also known as deoxyribonucleic acid, is the material that is responsible for determining genetic traits in all humans and nearly all animals. DNA can be looked at in two different ways- either as a linear strand, or as a 3D arrangement, when DNA spontaneously folds into itself for cell division or to fit inside a nucleus. In the 3D arrangement of DNA, regions that are many base pairs apart in the linear structure end up interacting with each other when folding. These interactions are critical in accounting for different genetic phenomena in individuals. There is a technique known as Hi-C, that is able to capture these interactions in the DNA and display them on a contact map for researchers to analyze. However, Hi-C experiments are expensive to replicate especially during sequencing, and only low-resolution data can be obtained, meaning that only the broad-scale interactions can be recorded. As a result, scientists have proposed the use of training deep learning models with artificially downsampled datasets to improve Hi-C resolution without incurring the same costs. Our study aims to comprehensively study the performance of the deep learning methods on real-world low-resolution data to assess their applicability. Here we show that deep learning methods trained with artificially downsampled data do not perform well on real-world low resolution data, and therefore, need to be retrained with real-world low quality data in order to increase performance. An implication of the work that has been done by this project is that scientists can now work on implementing the training methods that the project has shown to work on low-quality Hi-C data to approximate high resolution Hi-C maps.

Sultan Daniels

C26

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Christopher Rose (School of Engineering)

Finding a Bound for Information Transmission Between Two Bodies Under a Gravitational Force

According to Newton's Law of Universal Gravitation, if an object is a certain distance away from another, it will experience a force that is proportional to the inverse-square of that distance. Since force is proportional to the acceleration of a mass, the force of gravity determines this body's next move. Consequently, not only must this body know of the other's existence, it must also know of its exact location and mass. As the objects are not in the same place, Newton's Law shows that these two bodies have a method of communicating this information to one another. But how well can they communicate? Theoretical problems arise when sending a perfectly precise message. This is because perfect information requires an infinite number of bits to encode it. As every bit of information that is transmitted must contain energy to get it from one place to the other, it is evident that perfect information transmission is not physically realizable. This is because an infinite amount of energy would be needed to propagate these signals. Real-world signals are subject to many random processes in nature. These random processes introduce noise into a message that will be read by the recipient. As Newton's Law illustrates, the signal that each body receives from the other is the gravitational force. In our project, we are studying a two-body system in accordance with Newtonian Mechanics, however, the force in this system consists of the original Newtonian gravitational force plus a random process that is proportional to the magnitude of that force. We will compute the statistics of the ensuing equations of motion, specifically the mean and the variance. These values can then be compared to the empirical data for astronomical orbits which includes their errors. Since empirical observations support Newton's Law, we deduce that the noise present in the force needs to have a magnitude small enough so that the equations of motion lie within the error bounds of the observations. This bound on the noise energy can lead us to a calculation for the amount of information that can be transferred between the two bodies.

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Thomas Serre (CLPS) Pelgrim Madeline (PhD Student (Non-faculty))

Panoptic Object Segmentation for Dog Eye-Fixation Analysis

The research project aims to identify and separate a variety of objects present within video scenes captured by headmounted cameras on dogs. Through the application of novel computer vision architectures, we perform object segmentation (both instance and semantic segmentation) on the video scene frames.

The primary model used is a Feature-Pyramid Network + ResNET101 backbone MaskRCNN (region-based convolutional neural network) that learns the salient features of objects within the frame/scene (from the head-mounted camera) and proposes: A bounding-boxes enclosing each object instance predicted A binary mask that precisely identifies the object's pixel-wise location in the scene. This is corroborated with eye-tracking data from the headmounted cameras to obtain statistical information on the frequency and types of objects (static vs non-static or natural vs man-made objects) that dogs "prefer" to fixate on. A transfer learning approach is used, with a base model trained on MSCOCO and re-trained to integrate a total of 45 new classes from OpenImagesV6, CityScapes and the MSCOCO dataset.

Oren Lederberg

C28

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Ming Xian (Chemistry)

Understanding 1,2,4,5-Tetrazine Cyclization Reaction for Usage as a Fluorescent Probe

