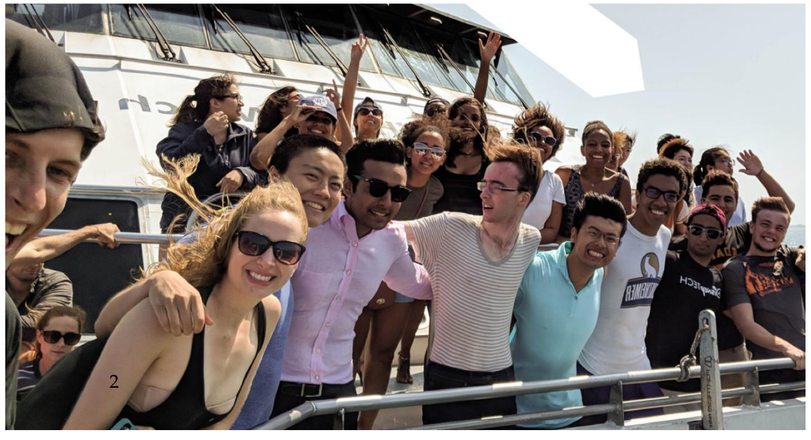

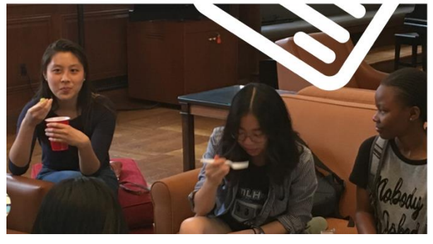

2018 ABSTRACTS

PBPSS

PRISE | BLISS | PRIMO | SHARP | SURGH

HARVARD SUMMER UNDERGRADUATE RESEARCH VILLAGE

ABSTRACT BOOK 2018

EDITORS-IN-CHIEF:

Truelian Lee, Kai Trepka

EDITORIAL COMMITTEE:

Rachelle Ambroise, Jamie Caines, Ralph Estanboulieh, Maclaine Fields, Bella Ganthier, Beverly Ge, Noah Houghton, George Hu, Anahita Iyer, Stacy Jo, Allison Kao, Marinna Okawa, Alyssa Panton, Arielle Rothman, Pratap Singh, Trang Truong, Katherine Venturo-Conerly, Michelle Walsh, Margaux Winter, Leon Yang, Ryan Zhang, Annie Zhao

PEER EDITORS:

Maria Altshuller, Stephen Casper, Sambuddha Chattopadhyay, Brenda Chiang, Audrey Effenberger, Mohamed El-Abtah, Leo Garcia, Eliane Grace, Jonathan R. Honey, Lourdes Kaufman, Angela Kim, Katelyn Li, Yiping Li, Winston Michalak, Cal Miller, Arjun Mirani, Simon Shen, Natalie Sherman, Wesley Shin, Filippos Sytilidis, Joanna Tao, Evan Thompson, Tori Tong, Akash Wasil, Piper Winkler, Nicola Young

COVER DESIGNER:

Sinead Danagher

PARTICIPATING PROGRAMS:

Program for Research in Science and Engineering (PRISE)
Build Learning through Inquiry in the Social Sciences (BLISS)
Program for Research in Markets and Organizations (PRIMO)
Summer Humanities and Arts Research Program (SHARP)
Summer Undergraduate Research in Global Health (SURGH)

Office of Undergraduate Research and Fellowships
Harvard University
Cambridge, Massachusetts

Contents

Letter from the Director

Dear HSURV Community,

I am delighted to introduce this thirteenth collection of research abstracts from the 2018 Harvard College Summer Undergraduate Research Village, comprised of PRISE (Science and Engineering), BLISS (Social Sciences), PRIMO (Markets and Organizations, co-hosted by Harvard Business School), SHARP (Humanities and Arts), and SURGH (Global Health, co-hosted by the Harvard Global Health Institute). Once again, these outstanding undergraduate scholars have done exceptional work guided by Harvard faculty, postdocs, graduate students, and other investigators in virtually every Harvard School, affiliated teaching hospitals, and research enterprises across Boston and Cambridge. Combined with the lively and energetic residential community at Winthrop House, the Summer Undergraduate Research experience is an enduring testimony to the compelling value of developing strong social and intellectual ties among emerging young researchers across the full range, breadth, and diversity among scholarly interests and pursuits in a rich, vibrant environment.

This historical collection of abstracts could not have been possible without the outstanding and indefatigable effort of the group of Research Village editors whose mission it has been to collect, organize, and publish the works of all of the Fellows. Along with this summer's Program Assistant Fellows, who have helped with all of the fellow-initiated activities, I would like to thank this group especially for taking on the particular challenge to record the research projects of the Research Village community this summer.

To the Summer Undergraduate Research Village Fellows of 2018, I wish you every success in your further intellectual growth and academic trajectory. Your engagement, enthusiasm, and inclusiveness are inspiring, and I hope the personal and collegial relationships you have cultivated these past ten weeks continue to grow and flourish long after your HSURV summer.

All best wishes,

Gregory A. Llacer
Director, Harvard College Office of Undergraduate Research and Fellowships (URAF)
Director, Harvard College Program for Research in Science and Engineering (PRISE)

Letter from the Editors

Dear HSURV Community (and Beyond),

It takes a village to raise a child, and it took HSURV to transform us into the researchers that we are today. It has been a privilege to work alongside top faculty these past ten weeks, and the time could not have flown by faster. HSURV is not just a research program; it is a testament to the ability of undergraduates like us to pursue our passions and delve into work that can potentially change the world.

To celebrate our work and provide a taste of our invigorating and diverse research, the Editorial Board has worked hard to compile this abstract book. However, this book alone cannot fully encapsulate all that we have gained this summer. The Research Village has given us an opportunity to interact with insightful mentors and passionate peers in an interdisciplinary, residential setting. From discussing research over the dinner table in Gore Hall of Winthrop House, bonding over cricket with the Emmanuel Fellows from the University of Cambridge, and attending the enlightening Distinguished Speaker talks this summer, we have learned that research does not just belong in the lab and library.

This summer would not have been successful without a confluence of support from a variety of sources. We would like to thank our professors, mentors, and peers for inspiring us to venture out into the world of research and the Winthrop summer staff for their generous hospitality. Thank you to the PAs and proctors for guiding us and providing us with fun activities throughout the summer. Elizabeth Perten from URAF and our esteemed PA Sean Gibney, as well as our numerous peer editors, were also integral to the completion of this book. And of course, we must thank Greg Llacer and the rest of the URAF staff, as well as all the PBPSS fellows of the Research Village, for making this a summer one that we will never forget.

Sincerely,

The 2018 HSURV Abstract Book Editorial Board

Program Overview

According to the Office of Harvard Undergraduate Research and Fellowships, the 2018 Harvard Summer Undergraduate Research Village is a 10-week residential community that comprises Research Fellows from the following programs:

PRISE
The Program for Research in Science and Engineering aims to build community and stimulate creativity among Harvard undergraduate researchers in the life, physical/natural, engineering and applied sciences. Selected fellows work on projects with Harvard-affiliated researchers and participate in extremely rich evening programming (that includes both social and academic activities).

BLISS
Build Learning through Inquiry in the Social Sciences is designed to provide a formative and substantive social science research experience and to promote community, creativity, and scholarship. A diverse cohort of BLISS Fellows works on pre-designated research projects led by Harvard faculty. In addition to conducting full-time research, BLISS Fellows participate in rich variety of programming, including social and academic activities.

PRIMO
The Program for Research in Markets and Organizations aims to build community and stimulate creativity among Harvard undergraduate researchers in business and related fields. Students are selected to work in research areas which span diverse topics (finance, organizational behavior, marketing, etc.), disciplines (Psychology, Economics, Sociology), and methods (quantitative or qualitative). Fellows are placed with pre-designed faculty projects at Harvard Business School and participate in enrichment activities such as faculty lectures, professional development workshops, presentation opportunities, and social events.

SHARP
The Summer Humanities and Arts Research Program aims to build community and stimulate creativity among a small cohort of Harvard undergraduate researchers in the humanities and arts. SHARP fellows work on research projects with Harvard-affiliated faculty, researchers, and senior library and museum staff. Fellows live together in one of the Harvard College houses and participate in rich evening programming that includes both social and academic activities. To participate in SHARP, you must apply and be selected to work on one of the available SHARP research projects.

SURGH
The Summer Undergraduate Research in Global Health program aims to build community and stimulate creativity among a small cohort of Harvard undergraduate researchers in global health. SURGH fellows work on research projects with Harvard-affiliated faculty and researchers. Fellows live together in one of the Harvard College houses and participate in rich evening programming which includes both social and academic activities. To participate in SURGH, you must apply and be selected to work on one of the pre-designated SURGH research projects.

Abstracts

ANTHROPOLOGY

3D Modeling of Egyptian Artifacts

Andréa Martinez
BLISS Fellow
Near Eastern Languages and Civilizations, 2020

Near Eastern Languages and Civilizations
Advisor: Peter Der Manuelian

Because access to museum artifacts often involves entrance fees, university IDs, and travel expenses over long distances, it is a class-based privilege inaccessible to many. However, new advances in 3D object scanning may provide access for anyone with an internet connection. The Harvard Semitic Museum is one of the pioneers in this movement utilizing the Artec Space Spider 3D portable scanner to capture and render 3D models of its Egyptian collection for online publication. One of the goals of this project is to also create a manual of best practices for scanning and modeling ancient artifacts for research. The Artec Space Spider is a structured light-based scanner that collects data points from the surfaces of artifacts. These points can be manually aligned, edited, and fused together to form a lifelike digital model. The resulting models are precise to 0.1 mm of error and can be used by researchers, students, and the general public for teaching, research, learning, and enjoyment. Additionally, the models, unlike the actual artifacts, will not decay with age (provided they are maintained digitally). The 3D models thus also serve as a conservation and collections management data. Ultimately we seek to provide access to artifacts for a broader audience, regardless of individual resources or privilege.