1,2,4,5-Tetrazines and olefins are robust bio-orthogonal coupling partners with imaging and diagnostic applications because they do not interfere with biological reactions. For example, these coupling partners have been utilized to selectively label cancer cells, modify DNA, and monitor cellular metabolisms with excellent kinetics. Despite these advances with 1,2,4,5-tetrazines in bio-orthogonal chemistry, they are seldom used in therapeutic applications. Recently, we discovered an intramolecular cyclization reaction between 1,2,4,5-Tetrazines and olefins resulting in a fluorescent compound. My work focused on studying the two synthetic steps to prepare the coupled 1,2,4,5-Tetrazine and an electron deficient olefin, an alpha,beta-unsaturated ester, in order to produce a library of eight 1,2,4,5-Tetrazine and alpha,beta-unsaturated ester coupled compounds. I focused on how changing the sterics surrounding the olefin and the electron density of the tetrazine would affect the yield of the overall synthesis. The yield is of critical importance because it provides a strong foundation to draw conclusions regarding the mechanism and details surrounding optimal conditions for future usage of the reaction. Finally, work was conducted to study the yield of the actual fluorophore, the kinetics of the cyclization, and the strength of the fluorescence. Having details surrounding the yield of the synthesis, but more importantly the kinetics and fluorescence details of the cyclization allows for future therapeutic applications by using the fluorophore as a fluorescent probe for the detection of chemical environments such as areas of high oxidative stress frequently seen in cardiovascular diseases. This will be achieved by having the detected compound as a leaving group that will eliminate to form the necessary olefin for the cyclization. By the end of this project, we hope to create a library of chemical reactivities specific to this newly discovered reaction and use this information to synthesize a sulfur dioxide releasing agent for treating cardiovascular diseases. This library will develop a more complete understanding of the reaction and its implications in drug development.

Home Institution: Brown University
Summer Research Program: Research Assistant for Systems@Brown
Faculty Mentor: Malte Schwarzkopf (Computer Science)

Privacy by Design - Making Applications Comply with GDPR-like Legislation by Default

Be it the EU's General Data Protection Regulation (GDPR) or the California Consumer Privacy Act (CCPA), governments have enacted a flurry of new laws seeking to protect people's privacy. Yet compliance with these laws in the software industry has been spotty at best; privacy breaches abound and companies are paying millions in fines as a result. Today's storage systems were simply not designed with privacy laws in mind and hence many developers rely on error-prone manual scripts, imprecise crawlers, and band-aid techniques to handle privacy-related requests. In this research project, I developed a database proxy that allows applications to interface with Pelton, a database optimized for privacy compliance developed by a team of researchers at the Brown Systems Research Group which I am a part of. Pelton provides a correct and complete response to privacy requests by organizing data primarily by user: each user has their own micro-database which contains all data related to them and which they can download or remove at any time. The proxy developed in this project acts as the connecting layer between real world applications and the privacy-by-construction database Pelton - the proxy appears as a standard MySQL database while internally converting application queries to a format that Pelton can understand and converting Pelton responses to a format that the application can use. As far as the application is concerned, connecting to the Pelton proxy is the same as interacting with any standard MySQL database - except that privacy-related queries are handled by design.

Home Institution: Brown University
Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty
Mentor: Iris Bahar (Computer Science)

I will be sharing a video demonstration of the project simulation instead

In the future, physical systems from simple tools to complex machines will be built, used, and repaired by humans and robots working together. Joint work requires a robot to perceive, understand, and share the semantics of its environment with a human partner. A robot must be able to interpret a user's commands in a context that accords with that user's goals and model of the world. The goal of this research project is to develop a framework for constructing this common representation that serves as conceptual common ground between the human and the robot by extracting object causal models from human input and Embedding them within hybrid machine learning algorithms.

Home Institution: Brown University
Summer Research Program: Boise State Data Driven Security REU
Faculty Mentor: Liljana Babinkostova (Boise State Mathematics department) Serra Edoardo (Boise State Computer Science Department)

Side Channel Attacks Against GIFT Lightweight Block Cipher

Computing devices continue to be increasingly spread out within our everyday environments. Computers are "embedded" into everyday devices in order to serve the functionality of electronic components or to enable new services in their own right. In 2016, the National Institute of Standards and Technology (NIST) initiated the first call for new lightweight cryptographic proposals to strengthen the cryptographic defense of networked devices against

cyber attacks and to protect the data created by those devices. Lightweight Cryptography allows for the encryption of sensitive information from devices with constraints of power usage, processing power, storage, and more. SideChannel Attacks (SCA) analyze additional information devices release beyond the transmitted message, such as timing, heat, sound, or power consumption to reveal encrypted content. GIFT, a lightweight block cipher, is one of ten candidates in the final round of NIST's lightweight cryptography competition to create a new standard for constrained devices. GIFT has been shown to be vulnerable against Correlation Power Analysis (CPA), a type of nonprofiled Side-Channel Attack. Deep Learning based Side-Channel Attacks have shown promise in overcoming countermeasures such as masking. Our research focuses on the effectiveness of Deep Learning-based Side-Channel Attack against GIFT with and without masking countermeasures. We provide a comparative study of Side-Channel Attacks against GIFT that have produced results against other block ciphers.

Thomas Kim and Scott Kim

C32

Home Institution: Brown University
Summer Research Program: Prof. Iris Bahar's Lab, ERC
Faculty Mentor: Iris Bahar (Computer Science and Engineering)

Camera less POMCP implementation on VX300 using force sensors

We have been working on implementing a Partially Observable Monte-Carlo Processing (POMCP) solver for Partially Observable Markov Decision Problems (POMDP) on a physical robot, specifically the ViperX 300 robot arm developed by Trossen Robotics. We used various methods to manipulate the robot arm, using serial communication and ROS (Robot Operating System), a framework for robot software development. In order to work on a valid POMDP, we needed to eliminate some observability from the system, which we did by removing the usual camera input from the system. Instead, we attached some force sensors to custom grippers for the robot and used those, in addition to the robot's knowledge of its own position and the position of a known object, to use POMCP to learn the pose of the object, and then pick it up and place it in another area.

Electa Cleveland and Angela Zhu

C33

Home Institution: Brown University
Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA)
Faculty Mentor: Björn Sandstede (Applied Mathematics)

Quantitative Comparison of agent-based Zebrafish Models

During their early development, zebrafish (*Danio rerio*) develop stripes on their skin through complex interactions between different pigment cell types. Zebrafish pattern formation is a widely studied topic in developmental biology, as zebrafish skins are translucent and embryos develop outside of the mother. Interactions between pigment cells are now understood to govern zebrafish stripe formation. Our faculty mentor's lab developed a mathematical model of zebrafish pattern development to explain which pigment cell interactions are essential for stripes to form. A team of researchers at Bath recently proposed a second model for zebrafish patterns. The focus of our UTRA has been comparing the two models to each other and to biological measurements from real zebrafish using quantitative techniques.

Both models treat cells as agents and describe their positions as a function of time using stochastic differential equations, supplemented by discrete rules for cell birth, differentiation, death, and shape change. The models also have fundamental differences in their design: the Bath one structures its cells on a lattice and simulates time continuously using a Gillespie algorithm. In contrast, the model proposed by our faculty mentor, Prof. Björn Sandstede, is off-lattice and relies on discrete time steps, updating the simulation once per day.

Prof. Sandstede's lab recently developed the first methodology to quantitatively compare the outputs of agent-based models. This new technique uses topological data analysis to quantify agent-based patterns. During our UTRA, we

optimized this technique for both models. We then used it to obtain a quantitative comparison of 1000 simulations of each model. Although both properly simulated the development of two stripes and three interstripes, we found several significant quantitative differences in their average number of stripe and interstripe breaks, stripe straightness, cell-to-cell spacing, and cell densities. Finally, we compared our quantitative measurements for the two models to published empirical measurements in real zebrafish to determine the biological accuracy of the models. This work thus constituted the first quantitative comparison of agent-based models.

Elena Song, Arvin Soepriatna and Jenny Wei

C34

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA)

Faculty Mentor: Karen Coulombe (School of Engineering)

Engineering Bioelectric Sutures for Heart Repair

Heart attacks reduce heart function as stiff scar tissue develops throughout the ischemic area. A promising therapy is the implantation of engineered heart tissues (EHTs) constructed with cardiomyocytes differentiated from human-induced pluripotent stem cells (hiPSC-CMs). Despite their ability to beat and propagate electrical signals in vitro, electrically integrating EHTs with host hearts remains a significant challenge. Our project aims to develop electrically conductive biological sutures, termed bioelectric sutures, using fibrin threads coated with hiPSC-CMs. We hypothesize that bioelectric sutures will bridge electrical signals between the host heart and the implanted EHT to achieve synchronous beating. The first part of our project involves prototyping various 3D-printed molds to optimize CM attachment onto fibrin threads. Uniform distribution of CMs will ensure that bioelectric sutures effectively propagate electrical signals between host hearts and EHTs. The second portion involves using immunohistological staining to characterize cardiomyocyte gap junctions, alignment, and uniformity around the thread. We discovered that deep, narrow wells with tapering hemispherical bottoms resulted in increased density and uniformity of hiPSCCMs around threads, which improved electrical propagation as shown by optical mapping. Additionally, we created molds that enabled effective electrical stimulation of coated threads to improve maturation. We optimized antibody staining protocols in similar 3D tissues and showed that Triton-X improved antibody permeabilization. We also identified the best antibody dilutions for assessing maturation (MLC2v/MLC2a) and phenotype (cTnI/vimentin). Fluorescence imaging of stained threads confirmed the formation of cell-to-cell connections, an average radial thickness of 2-4 cells, and that cells preferentially aligned with the threads. Successful engineering of bioelectric sutures can establish a long-lasting bridge between an EHT and host heart, thereby improving EHTs' functional integration. The development of a coupled implant would help establish a heart repair therapy for patients experiencing conduction abnormalities and heart failure with reduced systolic function.