APPLIED MATHEMATICS

Circulating Tumor DNA Analysis as a Molecular Basis to Monitor Meningioma

Meriton Ibrahimi
PRISE Fellow
Applied Mathematics, 2019

Brigham and Women's Hospital, HMS
Advisor: Wenya Linda Bi

Meningiomas account for over one-third of all intracranial tumors. While they are usually benign, high-grade meningiomas display aggressive behavior and higher rates of recurrence. Close monitoring of these lesions is therefore crucial. Liquid biopsies, which sample non-solid biological tissue (primarily blood) for biomolecules, present a non-invasive form of continuous monitoring. Circulating tumor DNA (ctDNA) has been detected in liquid biopsies from various cancer types, including glioma at low levels. We therefore postulate that meningiomas, which form from the meninges outside the blood-brain barrier, secrete detectable levels of ctDNA for tumor monitoring. We submitted ten samples of ctDNA extracted via blood biopsy from patients presenting meningiomas for low-pass whole-genome sequencing. The sequenced data will be analyzed for copy number variations (CNVs) associated with meningiomas using the Broad Institute's Genome Analysis Toolkit (GATK). Results will look at detection rates in conjunction with correlation of meningioma grade and recurrence. If our hypothesis is supported, then a larger follow-up study will ensue to validate findings and determine the clinical significance of using ctDNA analysis for non-invasive monitoring of meningiomas.

Making Mistakes in School Choice

Claire Shi
PRIMO Fellow
Applied Mathematics, 2021

Harvard Business School
Advisor: Scott Duke Kominers

Each year, thousands of middle school students are matched to high schools using matching algorithms. One popular algorithm is Immediate Acceptance (IA). Recently, market designers have been advocating for Deferred Acceptance (DA) to replace IA, largely because IA is *not* strategy proof. This means that ranking schools truthfully in order of preference is weakly dominated by strategically ranking schools in concordance with one's chances of admission. However, despite DA being strategy proof, salient empirical evidence has suggested that a non-trivial proportion of students still misrepresent their preferences. This tendency to strategize or make mistakes in DA could be attributed to the high-stakes environment (that is school choice), or to misunderstandings of the algorithm. Consequently, we ask the following questions: how do students who make mistakes affect the welfare of their peers? Is DA, despite its pareto-inefficiency, more robust than IA for those who strategize *incorrectly*? In other words, how severely is the student "hurt" in IA compared to DA if she wrongly guesses the priorities of schools and therefore fails to strategize to her advantage? Taking a theoretical approach, the analysis appears to suggest that if there exist students who make mistakes and correctly rank schools by their probability of admission, then DA with mistaken students is weakly better for truthful students than DA without mistaken students. Further, it appears that the more heterogeneity between student preferences, the more successfully DA protects students who strategize incorrectly from welfare loss. By taking into account mistakes, these results may help market designers better understand how students interact with IA and DA.

Pension Funds Around the World

Lydia Wang
PRIMO Fellow
Applied Mathematics, 2020

Harvard Business School
Advisors: Victoria Ivashina, Josh Lerner

Public pensions are a significant source of long-run capital for corporations and projects. One recent phenomenon that has affected pension funds is the low level of interest rates that followed the Great Recession of 2007-2009. Since the Great Recession, interest rates have continued to stay very low. Due to these lower interest rates, pension funds have not been able to achieve high enough returns from their fixed income investments. Since interest rates are unlikely to increase significantly and quickly, we hypothesize that many large pension funds have battled lower returns by increasing investment in riskier alternative assets, such as private equity and real estate. To explore this idea, we are building a data set of the 300 largest pension fund institutions in the world between 2008 and 2017, gathering information about these institutions' allocations from their annual reports or from SEC filings. We will marry this data with information about the nations' economic and political features and about the pension funds themselves, which will allow us to do analyses with panel data. Moreover, we can exploit changes in political leadership to get plausibly exogenous shifts to understand the potential consequences of these investments.

Improving the Outcome of Care for Opioid Use Disorder (OUD) Patients

Megan Zhao
PRIMO Fellow
Human Evolutionary Biology, 2019

Harvard Business School
Advisor: Robert Kaplan
Mentor: Mahek Shah

On average, over a hundred people die from opioid overdose a day in the United States, making opioid overdose a widespread national epidemic that has disproportionately impacted the Northeast. Drug overdoses have become among the leading causes of death in Americans under the age of 50. In light of this critical issue, two interventions are necessary: reduction of the incidence of newly addicted patients by reducing the frequency and dosages of prescriptions for relief of pain as well as using evidence-based treatment for currently addicted patients. Through the use of Medically Assisted Treatment (MAT), OUD treatment is approached as a chronic disease, which is essential for improving outcomes for these patients. However, current reimbursement for OUD patients does not cover the costs comprised of MAT, behavioral and social services. Thus, combatting the opioid epidemic requires a more comprehensive and integrated costing of care for OUD patients so that clinics can receive proper compensation in providing evidence-based care. With a focus on MGH Bridge Clinic and RIZE Massachusetts, process mapping of these healthcare settings increases their efficiencies by lowering costs of care and maximizing the utility of each staff member. Process maps accounts for every step of care that an OUD patient receives, including the interventions taken when the patient is both inside and outside of the clinic. In creation of process maps, Time-Driven Activity-Based Costing can be applied to estimate the costs for one cycle of care that OUD treatment bundle payment should cover, thus allowing more effective and efficient care to be delivered to OUD patients.

ASTROPHYSICS

Probing the Evolution of Supermassive Black Holes in Various Galaxy Environments

Natasha Sarah Abrams
PRISE Fellow
Astrophysics, 2021

Smithsonian Astronomical Observatory
Advisor: Akos Bogdan

Every massive galaxy has a supermassive black hole at its center, which co-evolves with its host galaxy. Galaxies can be found in a variety of environments including clusters, groups, and isolated locations (in order of decreasing frequency of galaxy mergers). Since mergers and other environmental factors are known to impact galaxy evolution, studying properties of older (elliptical) galaxies in different environments may reveal how they and their respective supermassive black holes evolve. In the framework of this project, I studied isolated galaxies, galaxies in groups, and galaxies in clusters. Specifically, I studied the X-ray luminous gas in these galaxies based on observations collected by the Chandra X-ray Observatory. I generated surface brightness profiles that were fit using a β-model and measured the temperature of the hot gas by fitting the X-ray spectra using XSpec. Assuming the gas is in hydrostatic equilibrium, I computed the total gravitating mass of the galaxy. Using the total mass within a characteristic radius and previously measured black hole masses, I derived the black hole mass to total mass ratios and compared the values for galaxies of various environments. By probing these ratios, I can infer if black holes residing in the center of isolated galaxies, those in groups, and those in clusters undergo different evolutionary processes.

BIOMEDICAL ENGINEERING

Cellular Adhesion and Biofilm Formation on Liquid-Infused Silicone Ear Tubes

Eva Cai
PRISE Fellow
Biomedical Engineering, 2021

School of Engineering and Applied Sciences
Advisor: Jennifer Lewis
Mentor: Nicole Black

Middle ear infection is the most common infliction for which medical care is provided to young children in the US, affecting more than 80% of children by the time they are three years old. To reduce the pressure and pain from recurrent middle ear infection, tympanostomy tubes (ear tubes) are implanted in the tympanic membrane to drain effusion from the middle ear cavity and ventilate the space to prevent further infections. However, commercially available ear tubes are limited in their ability to transport fluid or deliver drugs, as keratinocytes from the tympanic membrane and bacteria from effusion and otitis media adhere to their surfaces. We aim to overcome these limitations through the design and fabrication of liquid-infused silicone tympanostomy tubes. Using stereolithography, we first created high-resolution molds for silicone ear tubes. Next, we investigated keratinocyte adhesion, bacteria adhesion, and biofilm formation on both commercial (controls) and liquid-infused 3D tympanostomy tubes to predict rates of occlusion. Our preliminary findings indicate that liquid-infused silicone ear tubes significantly reduce cellular adhesion, while simultaneously allowing to tailor both fluid flow and drug delivery through their open lumens. Ultimately, these novel tympanostomy tubes may provide a minimally-invasive and cost-effective strategy for improving the lives of millions of patients with chronic middle ear infection.

Chondrocyte Invasion into RGD-Functionalized PTFE Mesh

Kasoorelope Oguntuyo
PRISE Fellow
Biomedical Engineering, 2019

School of Engineering and Applied Sciences
Advisor: David Mooney
Mentor: Joshua Grolman

Anterior cruciate ligament (ACL) rupture occurs in 68.6 out of 100,000 people per year. Treatment methods include surgical replacement with tendon grafts, which are subject to donor site morbidity and host-graft rejection. Therefore, synthetic replacements present an opportunity to bypass these negatives. One such option, polytetrafluoroethylene (PTFE), is a polymer with properties of high tensile strength and stiffness, making it desirable for use as a biological scaffold for ACL replacement. Though PTFE exceeds the mechanical properties of the natural ligament, the presence of fluorine in the material prevents the infiltration and attachment of cells such that the material fails *in vivo*. As such, PTFE has been removed from consideration as an ACL prosthesis. We are working to manufacture an electrospun mesh of PTFE functionalized with a cell adhesion peptide to enhance attachment. Infiltration of chondrocytes, cells found in ACL tissue, into these meshes will then be measured with confocal and scanning electron microscopy (SEM). We believe that controlling the degree of substitution on the PTFE fibers, as well as the directionality of the fibers and porosity of the meshes, will allow us to increase the amount of infiltration of the chondrocytes. Thus far, we have developed an electrospinning protocol and will soon quantify the size of the produced fibers and pores with SEM. If the hypothesis is supported and infiltration is increased, it could improve PTFE's viability as an ACL replacement and provide an opportunity for an improvement in ruptured ACL treatment.