Michael Bregar

C35

Home Institution: Brown University

Summer Research Program: LANS

Faculty Mentor: Stephanie Jones (Neuroscience)

Modeling and Simulation of Noise Caused by Time-Changing Magnetic Fields of Domain Walls in Magnetic Tunnel Junctions

With the conception of quantum computers and quantum devices, the possibilities for solving computational as well as simulating reality are practically endless. In trying to construct such devices and understand quantum materials, a large amount of research has been conducted recently on magnetic tunnel junctions (MTJ) sensors. Increasing the sensitivity of MTJs would allow the observation of quantum phenomena such as quantum entanglement and would also help in the development of quantum materials for quantum computing. One major challenge in increasing the sensitivity of MTJ sensors is the reduction of noise while maintaining large enough tunnel magnetoresistance (TMR) ratios. In this study, the electric noise caused by the time-changing magnetic field of the domain walls was investigated and modeled using

Python. The velocity of the domain walls was found from various experiments and theoretical research papers and used to determine the current density. Then, using the strength of magnetization, the time-changing magnetic field and thus the electric field were determined using Maxwell's equations.

Kenneth Loi

C36

Home Institution: Brown University
Summer Research Program: LANS
Faculty Mentor: John Marston (Physics)

Biophysical modeling of Alzheimer's disease mediated changes in magnetoencephalography (MEG) alpha oscillations

The lack of a mechanistic understanding of Alzheimer's disease (AD) presents a major challenge in both prevention and therapeutic intervention. Recent studies have demonstrated that macroscale neural activity in the form of neural oscillations measured in humans with magneto- or electroencephalography (MEG/EEG) are perturbed during Alzheimer's disease. Neural oscillations reflect massively coordinated activity and are presumed to regulate cognitive function. Therefore disruption(s) of neural oscillations in AD are suggestive of a breakdown of the communication of large neuronal populations, potentially leading to AD symptomatology. Alpha oscillations disturbances have been shown to be associated with the loss of excitatory and inhibitory (E/I) balance as well as amyloid-beta plaque, which are common hallmarks of AD. This investigation seeks to elucidate the possible cellular origins of the macro-scale oscillatory disturbance in Alzheimer's by utilizing the Human Neocortical Neurosolver (HNN), a computational neural modeling software (<https://hnn/brown.edu>). HNN's foundation is a biophysics-based model of a canonical cortical column developed in the lab of Dr. Stephanie Jones, uniquely designed to simulate the cellular and circuit origin of human MEG/EEG signals (Neymotin et al eLife 2020). The details included in HNN's model enable a bi-directional interpretive bridge between human recordings and invasive microcircuit recordings that can be performed in animal models. In this project, we will apply HNN to uncover microcircuit dynamics that can produce characteristic changes in the alpha band oscillations of MEG/EEG data in Alzheimer patients. We will first characterize each parameters' independent effect on alpha oscillations to predict the parameters' role in their disturbance. To more rigorously explore the space of model parameters, we will employ simulation-based inference (SBI), a framework of machine learning algorithms and neural density estimators, to predict the mechanisms underlying the measured alpha waveform. This work addresses the growing need for safe and highly effective ways to collect and interpret data, underscoring the relevance of MEG/EEG recordings and biophysics-inspired interpretive tools like HNN that can link human recordings to the wealth of knowledge of microcircuit changes modeled in vitro and in animal studies

SOCIAL SCIENCES PRESENTATIONS

Gabrielle Shammash

D1

Home Institution: Brown University

Summer Research Program: Part of IAPA 1804T

Faculty Mentor: Geri Augusto (Africana Studies and International and Public Affairs)

Rethinking Development Archives

How can we reorient our understanding of development studies to center around grassroots initiatives and marginalized voices? And what genre of “final product” will be of use to future scholars? Using the first question to answer the second, we created a “finder’s aid,” diving sources into four thematic categories: “Gender,” “Urban, Rural, Space, and Place,” “Sustainable\Development,” and “Borders and Belonging.” We started with a “wide” bibliography of fifty sources that ranged from academic journals and newspaper articles to photography and music. Then, evenly spread through the four concepts, we created fifteen annotated bibliography entries, critiquing each source on its own and concerning the others. The four themes function much like a web, with some sources and lines of inquiry flowing between them. Each source with an annotated bibliographic entry is linked to three other sources from the wide bibliography for further research. Visually our sources are spread across space and time, although they focus on contemporary Asia and Africa. In Africa, the guide cover topics ranging from ethnic minorities in Morocco to religious organizations in Senegal. In Asia, we start in Singapore, exploring the city-state as a model of non-western development ideals while struggling with a sense of identity. Then, we move north and west to cover the experiences of religious minorities in Korea and development theories in India. Through the annotated bibliography, we primarily compare the work of non-western academics, journalists, and artists to each other without constant comparison to standards set by North American and European institutions. Overall, the bibliography is a guide for rethinking development studies not as an aid pipeline from the West to the Global South but as a place that amplifies disenfranchised voices.

Aaron Castillo and Yaideliz Ramos

D2

Home Institution: Brown University

Summer Research Program: Ginsberg Aging Research Fund @ Center for Gerontology Faculty

Mentor: Maricruz Rivera-Hernandez (Health Services, Policy, and Practice)

Improving Insurance Plan Choice and Decision-Making Among Medicare Advantage Seniors During the COVID-19 Pandemic

The Medicare Advantage (MA) program covers the same benefits of Original Medicare, but may offer extra benefits and lower out-of-pocket expenses through private insurance companies. The MA program enrollment has almost doubled over the last decade, particularly between low-income individuals and racial/ethnic minorities such as Black and Hispanic communities. To provide information about MA plans, the Centers for Medicare & Medicaid Services (CMS) have developed online resources such as the CMS plan “comparison tool”, and the CMS five-star rating system. However, previous research has shown that older individuals prefer person-to-person interaction to receive information about MA plans. To do so, seniors can obtain Medicare unbiased education from the State Health Insurance Program (SHIP) and non-profit organizations, unlike insurance agents/brokers who may potentially be biased. This research project will help fill the gaps in knowledge regarding the means by which seniors learn and/or obtain information about MA plans, from both the community and private organizations’ perspectives. To achieve this, we have performed semi-structured interviews of members of the stakeholder’s organizations over the Zoom platform, and have offered raffle prize incentives. For the qualitative analysis, the interviews have been coded using a combination of a priori and emergent codes. We identified the major interconnected themes regarding decisions, difficulties, online resources and specific strategies to help older adults choose their MA plan. Preliminary results have

shown that although CMS tools are helpful for beneficiaries and stakeholders, they are not used enough. Also, there has been dissatisfaction with the updated Medicare.gov plan finder tool among SHIP counselors. However, further analysis is needed and understanding these outcomes will help identify recommendations from stakeholders regarding the necessary tools for consumers choosing a MA plan.

Alexander Daskalopoulos

D3

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Joo-Hyun Song (CLPS)

Goal competition during reaching: A nonlinear dynamical systems approach

During most daily activities, there are multiple opportunities for action. For example, when reaching in a cluttered environment, multiple objects compete for attention. Previous work demonstrates that distracting non-target objects divert the hand path away from the target object. However, in many circumstances, people select a target from multiple competing options. Walking path selection in environments with multiple competing goals has been described using online steering dynamics models that link perception and action through simple control laws without explicit path planning. The goal of this project is to test the validity of a modified steering dynamics model, which explains walking paths and decision-making (i.e., route switching) in terms of the dynamics of attractors, repellers, and bifurcations, in the context of goal-directed reaching actions among competing goals.

Czenilriene Santander

D4

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA)

Faculty Mentor: Nicole Nugent (Departments of Psychiatry and Human Behavior, Pediatrics, and Emergency Medicine at the Warren Alpert Medical School of Brown University)

Observations of Social Support Systems on Teen Mothers Post-Trauma: A Study of Two Cases

A potentially traumatic event that ultimately results in hospitalization can have a great effect on both the injured adolescent and those who are regularly a part of their lives. Though adolescent resilience can vary from individual to individual, it is possible that their relationships and support systems hold influence on their ability to recover from trauma or injury. In the case of teen mothers, recovering from an event that results in hospitalization only adds to the many responsibilities these young women must face. Using the unique nature of the data collected by the Electronically Activated Recorder (EAR), we are able to observe the 2-week period following a trauma event for two cases of teen mothers enrolled in the ED EAR study. The EAR data provided an opportunity to observe the support systems available to these cases, revealing how one case appeared to have more partner support whilst the other had more parental/peer support. In addition, both parents and adolescents involved in both cases responded to surveys that give insight into general familial functioning, possible parent-child conflict, child's perceived adequacy of social support, child loneliness, parental stress, etc. Combining EAR data, self-report survey results, and interviews, we aim to construct an in-depth analysis of the support systems available to these two cases in the 2-weeks post-discharge and draw conclusions as to the effect of parental, partner, or peer support on these teen mothers post-trauma.