Investigation of Novel Oil-Infused Tympanostomy Tubes

Arin Stowman
SURGH Fellow
Biomedical Engineering, 2019

School of Engineering and Applied Sciences
Advisor: Aaron Remenschneider
Mentor: Nicole Black

Otitis media, or an ear infection, affects people all over the world, with over 700 million patients annually. It is commonly treated by inserting ear tubes, or tympanostomy tubes, which ventilate the middle ear space and transport both effusion out of and antibiotic droplets into the middle ear. In this study, *in vivo* tests are used to determine how a novel oil-infused silicone elastomer tube interacts with the eardrum and addresses issues associated with tympanostomy tubes, such as otorrhea, occlusion, scarring, and persistent perforation. Preliminary studies optimize tube diameter and flange shape for insertion, droplet delivery, and short-term perforation healing. We insert and endoscopically analyze the tubes for one month to determine how easily they can be put in and remain without causing inflammation; after removal, perforation healing time will be documented. We assess drug delivery capabilities by applying fluorescently labeled otic drops and calculating the amount delivered to the middle ear during histological analysis. Subsequent studies determine the effects of the optimized tubes on the membranes over longer periods of time. They include hearing tests, ABRs and DPOAEs, conducted before insertion, after insertion, 6 months after insertion before the tubes are removed, and upon membrane healing. The findings from these studies will hopefully show that these new tubes are less invasive and deliver antibiotics more readily, and thus are better equipped to prevent bacterial and cellular adhesion while also allowing for quicker healing times.

Plasmid Engineering and Genomic Knockouts Improve Secretion of Recombinant Proteins in *Escherichia coli* Nissle

Siva Emani
PRISE Fellow
Biomedical Engineering, 2021

Wyss Institute
Advisor: Neel Joshi
Mentor: Anton Kan

Therapeutic applications of engineered probiotic bacteria rely heavily upon efficient production and secretion of synthetic product. This study utilized a plasmid-engineering approach to optimize sustained long-term secretion of fluorescent reporters and bacterial biofilm proteins in Nissle E. Coli, a well-classified species prominent in the human microbiome. Five major aspects of sustainable secretion were targeted in the study: production, folding and maintenance, inner membrane secretion, outer membrane secretion, and engineered plasmid retention. Commercially available plasmids were altered using PCR and Gibson Assembly to express recombinant protein tagged for secretion along with other proteins including chaperones, secretion pathway proteins, and plasmid stabilizing proteins. Certain genomic knockouts were also produced to reduce protein degradation and competition for channel access. Growth and protein secretion were measured using OD and fluorescence measurements following 24 hours of growth. Preliminary results demonstrate an inverse relationship between per cell protein secretion and cell viability. Upregulation of outer membrane channel proteins seems to increase secretion while upregulation of inner membrane channel proteins decreases cell viability but improves secretion efficiency. Knockouts that lacked competitors in protein secretion tended to secrete more efficiently than the wild type. Long-term plasmid stability was improved through the usage of a Nissle-specific plasmid backbone that demonstrates high retention. The findings of this study indicate promising methods of promoting sustainable secretion by balancing per cell production and overall growth, providing an instructive framework for engineering high-yield peptide-secreting probiotics for therapeutic application.

Schwann Cell Reprogramming for Peripheral Nerve Injury-Assessing the Effects of Alternatively Activated Schwann Cells

Do Hyun Kim
PRISE Fellow
Biomedical Engineering, 2019

Massachusetts General Hospital, HMS
Advisor: Cathryn Sundback
Mentor: Emmanuel Ekwueme

Mature myelinating Schwann cells (SCs) offer stabilization and insulation for more rapid signal transmission. In the presence of nerve injury, myelinating SCs "reprogram" themselves to a transient, regenerative state referred to as Bungner cells; these cells provide neuroprotective and pro-neurogenic signals for regenerating nerves. This reprogramming occurs after a sequence of events initiated by peripheral nerve injury and may be facilitated by cellular signaling mechanisms including cJUN and PI3K activation. In this project, we examine the signaling mechanisms governing SC reprogramming and explore their roles in neural neuroprotection and neurogenesis *in vitro*. We hypothesize that the PI3K pathway is upstream of the cJUN, so we expect that IGF1-treated SCs will express greater neuroprotective and neuroregenerative capabilities than those of TGFβ1-treated SCs. First, we will alternatively activate SC by treating with soluble growth factors TGFβ1 (cJUN) and IGF1 (PI3K). Next, we will characterize alternatively-activated SCs based on their cell metabolic activity, proliferation, morphologhy, gene expression, and protein expression. Subsequently, we will employ indirect and direct co-culture with motor neurons to test the neuroprotective and neuroregenerative capabilities of the SCs. We expect that our results will allow us to examine how the alternative activation of SC leads to peripheral nerve regeneration. The understanding of the cellular signaling mechanisms governing alternatively activated states of SC can be harnessed to enhance peripheral nerve regeneration after injury.

Biodegradable Polyurethane Inks for 3D-Printing of Biomimetic Tympanic Membrane Grafts

Michelle Walsh
PRISE Fellow
Biomedical Engineering, 2020

School of Engineering and Applied Sciences
Advisor: Jennifer A. Lewis
Mentor: Nicole Black

The tympanic membrane (TM), commonly known as the eardrum, is an exquisite structure that captures and transmits sound. However, its fragile tissue is easily damaged through traumatic injury or middle ear infection, which annually afflicts over 30 million individuals worldwide. TM surgical correction is invasive and imperfect, as over 15% of corrections fail. Additionally, current repair materials, such as temporalis fascia, do not recapitulate the TM's finely-tuned acoustic and mechanical properties, including its organized circumferential and radial collagen fibers that aid in sound conduction. Our group seeks to advance TM repair by 3D-printing biodegradable TM grafts that promote tissue regeneration and do not require invasive surgery. Towards this aim, we are synthesizing biodegradable polyurethane elastomer inks from polycaprolactone-diol (PCL) and 1,4-diisocyanatobutane (BDI). By modifying the BDI:PCL ratio, we optimize ink printability, mechanical properties, and bioresorption. TM grafts are 3D-printed with varying circumferential and radial fibers, utilizing high-operating-temperature direct ink writing. Upon printing, these inks undergo densification hardening, yielding the desired directional fiber stiffness for sound conduction, as well as cellular alignment for long-term TM remodeling. 3D-printed graft morphology is characterized through Fourier transform infrared spectroscopy, atomic force microscopy, and small-angle X-ray scattering. To elucidate cell alignment, grafts are seeded with human neonatal dermal fibroblasts. Preliminary results demonstrate that directional stiffness of polyurethane grafts facilitates fibroblast alignment along the print-path, allowing guided remodeling into custom architectures. Our biodegradable polyurethane inks thus enable the rapid fabrication of novel TM grafts for customizable tissue repair and regeneration.

Optimization of Ionic Liquid CAGE for Drug Delivery

Joel P. R. Balkaran
PRISE Fellow
Biomedical Engineering, 2020

School of Engineering and Applied Sciences
Advisor: Samir Mitragotri
Mentor: Eden Tanner

Many drugs, especially proteins or other sensitive compounds, can only be administered by injections. In the case of chronic illnesses, these injections cause daily discomfort and an increase in patient non-compliance. I am conducting research on non-invasive transdermal drug delivery, specifically with the use of the ionic liquid (IL) choline and geranic acid (CAGE). Through previous research, CAGE has been found to be more effective and safer in transdermal delivery of insulin compared to other industry standard transdermal delivery agents. However, its detailed mechanisms have not been fully fleshed out. This research project attempts to demystify how CAGE works by comparing it to other similar ILs that were chosen based on their ease of synthesis and their similarity to either the geranic acid or the choline molecule. The resulting ILs had various parameters tested alongside that of regular CAGE and the ILs: viscosity, conductivity, water content, 1D and 2D NMR spectroscopy. In addition, the diffusion rates of drugs in the presence of these ILs across the skin were measured using porcine diffusion cells at 37°C. The result of these experiments showed that CAGE (in a 1:2 ratio of cation to anion) is the most effective of the ILs at transport across the skin and preliminary data suggests this is because of the unique interactions of CAGE with skin lipids compared to those of CAGE's individual ions. This information can now be used to determine how to optimize CAGE for each individual drug identified for further study, with the end goal of developing a method for choosing the best CAGE variant for particular drugs.