Alison Kim

D5

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Lauren Bohlen (Behavioral and Social Sciences)

The Impact of the Covid-19 Pandemic and Technology Use on Women's Physical Activity Levels

The Covid-19 pandemic and the associated business closures, and recommended guidelines for social distancing, impacted what were already low levels of physical activity across the population in the past year. Many people used technology as a way to help them remain physically active in light of the many changes during this time. The purpose of this research was to understand how the Covid-19 pandemic impacted physical activity levels in a sample of low-income women in the Rhode Island and Southeastern Massachusetts area. Participants completed three surveys over the span of two weeks, and participated in two individual interviews, separated by one week. Quantitative analyses were conducted using statistical software SPSS, and included correlation analyses, and paired sample t-tests. Interview data were double and triple-coded, and codes entered into Nvivo for analysis. The preliminary results indicate that participants' physical activity was significantly lower than it was before the pandemic, and that this was associated with their technology use. Those with a greater perceived ability to use the internet for health information spent more time performing recreational activities per week since the pandemic. Moreover, greater physical activity levels before the Covid-19 pandemic are significantly associated with greater physical activity levels since the pandemic. We are further exploring predictors of the decline in women's physical activity since the pandemic, including a rich qualitative understanding of their reported barriers to activity since the pandemic. The results of this research could be used to support interventions to increase physical activity in these populations, and to help develop resources should widespread closures like those seen during the Covid-19 pandemic occur again in the future.

Selene Schiavone

D6

Home Institution: University of Puerto Rico Rio Piedras

Summer Research Program: Leadership Alliance-Summer Research Early Identification Program (SR-EIP) Faculty

Mentor: Frederike Petzschner (Robert J. and Nancy D. Carney Institute for Brain Science)

The influence of perceived control and received reward on slot machine gambling

Disordered gambling poses a severe financial and social burden on individuals and their families. This disorder has recently become the focus of addiction research since it's currently the only behavioral addiction that's recognized by the Diagnostic Statistical Manual (DSM) and can thus serve as a blueprint for studying addiction in the absence of substance abuse. Specifically, previous research has indicated that maladaptive reward learning is a key component in the development of disordered gambling, such as a heightened reward expectancy and alterations in the perception of control. Slot machines are, thereby, the most addictive gambling devices and are designed to tap into an individual's reward processing and sense of control. However, there are few studies that have evaluated how these elements influence behavior in a naturalistic slot machine-like environment. This investigation uses programming techniques to track the behaviors of gamblers through a slot machine-like experiment and identify key differences between recreational and disordered gamblers in terms of the cognitive distortions mentioned above. Participants played four different slot machine tasks with specific combinations of perceived control (high/low) and reward magnitude (high/low). By analyzing the change in their gambling behaviors, we'll test the hypothesis that pathological gamblers are influenced by the illusion of control and received reward. This combination of computational modeling and behavioral data may help us understand who is at risk of developing an addiction or at risk of relapsing, while also promoting the development of new tools and data processing technologies that may improve the diagnosis/prognosis of mental disorders.

Home Institution: Brown University
Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA)
Faculty Mentor: Sarah Helseth (Brown University School of Public Health Center for Alcohol and Addiction Studies)

Reducing Cannabis Use Among Justice-Involved Youth: Caregiver Perceptions of Mobile Health Apps

Over half of justice-involved youth (JIY) test positive for illegal substances at the time of their arrest, 92% for cannabis (NCASA, 2004), increasing their risk for later SU disorders (Flory et al., 2004) and recidivism (Van der Put et al., 2014). JIY face a tremendous SU treatment gap, as only 48% of those identified as needing SU treatment services receive them (Johnson et al., 2004). Mobile health (mHealth) apps are especially appealing for delivering effective cannabis use interventions to underserved JIY, in part because they are more accessible and require fewer resources than traditional approaches (Bath et al., 2018). Youth perspectives of mHealth are well established, but their caregivers' are not. As gatekeepers to youth services, caregiver perspectives must be explored prior to cannabis app development.

This qualitative study collected caregiver opinions, preferences, and concerns related to mHealth apps targeting cannabis use among JIY, to help reduce any usage barriers, ultimately promoting their efficacy and sustainability. In-depth interviews were conducted with caregivers (n=8) of JIY with past-year cannabis use. Questions delved into participants' perceptions of the feasibility and acceptability of mHealth interventions and their children's potential use of an mHealth app to reduce cannabis use. Caregivers were all biological parents (100%) and were predominantly non-Hispanic white (63%) cis-women (75%). Qualitative coding employed an a priori framework based on the Behavioral Intervention Technology model (BIT; Mohr et al., 2014), encompassing the theoretical (i.e., clinical aims, usage aims, behavior change strategies) and instantiation (i.e., elements, characteristics, and workflow) aspects of specific mHealth features. Emergent codes that did not fall within the BIT framework were also captured.