Modification and Characterization of Nanoparticles for Immune Modulation

Alexandra E. Fehnel
PRISE Fellow
Biomedical Engineering, 2021

School of Engineering and Applied Sciences
Advisor: Samir Mitragotri
Mentor: Anvay Ukidve

Red blood cell hitchhiking technology has enabled efficient delivery of nanoparticles to vascularized organs like the lungs and kidneys while avoiding the mononuclear phagocytic system (liver and spleen). The primary step of this technology involves non-covalent adsorption of nanoparticles. For the most part, attachment of these nanoparticles to the RBC surface appears to be mediated by hydrophobic interaction, but the exact mechanism remains elusive. The aim of this project is to decode the exact mechanism of nanoparticle attachment to the RBC membrane. The first approach taken is using a protein, Ovalbumin, to cap the hydrophobic surface of polystyrene nanoparticles and see the effect of this capping on RBC attachment and subsequent detachment. Increasing the protein concentration on nanoparticle surface decreases the hydrophobicity and makes other interactions like H-bonding and protein-protein interactions mediated by cysteine rich domains more dominant. Our ultimate goal is optimize this protein capping on nanoparticle to achieve higher binding strength (validated by performing in vitro shear study) which will in turn help in increasing the circulation time of nanoparticle that will be further validated by performing in vivo biodistribution experiments.

Static Computed Tomography for Clinical Use

Jamie Caines
PRISE Fellow
Engineering Sciences, 2021

Massachusetts General Hospital, HMS
Advisor: Rajiv Gupta
Mentor: Avilash Cramer

Standard computed tomography (CT) for medical imaging is accomplished through thermionic electron emission with a single source mounted on a rotating gantry to acquire images. The high cost, large size, and high angular momentum precludes the use of such scanners in certain military regions, space stations, and less developed communities. These limitations are unfortunate, given the importance of CT in correctly diagnosing strokes and traumatic brain injuries. Static CT allows for image acquisition without the massive rotating gantry. This project utilizes photocathode emission to accomplish CT imaging, where a UV photon triggers the ejection of an electron from a photoemissive substance. The prototype consists of rapidly pulsable x-ray elements that allow for x-ray generation from multiple points, and its modular design promotes simple disassembly for mobile use. A high voltage (HV) system has been built to power this device. It was rendered safer by installing emergency stop switches and other safety relays to allow for quick and complete shutdown of power. The control interface for the HV system was updated to reflect these changes, and the system now provides multiple ways to stop a running sequence in the event of an emergency. Thus far, the safety updates for the HV system have been completed, and a schematic and circuit diagram initialized. The user manual for the device will include the full HV system schematic for documentation purposes. The successful completion of this project will allow for more widespread use of CT in diagnosing injuries.

Fabricating Therapeutic Loaded Bandages for the Treatment of Chronic Wounds in Diabetic Patients

Evan Thompson
PRISE Fellow
Biomedical Engineering, 2021

School of Engineering and Applied Sciences
Advisor: David J. Mooney
Mentor: Sahar Rahmani

Diabetes mellitus is one of the world's fastest-growing chronic diseases, affecting over 400 million people worldwide. Diabetes impairs the body's ability to properly produce or respond to insulin, leading to a variety of health complications. These include a 25% lifetime risk of developing a diabetic foot ulcer (DFU), a non-healing wound that often leads to lower limb amputations. Current treatments are often insufficient in healing and preventing the recurrence of DFUs. Thus, the goal of our study is to develop therapeutic bandages to enhance the treatment of DFUs by targeting their impaired healing mechanism. In our study, alginate bandages were fabricated according to an established protocol in the Mooney lab and were loaded with one of two pro-healing factors (Substance P or MCP-1). The release kinetics of these factors were analyzed via enzyme-linked immunosorbent assays, and the release profiles of Substance P and MCP-1 from the bandages were optimized to be above the therapeutic levels for both factors at 1.5 (mu)g/ml and 60 ng/ml, respectively, over a 10-day period. The bandages were tested in a murine model to assess their capability for wound healing based on two factors: the size of wounds after a given number of days and the cells recruited via fluorescence-activated cell sorting. These data are currently being analyzed to determine the efficacy of the bandages and their potential to enhance healing in DFUs, improving the lives of diabetic patients.

Tympanostomy Tubes – The Global Spectrum

Stacy Jo
SURGH Fellow
Integrative Biology, 2021

Massachusetts Eye and Ear
Advisor: Aaron Remenschneider
Mentor: Ida Pavlichenko

Otitis media (OM) is the most common ear infection in pediatric patients, affecting approximately 709 million patients worldwide each year. Recurrent acute OM and OM with effusion are both treated by inserting tympanostomy tubes (TTs), in order to drain fluid, improve ventilation, and allow for local antibiotic treatment within the middle ear. However, patients in areas with the highest OM prevalence rates who could benefit the most from this treatment are not receiving the medical care they need due to low resource settings and high costs of surgical implants. By performing extensive literature review on the global prevalence of otitis media itself, a foundation of knowledge was built regarding the areas where TTs were most valued in treatment or most needed. Then additional review on TT features and geometries was conducted, forming a current record of commercially available models of the most widely used TTs, their selection criteria/guidelines and potential complications. While this process is ongoing, initial findings revealed not only a lack of international consensus of optimal TT designs or materials, but also a lack of fundamental guidelines for treating OM itself (with outdated documentation collected from 1980-2012). Therefore, recent records of OM prevalence in developing nations must first be consolidated with clear representation of TT placement techniques, their rate of placement, and the procedure cost. This research will provide a superior understanding of the common challenges in TT usage in the global context and contribute to creating functional, cost-efficient TTs that will reach those in greatest need of them.

EEG Signatures of Sevoflurane General Anesthesia in Children Age 0 to 3 Years

Angela Kim
PRISE Fellow
Neurobiology, 2021

Boston Children's Hospital, HMS
Advisor: Charles Berde
Mentor: Laura Cornelissen

General anesthetics generate specific brain oscillations in the electroencephalogram (EEG) that provide important information about a patient's level of surgical anesthesia. Phase-amplitude coupling indicates how low-frequency oscillations modulate high-frequency oscillations and provides a useful metric for anesthetic depth. Although the adult EEG is characterized by slow-delta oscillations (0.1-4Hz) that modulate frontal alpha oscillations (8-12Hz) during loss of consciousness, little is known in children. Current brain monitoring systems inadequately reflect the extent to which a pediatric patient is anesthetized because they were developed using adult brain dynamics. Our aim was to characterize frontal EEG signatures in children under sevoflurane general anesthesia and how these signatures change with age. Multielectrode EEG signals were recorded from children aged 0-3 years old receiving sevoflurane general anesthesia for elective surgery. Frontal electrodes were selected (F3, F4, F7, F8). Five-minute artifact-free epochs were identified during steady-state anesthesia ($\sim$2.6% end-tidal sevoflurane). We used multitaper-spectral methods to analyze the power of oscillating frequencies as a function of time, and we applied phase-amplitude coupling methods to establish the relationship between slow-wave and alpha oscillations. Spectral analysis confirmed that slow oscillations were present across all ages, while alpha oscillations emerged at 3-4 months of age. Preliminary results indicated that higher frequencies such as alpha are coupled to slow oscillations at surgical levels of anesthesia, and ongoing analysis aims to investigate the relationship between phase-amplitude coupling and anesthetic depth. These findings may help guide development of pediatric brain monitoring tools, creating more sensitive systems for better anesthetic dosing.

CHEMICAL AND PHYSICAL BIOLOGY

Unraveling Cellular and Tissue-Wide Complexity through Synthetic and Natural Electrophysiological Systems

Rajath Salegame
PRISE Fellow
Chemistry and Physics, 2021

Chemistry and Chemical Biology
Advisor: Adam Cohen
Mentor: Harry McNamara

A cell is an electrical system that modulates its membrane voltage by allowing ions to flow across a lipid bilayer in response to external stimuli. These voltage changes form complex patterns in space and time, and can modulate downstream signaling pathways. However, the role of electrical signaling in the development of skeletal myocytes (muscle) is currently unknown. Specifically, we are interested in the spatiotemporal pattern by which membrane voltage transitions from 0 mV in stem cells to -90 mV in myocytes. Earlier experiments in a simple model system suggest that electrical polarization may occur in a stepwise fashion, spreading as a domain wall through the tissue. To test this hypothesis, we are performing optogenetic experiments in cultured induced pluripotent stem cells (iPSCs) as they differentiate into skeletal myocytes. Additionally, we are optimizing a cAMP mapping assay to test whether electrical patterns in tissues can cause patterns in the spatial distribution of cAMP. These studies provide deeper insight into how electrical signaling can create complex cellular and tissue-wide behavior.

mTOR's Involvement in Contralateral Cell Cycle Re-Entry in Axolotls

Gabriel Dardik
PRISE Fellow
Chemistry, 2021

Brigham and Women's Hospital, HMS
Advisor: Jessica Whited
Mentor: Kimberly Johnson

A major focus of medical research is discovering a method to stimulate limb regeneration in humans. Since axolotl salamanders can regenerate entire limbs after amputation, they are a promising animal model to study limb regeneration. Past research has indicated that post-amputation, a systemic signal induces cells all around the body to re-enter the cell cycle, before regenerative activity is focused to the site of injury. It is known that mTOR, a kinase that regulates cell growth and proliferation, is systemically upregulated after an amputation event. Our goal is to investigate mTOR's connection to the systemic signal pathway, and determine whether it is upstream or downstream of the signal causing contralateral cells to re-enter the cell cycle. We injected axolotls with rapamycin (an mTOR inhibitor), amputated their limbs, and harvested the stumps and remaining limbs a week later. We then performed a Western blot on tissue lysate to confirm the knockout of mTOR, which we verified with a ps6 stain on cryosectioned tissues, and we will perform an EdU stain to determine if cells were actively dividing. If EdU positive cells are present in the tissue in the absence of mTOR, this will suggest that mTOR is downstream of the "systemic activator" and is not necessary to stimulate cell cycle re-entry. If there is a decrease in EdU+ cells, this suggests that mTOR is likely necessary to stimulate cell cycle re-entry, and is upstream of the "systemic activator." Determining the role of mTOR in relation to contralateral cell cycle re-entry will help elucidate the mechanisms mediating regeneration in axolotls. Since this pathway is conserved in humans, it may be a first step towards stimulating human limb regeneration.

Employing Locally Generated DNA Damage to Probe 3D Genome Architecture

Eric Zhou
PRISE Fellow
Comparative Literature and English, 2020

Chemistry and Chemical Biology
Advisor: Brian Liau
Mentor: Allison Siegenfeld

Although the linear sequence of the human genome is well-characterized, its 3D structure in the nucleus is still difficult to ascertain. In this study, we developed methods that employ locally generated singlet oxygen ($^1O_2$), a highly reactive, excited state of molecular oxygen, to strategically induce oxidative DNA damage in a spatially-dependent manner. The location of the damage was then determined to yield information on DNA's 3D positioning in the nucleus. $^1O_2$ oxidizes guanine (G) to form 8-oxoguanine (8-oxoG) within a limited diffusion radius inside the nucleus. Taking advantage of this property, we localized oxidative DNA damage to the nuclear lamina, the fibrillar meshwork coating the inner nuclear envelope, to study genomic structure around the lamina. First, dibromo-fluorescein, a small molecule photosensitizer that generates $^1O_2$ upon irradiation with blue light, was covalently linked to lamin B1, a nuclear lamina protein. The cells were fixed, irradiated with blue light and labelled with antibodies against 8-oxoG and lamin B1, which were visualized using immunofluorescence microscopy. The results show that 8-oxoG is formed near the source of $^1O_2$ production at the nuclear periphery, demonstrating that our approach is feasible. Since 8-oxoG is mutagenic, leading to G to thymine (T) mutations after DNA replication, our current goal is to determine the localization of the damage by high-throughput sequencing while dynamically visualizing 8-oxoG formation in living cells using fluorescent microscopy. We anticipate that this dual sequencing & microscopy-based approach will be applicable to investigating higher-order chromatin structures in addition to the nuclear lamina.

Production and Catabolism of Essential Micronutrients by Gut Bacteria as It Relates to Childhood Malnutrition and Environmental Enteric Dysfunciton

Hilina Woldemichael
PRISE Fellow
Molecular and Cellular Biology, 2021

Chemistry and Chemical Biology
Advisor: Emily Balskus
Mentor: Lauren Rajakovich

Previous studies have shown bacteria to synthesize and degrade vitamins and other essential micronutrients. Children suffering from malnutrition and environmental enteric dysfunction (EED), a disease characterized by malabsorption of nutrients, stunted growth, and gut membrane permeability, lack adequate levels of these micronutrients. We hoped through this project to elucidate the microbiome's effect on treatment for EED and child malnutrition. We focused on folate, a vitamin essential for proper infant development, and niacin, a precursor to nicotinamide adenine dinucleotide (NAD), a compound involved in several metabolic processes. To investigate the ability of bacteria to produce folate, we transformed cultures of infant gut bacteria, *Bifidobacterium infantis*, and *Bifidobacterium adolescentis* with a plasmid coding for pabB and pabC, which are proteins thought to be responsible for folate production. We monitored the activity of the pab proteins and amounts of folate produced by the bacteria in folate-deficient media *in vitro*. To investigate niacin catabolism in bacteria, we cultured *Pseudoflavonifractor capillosus*, a gut bacterium with genes similar to those of niacin-catabolizing bacteria, with niacin. We then monitored bacterial growth and the degradation of niacin. Thus far, *P. capillosus* has successfully been propagated in minimal media and the pab genes have been isolated from *Bifidobacteria*. If our results support that gut bacteria both create and break down essential nutrients, there will be potential to more effectively treat EED and malnutrition. Existing therapeutics yield only short-term improvements on patient health, so there is a need for long-term alternatives to be discovered.

Optimization of an Improved Synthesis of the Minimalist Tag, a Diazirine Alkyne Tag for Measurement of Small Molecule-Protein Interactions

Carter Nakamoto
PRISE Fellow
Chemical and Physical Biology, 2021

Chemistry and Chemical Biology
Advisor: Christina Woo
Mentor: Hope Flaxman

The Woo Lab has developed Small molecule Interactome Mapping by Photo-Affinity Labeling (SIM-PAL), a technique that utilizes mass spectrometry to characterize the interactions between small molecules and the proteome by identifying specific binding sites on individual proteins. This method involves attaching the "minimalist tag" containing a diazirine, which will crosslink to nearby proteins when exposed to UV light, and an alkyne, which can undergo click chemistry, to the molecule of interest. The small molecule with the embedded tag is incubated with live cells and binding interactions are captured by photolysis. Subsequently, click chemistry allows the attachment of cleavable biotin, which can be pulled down to facilitate isolation, and specific stable isotopes, which can be clearly identified via mass spectrometry. This project involved optimizing a new synthesis of the minimalist tag with the potential to prepare it in two steps from commercially available materials in high overall yields, as compared to the synthetic route developed by Yao and co-workers (six steps, 70% yield). Reaction conditions, including temperatures, solvents, equivalences, workups, mixing times, extractions, and purifications, were varied to optimize the new synthetic route. Results were monitored and compared against synthetic standards using thin layer chromatography, mass spectrometry, and nuclear magnetic resonance. Optimization of the minimalist tag will make access to small molecules for the SIM-PAL workflow more efficient, enabling additional analysis of the protein interactome. This will improve our understanding of a broad range of cellular pathways in addition to helping to advance drug discovery and development.

Developing a High-Affinity Binding Interaction between the Anthelmintic Bt Protein Cry5B and the Nematode Cadherin CDH-8

Simon Shen
PRISE Fellow
Chemistry and Physics, 2020

Chemistry and Chemical Biology
Advisor: David Liu
Mentor: Mary Morrison

Helminths are worm-like parasites that currently infect over 1.5 billion people worldwide, causing severe iron-deficiency anemia. Many existing small-molecule anthelmintic treatments are unsafe for pregnant women or have become ineffective due to helminth resistance, creating a need for the development of alternative treatments. Recent studies demonstrated that the cadherin CDH-8 in helminths acts as a receptor for the *B. thuringiensis*-derived crystal protein Cry5B, which kills helminths without harming humans. In this work, we aim to use phage-assisted continuous evolution (PACE) to evolve variants of Cry5B with high binding affinity to CDH-8 so that it can be given to humans in a single dose. PACE was previously used to successfully evolve a similar protein-protein binding interaction between a widely-used agricultural pesticide and an insect cadherin to overcome resistance. PACE associates phage propagation with a biological function of interest, such as protein-protein binding, to allow for rapid and continuous selection of high-affinity binders. We must first identify fragments of CDH-8 that are compatible with the PACE environment: they must be well-expressed and soluble in *E. coli* and exhibit modest binding activity with Cry5B. We found cadherin repeat domains 7-8 of CDH-8 in *C. elegans* to be a promising fragment with up to two-fold higher Cry5B binding affinity compared to negative controls. Using homology to this *C. elegans* fragment, we identified and tested CDH-8 fragments from other helminth species. This diverse set of CDH-8 fragments will be used as protein-binding targets in PACE in order to develop Cry5B into a potential robust anthelmintic drug.

Optimizing Enucleation of Erythroid Progenitor Cells for Malaria Research

Maria Jose Acosta Robayo
SURGH Fellow
Sociology, 2020

School of Public Health
Advisor: Manoj Durainsingh
Mentor: Estela Shabani

Malaria remains a world-wide health concern causing 500,000 deaths annually. Clinical disease is caused when *Plasmodium* parasites invade and develop within red blood cells (RBCs). A major goal in global health research is identifying the RBC proteins required for *Plasmodium* invasion and growth, which could lead to novel therapeutics. To identify these proteins, we perform genetic modifications in erythroid progenitor cells, since mature RBCs lack a nucleus. A prerequisite for the success of this method is a homogenous erythroid cell line that can be genetically modified and is physiologically representative of the RBCs infected *in vivo* by*Plasmodium*. We have generated an immortalized erythroid cell line (ejRBCs) which shows normal differentiation, but low enucleation rates (2-10%). Previous work revealed that immortalization in early erythropoiesis and differentiation on stromal cells improves enucleation. My research is focused on determining the conditions needed to increase efficiency of terminal differentiation and enucleation in ejRBCs. Our first method used limiting dilution to select single-cell clones from the bulk EJs and identified those with better enucleation. We then tested various differentiation conditions such as (1) media composition, (2) timing of media changes, and (3) co-culturing EJs on a stromal cell line to better mimic the physiological niche during differentiation. Preliminary results show that differentiating EJs on stroma and low seeding densities improves enucleation. By improving the enucleation rate of EJs, my work will provide more homogeneous and physiologically relevant cells to study *Plasmodium* and RBC biology, thereby contribute to the global effort of malaria eradication.