Coding identified several emergent codes. Specifically, caregivers described their child's technology access and use, shared thoughts on behavior change apps, detailed specific needs of JIY, and discussed risks and concerns about the proposed app. Analyzing caregiver perspectives on mHealth apps for cannabis use is a vital first step to addressing unique SU service needs and barriers encountered by JIY and their families. Dissemination of caregivers' feedback will guide researchers building mHealth apps for vulnerable youth facing a range of public health concerns.

Home Institution: Brown University
Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA)
Faculty Mentor: Michael Frank (Cognitive Linguistic Psychological Science) Jaskir Alana (Cognitive Linguistic Psychological Science)

Sleep promotes state-abstraction in human reinforcement learning

The human ability to transfer information from what we know about one skill to a related skill is remarkable. For example, a guitarist can transfer what they know about the guitar in order to learn other string instruments. We aim to study the state-abstraction process and what role sleep plays in constructing abstractions which can be exploited to improve learning. In order to do this, we designed a task using predictions from cutting-edge algorithms in computer science.

Our task consists of a challenge where the participant is awarded if they correctly guess a three-button combination. The display consists of a keypad, each button with a different color (e.g. a 2x3 keypad with green, blue, red, yellow, orange, and purple keys). The participants guess keys in the combination one at a time. If that square was correct in that level, there is positive feedback and the participant can move onto the next key in the combination. If it is incorrect, there is negative feedback and the participant must keep guessing. The hidden rule in the challenge is that certain keys

produce the same outcome. For example, if the blue and red keys were in the same “cluster”, if pressing blue is rewarded, pressing red will also be rewarded. Picking any other key would not be rewarded.

In order to study how participants, carry out the challenge and learn the rule, we produced several versions of the challenge, varying the number of buttons in the clusters, the dimensions of the array, and the type of feedback the participant receives. The objective will be to study whether the participants can deduce the hidden rule through task abstraction and play the game more successfully when the combination changes but the clusters stay the same. Once we study how participants learn this initially, we will then study whether sleep aids formation of these abstract clusters. This would explore an understudied computational role for sleep in reward learning.

Kyla Mayo

D9

Home Institution: Dillard University

Summer Research Program: Leadership Alliance-Summer Research Early Identification Program (SR-EIP) Faculty

Mentor: Matt Nassar (Neuroscience)

Working Memory: Identifying Correlations between Memory Recall and GABA/Glutamate levels in the brain.

Within the brain, working memory is a prominent cognitive function that determines how well information is temporarily processed and stored. Many theories and models have been proposed to determine how to best optimize working memory in adults. The method “Chunking” which is a technique of grouping similar objects together, has been proposed as a way to make the most of one's working memory. To test this technique, a color reproduction task was administered and the data was stored in the MATLAB database to be analyzed and modeled to create observations and hypotheses. Within the color reproduction task, different clustering conditions were manipulated to get an accurate judgment of performance. To do so, a color wheel was used to identify cluster variance (difficulty level of colors ability to be chunked together). High cluster variance was harder to “chunk” compared to low variance, and a uniformed spacing condition was used as the control. It was shown that working memory in younger adults is more effective and produces less error compared to that of older adults. The difference between younger and older adult recall is due to lower memorization and random guessing from older adult participants. Originally it was believed that working memory resembled a slot, meaning memory was either remembered (stored in a slot) or completely forgotten. However, the data, which exhibits a normal to spread distribution, explains that objects not in the forefront of your sensory perception are more clouded with noise, making them harder to recall. This research has the opportunity to better expand working memory and identify the cognitive processes that lead to deficits in memory when aging. This will not only provide further insight into this cognitive phenomenon but also contribute to improving short-term memory and effective learning capabilities.

Hannah Joyce Joyce

D10

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Tara White (Neuroscience)

An Incentive Theory of Anger

Anger is a powerful, negatively valenced emotion with significant impact on human health and well-being. As such, there is potentially great value in better understanding the behavioral phenotypes associated with anger and their underlying neural substrates. We present a novel incentive theory of anger derived from assessments of emotion, personality, task-based functional magnetic resonance imaging (fMRI), and pharmacological challenge in healthy young adults. Two experiments were conducted to evaluate tiered hypothesis regarding the relationship between anger, exuberance, reward and approach. Experiment I found self-reports of anger to frustrative non-reward and exuberance to success events rose jointly in an incentive challenge task (N=39). Anger and exuberance responses were also positively associated with scores on the personality trait of social potency (SP), a measure of agentic extraversion that

relates to the sensitivity to reward. Experiment II used task-based fMRI and found anger was positively related to (a) task-induced exuberance, (b) trait SP and (c) fMRI BOLD response in right nucleus accumbens to d-amphetamine, a psychostimulant with dopaminergic and neurometabolic effects (N=10). Our findings are consistent with mechanistic contributions of dopamine to anger, indicating anger is an incentive state that facilitates the approach and acquisition of rewards that entail risk. Implications for neural mechanisms of anger, exuberance and its relevance to reward-motivated action and risk-taking are discussed.