Maternal Vaccination to Boost Neonatal Immunity

Francesca Noelette
PRISE Fellow
Molecular and Cellular Biology, 2019

Ragon Institute
Advisor: Galit Alter
Mentor: Madeleine Jennewein

The placenta is crucial to the health of a growing fetus. All necessary nutrients, even antibodies, travel across the placenta from mother to child. This project seeks to determine the viability of vaccinating pregnant mothers to boost immunity in neonates. Our goal requires an understanding of antibody transfer across the placenta and vaccine response in pregnant women. Knowing that cytotoxic antibodies cross the placenta to the fetus in higher quantities than other types of antibodies, immunofluorescence was conducted on placenta samples to determine the mechanism of this crossing by identifying the receptor that could transfer highly functional cytotoxic antibodies and was most abundant on the maternal side of the placenta. We also sought to know whether vaccine response in pregnant women led to production of antibodies that could bind the abundant receptors. Otherwise, the antibodies would not transfer at high enough quantities to provide the neonate with immunity. Therefore, plasma from pregnant women vaccinated for influenza was analyzed to determine the reactivity and type of their antibodies. Preliminary results indicate that FcgRIII receptors allow for the high transfer of cytotoxic antibodies, but research on the effect of the influenza vaccine on antibody production in pregnant women is still incomplete. Nonetheless, if vaccines that encourage the production of cytotoxic antibodies or antibodies that bind FcgRIII in pregnant women can be developed, it would be possible to provide greater immunity to neonates, making them less vulnerable to infectious disease during the first year of life.

Identification of Pancreatic Ductal Adenocarcinoma (PDAC) Tumor Antigen-Specific Nanobodies for Diagnosis and Treatment

Ralph Estanboulieh
PRISE Fellow
Chemical and Physical Biology and Computer Science, 2021

Boston Children's Hospital, HMS
Advisor: Hidde Ploegh
Mentor: Andrew Woodham

Pancreatic ductal adenocarcinoma (PDAC) accounts for 85% of pancreatic cancers and is one of two cancers for which the mortality rate in the US has risen since 1990. This reflects the ineffectiveness of current early-stage PDAC diagnostics and treatment. Antibodies (Abs) or their antigen-binding fragments are used as functional units of different immunotherapies, including chimeric antigen receptors (CARs). However, antibodies that recognize PDAC with high affinity are lacking. To overcome these challenges, we utilize camelid-derived variable fragments of heavy-chain Abs (also called nanobodies or VHHs) as the functional units for different cancer immunotherapies. VHHs are the smallest Ab fragments that retain antigen-binding capabilities. Their small size ensures superior tissue penetration compared to Abs and provides desirable pharmacokinetic properties. Moreover, VHHs are easily engineered for a range of applications, many of which the lab has pioneered. Alpacas were immunized with cell homogenates from human and mouse pancreatic organoids, creating VHH phage display libraries to be used for the identifying and characterizing PDAC tumor antigens. We are currently screening these libraries with various panning methods, some that enrich for membrane proteins via binding their glycosylated side chains to the lectin Concanavalin A (ConA) and others that optimize PVDF membrane-based panning to maximize the number of phages selected and cloned. The resulting VHHs will be produced recombinantly using simple bacterial systems, and then functionalized by appending different components to them like chemokines, radio-isotopes, drugs, and enzymes, as well as incorporating them in CAR -T cell systems for the diagnosis and treatment of PDAC.

Developing a Hydrogen-Specific In-Situ Mass Spectrometer (ISMS)

Andrea Rodriguez-Marin Freudmann
PRISE Fellow
Mechanical Engineering, 2020

Chemical and Physical Biology
Advisor: Peter Girguis
Mentor: Daniel Hoer

Hydrogen is an important part of microbial life in hydrothermal vents, as it provides valuable information about the processes that happen in this unusual marine environment. Mass spectrometers usually detect hydrogen accurately, but when ionized, the hydrogen in water causes the in-situ mass spectrometer (ISMS) to detect ions at mass 2 (hydrogen) which does not reflect the actual hydrogen concentration. Palladium (Pd) only allows small molecules to diffuse across it, and so first seems to be the perfect material for the membrane used in the ISMS, since only hydrogen can penetrate the instrument. Testing showed that dissolved hydrogen is unable to pass through the Pd membrane. Thus, a new design was tested, which operates using a double membrane: PDMS (polydimethylsiloxane) first, which allows gases in seawater to pass through, and Pd as the second, which should allow gaseous H2 diffuse across it. Another potential solution was to use a more sensitive mass spectrometry gauge, so the Simplicity Solutions VQM 830 was tested to see if it allowed more hydrogen to be visible. While the current ISMS did not create a vacuum good enough to use the VQM, adjusting the inlet system may allow the VQM to function. These modifications to the ISMS will allow a more accurate study of hydrogen concentration over time and location around hydrothermal vents, making it possible to better detect its effect on the marine environment.

Transposon Sequencing Reveals Strain-Specific Genes Required for *in vitro* Growth in *Mycobacterium abscessus* Clinical Isolates

Maria Altshuller
SURGH Fellow
Chemical and Physical Biology, 2020

School of Public Health
Advisor: Eric Rubin
Mentor: Chidi Akusobi

Mycobacterium abscessus is a type of nontuberculous mycobacterium that can cause pulmonary infections, particularly in immunocompromised or injured patients. Since *M. abscessus* is highly antibiotic-resistant and fast-growing compared to other mycobacterium species, and since there is a high rate of genetic variation between its different strains, *M. abscessus* infections are often difficult to treat. In this study, we put seven strains of *M. abscessus* through transposon sequencing (TnSeq), a technique in which transposon insertions are used to characterize the bacterium's genome. TnSeq involves inserting transposons into sites throughout many bacterial genomes and determining which genes are essential by counting the number of transposons inserted into each site: an essential gene would have few to no insertions, as these would disrupt the gene's essential function; a non-essential gene would have many insertions, as its function is not crucial to the bacteria's survival. Performing TnSeq on different strains of *M. abscessus* revealed genes that are more essential in some strains than others. We will select a few of these genes for more in-depth analysis, which will involve investigating how the differential essentiality of these genes affects the phenotypes of the different strains. Since TnSeq has never been used on *M. abscessus*, this analysis could produce a better characterization of the differences between *M. abscessus* strains, which may lead to more specialized treatments being used on different strains.

Causal Variants for Circadian Rhythms and Sleep and Their Functional Consequences in Human Cellular Models

Raymond So
PRISE Fellow
Chemical and Physical Biology, 2021

Massachusetts General Hospital, HMS
Advisor: Richa Saxena
Mentor: Jacqueline Lane

Though recent advances in genetic technology have allowed for the identification of many genetic variants associated with sleep-wake regulation, the identification of the causal variants and an understanding of their functional biology have not previously been pursued. In this project, the novel Massively Parallel Reporter Assay (MPRA) will be employed to test around five hundred genetic variants for their influence on the gene expressions of any of 21 target genes at the PAX8 and HCRTR2 loci. The PAX8 gene belongs to a family of genes that control tissue and organ formation during embryogenesis; the HCRTRT2 gene encodes for the sleep-wake regulating orexin receptor, which is a target for the insomnia drug Suvorexant. First, to assess allele-specific effects on reporter gene transcription, oligonucleotides to test these variants will be synthesized and transfected into the U2OS and neuronal cell lines. Genetic variants that reliably affect reporter gene transcription will be identified. Second, to understand the effect of these identified variants on cell-autonomous circadian rhythms, the identified variants will be introduced directly into the U2OS cell line via CRISPR-Cas9 gene editing technology, and gene expression of a luciferase reporter under the control of a circadian promoter from the gene BMAL1 will be used to measure changes in circadian rhythm timing, intensity, and length. These two experiments will identify the causal variants at these two loci, an important finding for understanding sleep-wake regulation and a crucial first step for creating a potential clinical cure for sleep disorders.

DNA Polymerization Influences the Homology Dependent Stability of Strand Exchange Products

Daniel Lu
PRISE Fellow
Philosophy and Physics, 2020

Physics
Advisor: Mara Prentiss

Researchers believe that in bacteria, the recombinase RecA must find a matching region of double-stranded DNA (dsDNA) to use as a template for the accurate repair of broken single-stranded DNA (ssDNA). Joining shorter, accidentally matching regions may cause undesirable and even fatal DNA arrangements. Despite decades of *in vitro* experiments, the *in vitro* accuracy of this search for matching dsDNA remains consistently and significantly worse than *in vivo* accuracy. In addition to the binding of the RecA and broken ssDNA to the dsDNA, we propose that considering the previously unexamined probability of progression of the *in vivo* polymerase DinB may improve *in vitro* accuracy. We mixed RecA with ssDNA to create RecA-ssDNA filaments, then introduced labeled dsDNA and other reagents like DinB to the filaments to facilitate recombination attempts with and without DinB and with different dsDNA lengths, label positions, and matching region lengths. The fluorescence of the dsDNA labels was measured to indicate the success and stability of binding to the dsDNA over time. Preliminary results show that the presence of DinB increases the stability of binding to the dsDNA and makes the proportional increase in stability from shorter to longer matching regions greater. This increase in differentiation suggests that DinB polymerase progression is more sensitive to homology (i.e. matching region) length than RecA-ssDNA filament binding alone. Thus, DinB polymerization likely plays an important role in homology recognition in bacterial cells, increasing both its stability and its accuracy.

CHEMISTRY

Permeability and Resistivity Tests for Flow Battery Cell Membranes

Winston Michalak
PRISE Fellow
Electrical Engineering, 2021

School of Engineering and Applied Sciences
Advisor: Michael Aziz
Mentor: Diana De Porcellinis

As renewable energy sources have become more frequently used to supply the power demands of modern society, flow batteries have become increasingly favored for their power efficiency and longevity. Flow batteries are comprised of an electrochemical cell connected to two electrolyte storage tanks, one containing positive electrolyte and the other containing negative electrolyte. The electroactive compounds within the electrolytes interact via ion exchanges across a semipermeable membrane that keeps the positive and negative electrolytes separated and prevents electrons from flowing between the electrolytes, thereby forcing them to flow through a wire positioned outside of the cell. The effectiveness of the membrane rests largely on its ability to keep the positive and negative electrolytes separated. To test the permeability of the membrane, ultraviolet-visible spectrophotometry on crossover cells and ion exchange capacity tests by titration were employed. The baseline commercial membrane for this application, FumaSep E-620 K, demonstrated excellent electrochemical stability and low permeability with many electrolytes, making it a favorable membrane to use. However, its resistance was higher than ideal. Alternative membranes are being examined to evaluate their resistivities and their permeabilities to important electrolyte molecules. Preliminary results indicate that polybenzimidazole membranes have very high crossover rates with most electrolytes. Other commercial membranes, including Nafion and Selemion membranes, showed varied results depending on the electrolytes used.

Implications of *Epipremnum aureum* and *Quercus rubra* on OVOC uptake emissions

Margaux Winter
PRISE Fellow
Chemistry, 2021

Chemistry and Chemical Biology
Advisor: Frank Keutsch
Mentor: Joshua Shutter; Joshua Cox

Oxidized volatile organic compounds (OVOCs) have many atmospheric impacts on both climate change and human health. Despite previous expectations that plants facilitate the uptake and deposition of OVOCs from the gas phase, new research suggests that plants can also emit OVOCs. Surface glands on plant leaves have the ability to store and release volatiles, while within-leaf reactions of OVOCs can oxidize organic compounds. To understand the bidirectional flux and chemical processing of OVOCs occurring within leaves and on leaf surfaces, our lab will expose *Epipremnum aureum* and *Quercus rubra* to formaldehyde and isoprene hydroxy hydroperoxide (ISOPOOH), respectively. Through our experiments with formaldehyde, the most simple and abundant carbonyl in the atmosphere, we hope to determine whether plants are sources of formaldehyde by determining the plant's compensation point (i.e., when the net flux of formaldehyde is zero). Previous research suggests that interactions between plants and ISOPOOH, a main OVOC in pristine conditions, act as new sources of OVOCs that are not due to gas-phase chemistry. Thus far, we have built the experimentation chamber, the electronics board to monitor these experiments, and characterized initial conditions of the chamber. Sensors and the electronics board were implemented to control experimentation conditions, from CO_2 concentration and relative humidity to the flow of OVOCs into the chamber. Leaf area (used in calculating photosynthetic measurements) was accurately determined using the Python-based program, Easy Leaf Area. Additional work was conducted on the laser-induced fluorescence instrument for formaldehyde detection, to improve the precision and accuracy of its measurements. This research will uncover the formation and deposition of OVOCs, providing data to increase the precision of atmospheric models.

COMPARATIVE LITERATURE

Catalogue of Uncommon Things: Scientific Romanticism in the Poetry of Keats

Piper Winkler
SHARP Fellow
Comparative Literature, 2021

Houghton Library
Advisor: Emilie Hardman

Modern analyses of Keats's poetry identify the author as a primary actor within the Romantic literary movement of the early nineteenth century, generally excluding considerations of the poet's extensive training within the field of medicine. As a licensed apothecary and student at Guy's Hospital in London, Keats engaged with scientific epistemology as a matter of course, so that a review of his poetry reveals a complex rapport between the disciplines of poetics and scientific philosophy. This study explores that rapport by linking four procedures central to nineteenth-century surgeries—the biopsy, anaesthesia, wound-dressing, and the autopsy—to their aesthetic manifestations in Keats's later poetry. Executed through close readings of Keats's poems and a survey of contemporaneous scientific and poetic literature, the connection of these scientific concepts to their influences upon Romantic verse reveals Keats's use of poetic form and philosophy as a method of overcoming creative limits imposed by trends of positivism within the medical world. Notable examples include Keats's theory of negative capability—the refusal to recognize scientific reason as the sole source of intellectual legitimacy—and the challenge to poetic form as an anatomical structure in the ode "To Autumn." These findings suggest that Keats incorporated scientific and medical themes into his poetic work as a means of representing the struggle between Romantic creativity and modern rationalism. Considering these results in the context of contemporary poetry, it is evident that Keats served as an early interlocutor between scientific and poetic philosophy, establishing the body as a site of intersection between medical study and poetic imagination.

COMPUTER SCIENCE

Transactional and Concurrent Data Structures

Zachary Yedidia
PRISE Fellow
Computer Science, 2021

Computer Science
Advisor: Eddie Kohler

As CPU manufacturers find it increasingly difficult to improve single core performance, they have been adding more cores in an effort to take advantage of parallelism, where multiple instructions can run at the same time, to increase overall performance. However, concurrent programming is difficult because simultaneous access to shared memory can cause undefined behavior, so programmers must be careful to order instructions that access shared memory locations. Transactional memory systems simplify concurrent programming by allowing blocks of instructions to run atomically, allowing programmers to avoid the use of explicit locks. One such system, STO (Software Transactional Objects), is attractive because it is implemented at the data structure level, rather than the level of individual memory words. STO facilitates specialized optimization for each data structure, thus improving performance over other kinds of transactional memory systems, and makes possible radically fast databases and other concurrent systems. Using STO, we are implementing and benchmarking a transactional version of a recently invented data structure called the Adaptive Radix Tree (ART), which we hope will provide better performance than the existing masstree data structure, which currently serves as the core of STO. The ART is promising because it combines comparable performance to hash tables, ordered data storage, and space efficiency. However, since ART is not built for transactional execution, naive integration with STO could slow it down. Early results indicate that the transactional ART is close to the speed of the original ART. We are still investigating which locking strategy provides the best performance.

Exploring Collaboration with Human-Computer-Human Interaction Interfaces

Yong Li Dich
PRISE Fellow
Computer Science and Folklore and Mythology, 2019

Graduate School of Education
Advisor: Bertrand Schneider

As technology continues to become more interwoven into our lives, there is an increased interest in analyzing its evolving effect on human interactions and abilities, such as 21st century skills such as the collaboration, creativity, critical thinking, and problem solving taught in schools. This paper is a continuation of a study on collaborative processes through physiological sensors. In the previous study, Empatica E4 wearable wrist bands were used to collect data from oscillatory systems such as the galvanic skin response (GSR) or electrodermal activity (EDA). The EDA values were picked as the physiological measure for synchrony to analyze for behavioral processes and identify markers of productive collaboration. The data came from 42 pairs (N=84) of participants who had limited to no coding experience to more accurately gauge the learning process of coding a robot. Participants were asked to program a Gogo widget robot to solve a variety of mazes. We explored four different index values for measuring how close a dyad's physiological signal values are, otherwise known as physiological synchrony: Signal Matching (SM), Instantaneous Derivative Matching (IDM), Directional Agreement (DA), and Pearson's Correlation (PC). Overall, we found PC to be positively associated with learning gains and DA with collaboration quality. With this insight, we moved to generalizing patterns by analyzing the characteristics of PC and DA to see what these measures could tell us about the qualities they were highly correlated with through video and graph observations done in parallel. Next, we plan to stream EDA values in real time and design different interfaces to depict these measures of physiological synchrony to analyze how this information could intervene with or affect human-to-human behavior. We will end by discussing other implications for measuring collaborative processes through physiological sensors.

Optimal Las Vegas Approximate Near Neighbors in ℓ_p

Alexander Wei
PRISE Fellow
Computer Science and Mathematics, 2020

School of Engineering and Applied Sciences
Advisor: Jelani Nelson

In the (r, cr)-*approximate near neighbors* (ANN) problem, one is given a database $\mathcal{D} \subset \mathbb{R}^d$ of n points and asked to construct a data structure which, given a query point $q \in \mathbb{R}^d$, returns a point in $\mathcal{D}$ within distance cr of q if there exists a point in $\mathcal{D}$ within distance r of q. Approximate near neighbor search has applications to a diverse set of areas in computer science, including machine learning, computer vision, and document retrieval. For these applications, the distance metric is an ℓ_p norm.

We show that high-dimensional approximate near neighbor search can be solved in a Las Vegas fashion (i.e., without false negatives) for ℓ_p ($1 \leq p \leq 2$) while matching the performance of optimal locality-sensitive hashing. Specifically, we construct a data-independent Las Vegas data structure with query time $O(dn^\rho)$ and space usage $O(dn^{1+\rho})$ for (r, cr)-ANN in $\mathbb{R}^d$ under the ℓ_p norm, where $\rho = 1/c^p + o(1)$. Furthermore, we give a Las Vegas locality-sensitive filter construction for the unit sphere that can be used with the data-dependent data structure of Andoni et al. (SODA 2017) to achieve optimal space-time tradeoffs in the data-dependent setting. For the symmetric case, this gives us a data-dependent Las Vegas data structure with query time $O(dn^\rho)$ and space usage $O(dn^{1+\rho})$ for (r, cr)-ANN in $\mathbb{R}^d$ under the ℓ_p norm, where $\rho = 1/(2c^p - 1) + o(1)$.

Our data-independent construction improves on the recent Las Vegas data structure of Ahle (FOCS 2017) for ℓ_p when $1 < p \leq 2$. Our data-dependent construction does even better for ℓ_p for all $p \in [1, 2]$ and is the first Las Vegas ANN data structure to make use of data-dependent approaches. We also answer open questions of Indyk (SODA 2000), Pagh (SODA 2016), and Ahle by showing that for ANN, Las Vegas data structures can match state-of-the-art Monte Carlo data structures in performance for both the data-independent and data-dependent settings and across space-time tradeoffs.