Kaitlyn Mundy

D11

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA)

Faculty Mentor: Amitai Shenhav (Cognitive, Linguistic, and Psychological Sciences) Yee Debbie (Cognitive, Linguistic, and Psychological Sciences)

Age-Related Differences in the Influence of Positive and Negative Motivational Incentives on Mental Effort

Aging is a biological process that affects cognitive as well as physical abilities. It is well understood that, relative to younger adults (YA), older adults (OA) experience increased costs of mental effort and more routinely avoid engagement in demanding tasks. However, while there has been extensive research into age-related alterations in cognitive function, the effect of motivational incentives of differing valence on cognitive control remains relatively unexplored across the entire adult lifespan. Here, we conducted an online study to examine age-related changes in the motivational influence of reward and punishment on the exertion of cognitive control. Participants (N = 194; 18-79 years) were recruited through Prolific to perform a self-paced incentivized Stroop task online, which required them to identify the ink color that a color word was written in (e.g. "green" written in blue ink). Throughout the task, participants earned large or small amounts of monetary reward for correct responses, and were penalized with either large or small amounts of monetary loss for incorrect responses. Consistent with extant cognitive control literature, linear mixed effects models run on the task performance data revealed that OA (65 years and older) showed no significant behavioral changes in response to the different positive and negative incentive conditions. In contrast, YA (18-39 years) performance was strongly modulated by both reward and punishment, responding faster and less accurately when the rewards were higher, while responding slower and more accurately when the penalties were higher. Interestingly, middle-aged adults (MA; 40-64 years) performed similarly to YA in response to high rewards, but did not appear to modulate performance in response to penalty level. In line with previous studies, YA participants responded more quickly than MA participants, while OA participants responded the slowest out of all three groups. Collectively, these findings reveal age-related differences in the interaction between motivation and the recruitment of mental effort to perform cognitively demanding tasks.

Rachel Ma, Ivery Chen and Flynn Begor

D12

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Sydney Skybetter (TAPS) Tellex Stefanie (Computer Science)

Choreorobotics 0101

Choreorobotics 0101 focuses at the intersection of dance and robotics to create interdisciplinary, exploratory final dances / projects. Three teams have been created (each focused on either beat detection, movement, or ethical frameworks) to examine existing methods and/or works that combine intersectional feminist thought with tangible performance-focused robotic dancers.

The Beat Detection team has been focused on developing a deep learning network for beat detection and developing syllabus material focused around foundational music theory covering topics such as rhythm, pitch, genres. The Movement team has been working on connecting the MOVO to ROS in order to control the robot's movement inside

Unity, as well as creating a graphical UI inside Unity that contains basic dance movements for the robot. The Ethical Frameworks team has been exploring different forms of media that cover topics of robotic autonomy, human-robot interaction, and the dangers and challenges of robotic advancement. The research that has been conducted over the last three months is in service of the development of the course 'Choreorobotics 0101' which will be taught in the Spring of 2022.

Carrie Deng and Rachel Huynh

D13

Home Institution: Brown University

Summer Research Program: SPRINT/Undergraduate Teaching and Research Awards (UTRA) Faculty

Mentor: Tayla Ash (Behavioral and Social Sciences)

Mukbang viewing demographics and its behavioral influence

Obesity, eating disorders, and unhealthy eating behaviors often have complex psychological and environmental triggers. Certain populations may also be more vulnerable to developing these pathologies. This project investigates how the viewership of sensationalist food-related digital content – in particular, a type of video called “mukbang” – could mediate the development of eating-related pathologies and could disproportionately affect certain demographics.

Mukbang is a Korean word that means “eating broadcast,” in which an individual films a video of him/herself eating a meal (usually while engaging with the audience or aiming to entertain through the audience with their eating) and then shares it on a social media platform like YouTube. Popular mukbang content creators often consume hypercaloric and hyperpalatable foods in the videos.

The proposed project will lay the foundation for future research into the public health impact of mukbang videos and other food-related digital content. Our results may help guide public health policies in the digital sphere regarding mukbangs and contribute to social media platforms’ re-assessment of algorithms that may recommend mukbang to vulnerable demographics.

Summer Research Programs at Brown

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