Web-Based, Large-Scale Volume Rendering

Sushant Achawal
PRISE-Emmanuel Fellow
Information and Computer Engineering, 2019

School of Engineering and Applied Sciences
Advisor: Hanspeter Pfister
Mentor: Johanna Beyer

The collection of image data from intricate networks of neurons in the brain has increased recently with developments in MRI and CT technology. The data consists of several adjacent 2D slices which can be combined to show a 3D volume using volume rendering. Viewing this data interactively, once segmented, allows neuroscientists to gain deeper understandings about brain function and its relation to particular neural pathways. However, the data can be as large as petabytes in magnitude which requires complex algorithms and hardware capable of parallel graphical processing in order to be rendered in real-time. This complexity greatly limits the type of device on which the data can be viewed. To facilitate the viewing of such data, we proposed a client-server solution in which a web application running in the browser can act as a user interface. The web-client is designed to support volume rotation, clipping, and transfer function editing by the user while all volume rendering algorithms run on the server equipped with the required hardware capabilities. The server uses WebSockets in C++ with the web application running in JavaScript. This solution should make volume rendering an accessible tool to help scientists while also allowing doctors to view MRI and CT data.

Curricle Project at metaLAB

Sinead Danagher
SHARP Fellow
Undeclared, 2021

metaLAB at Harvard
Advisor: Matthew Battles
Mentor: Jessica Yurkofsky

There is a wealth of information stored within the course catalogs of higher institutions of learning. Unfortunately, this information is not made readily accessible or digestible for students, faculty and others. To solve this disconnect, metaLAB is designing new course exploration and selection software for Harvard University affiliates. The project will culminate in the release of this software as part of a fully-developed website called Curricle, which will provide historical data and narratives mined from the course catalogs as well as a new dashboard through which students can explore courses and plan their academic paths. I worked specifically on the creation of this new dashboard, which will augment the existing website with tools that assist with academic planning for current students such as interactive academic trajectory visualizations. The development of this feature required me to research software precedents set by other universities, comparable software outside of academia, data visualization techniques, and the experiences and preferences of Harvard students regarding course selection as determined through interviews and surveys. The information gained from this research was used to help a team of visual technologists, designers and fellows improve the existing version of Curricle by expanding the historical data visualizations and student planning toolkit. This will enhance the preexisting academic advising arsenal provided to Harvard students and aid future users navigating the treasure trove of data buried in Harvard's course catalog.

Pairwise Independent Random Walks can be Slightly Unbounded

Shyam Narayanan
PRISE Fellow
Mathematics, 2019

School of Engineering and Applied Sciences
Advisor: Jelani Nelson

The expected value of the maximum distance of any 4-wise independent random walk on a line over n steps is known to be $O(\sqrt{n})$. This result and generalizations of it have been extremely beneficial in the analysis of streaming algorithms, since there exist k-wise independent random walks that can be stored in far fewer than n bits of space for small values of k, and variants of k-wise independent random walks have been valuable for tracking certain data. Our findings demonstrate that 4-wise independence is required by demonstrating a pairwise independent random walk with steps uniform in ± 1 and expected maximum distance $\Omega(\sqrt{n}\log n)$ from the origin. We also show that this bound is tight for the first and second moment: the expected maximum squared distance of a 2-wise independent random walk is always $O(n\log^2 n)$. Also, for any even $k \geq 4$, we show that the kth moment of the maximum distance of any k-wise independent random walk is $O(n^{k/2})$. The previous two results generalize to random walks tracking insertion-only streams and provide higher moment bounds than currently known. We also prove a generalization of Kolmogorov's maximal inequality by showing an equivalent statement that requires only 4-wise independent random variables with bounded second moments. These results bound the maximum distance of a random walk for various levels of independence between steps, and may have applications to probability theory and streaming algorithms.

Bolstering the Effectiveness of Corporate Compliance Programs Through Chatbots

Hyeon-Jae Seo
PRIMO Fellow
Applied Mathematics, 2020

Harvard Business School
Advisor: Eugene Soltes

As the criminal liability for corporations and their employees increases, so does the importance of adopting corporate compliance programs. Corporate compliance programs serve three crucial roles for corporations: preventing misconduct, detecting misconduct, and aligning corporate activities with regulation. Such programs can range from broad-ranging ethical principles to specific policies guiding employee behavior. For example, many organizations provide a code of conduct outlining proper and legal behavior for their employees. Although codes of conduct are common, research on how well employees understand and adhere to such codes is limited. Preliminary work suggests that they are not especially effective, as information contained in static codes of conduct are not easily retrievable. Furthermore, corporations have no way to understand if and how their employees engage with the codes.

In this project, we are developing a standalone, web-based chatbot that employees can use to ask questions pertaining to their company's code of conduct. In response, employees receive pertinent information in an easily digestible format. This chatbot will serve two primary purposes: to allow employees to more easily verify the legality of their decisions, and to use message-based data to identify and investigate potential instances of misconduct. Ultimately, the framework developed and tested in this project can be implemented in a wide range of companies to improve the efficacy of their corporate compliance programs.

End to End Optimization for Supervised Topic Models

Ben Barrett
PRISE Fellow
Applied Mathematics, 2019

School of Engineering and Applied Sciences
Advisor: Finale Doshi-Velez
Mentor: Mike Hughes

How can predictions using high-dimensional discrete data be made more interpretable without sacrificing predictive accuracy, especially when a subset of the dimensions are independent of the variable of interest? Topic models, which identify latent structure in discrete data, offer one approach. We introduce a pipeline for optimizing supervised topic models end-to-end. Specifically, we apply dimension weights to the data, to account for the varying predictive importance of each dimension. In each optimization iteration, we then estimate the parameters of our generative model for the input data, and perform supervised learning tasks using the learned parameters as predictors. Finally, exploiting the differentiability of our pipeline, we update our dimension weights based on the gradient of the loss function used in the supervised learning task. Incorporating topic models in our pipeline allows us to obtain easy-to-understand, low-dimensional representations of the input data. Meanwhile, iteratively updating our dimension weights alters the inputs from which the parameters of the generative model are inferred, yielding progressively better parameter estimates and thus improved predictions. Our pipeline differs from existing end-to-end optimization approaches in using tensor decomposition methods to estimate the parameters of our generative model for the data. Tensor methods are advantageous because they yield more stable estimates than alternatives and possess asymptotic convergence guarantees. Future work will comprise evaluating our pipeline's computational complexity and predictive accuracy on real-world datasets. By building interpretable predictive models, we hope to encourage their adoption in practical decision-making settings and help non-experts leverage the power of predictive analytics.

EARTH AND PLANETARY SCIENCES

Arctic Air Suppression and Extreme Cold Events in a Warm Climate

Pratap Singh
PRISE Fellow
Applied Mathematics, 2021

Earth and Planetary Sciences
Advisor: Eli Tziperman

Evidence from the Eocene period (50-35 million years ago) indicates that in warm equable climates (such as a possible future under climate change), frost-intolerant species such as crocodiles and palm trees survived year-round in regions as far north as Wyoming, which presently experience winter temperatures as low as -40°F. Conventional climate models are unable to explain such high temperatures in inland areas without resorting to unrealistically high levels of atmospheric CO_2. Recent studies, using highly idealized one-dimensional models of air columns, propose a mechanism of Arctic air suppression by low cloud formation: as warm, moist, oceanic air moves over land and cools, optically dense low clouds form and exhibit a strong greenhouse effect on inland areas. I investigate this phenomenon using a realistic three-dimensional model, examining output from the Community Atmosphere Model under various warming scenarios, and using the HYSPLIT particle-trajectory model to determine the origins of air masses that lead to extreme cold events resulting from Arctic air formation over North America. Preliminary analysis suggests such extreme cold events in present climate result from air masses moving over Arctic sea ice and land. I plan to next consider the trajectories leading to cold events in much warmer climates, representing the 22nd century under a business-as-usual scenario with no reduction in CO_2 emissions. I will also conduct a clustering analysis of the air trajectories. This work will help determine the mechanisms by which the Arctic warms, with important implications for future climate change modeling and prediction.

ECONOMICS

Managerial Talent and Economic Performance: Evidence from Discontinuities in Douglas MacArthur's Economic Purge

Emma Toh
BLISS Fellow
Statistics and East Asian Studies, 2020

Economics
Advisor: Melissa Dell

There is a lack of consensus regarding the extent to which managers affect a firm's overall performance. Some argue managerial talent depends on the organization or culture of the firm, while others claim it is intrinsic. This project investigates the impact of managerial capital using Japan's post-war economy as a quasi-experimental model. Following World War II, the Allied Forces attempted to eradicate Japan's militaristic, hierarchical culture through an "economic purge" in which senior managers from large Japanese firms, which were valued above an arbitrary one hundred million yen cutoff, were largely relocated to smaller firms in newer industries. Analyzing firm-level data from the US National Archives, this project uses a regression discontinuity design to compare the impacts of the purge on firms from which managers were removed to a constructed control group containing firms just below the one hundred million yen cutoff. Work on this project so far has focused on using Optical Character Recognition to process archival data, cleaning and merging this data to create functional and comprehensive datasets, and visualizing and regressing data subsets from immediately before and after the war. This project's findings will deepen our understanding SCAP (Security Content Automation Protocol) policies following World War II and inform businesses seeking to optimize their management, organizational structure, and productivity.

Analyzing The Market Design of Online Marketplace Startups

Michael Zarian
PRIMO Fellow
Applied Mathematics, 2021

Harvard Business School
Advisors: Tom Eisenmann, Scott Kominers

The secret to creating a successful startup has eluded many aspiring entrepreneurs, for many startups fail within the first few years of operation. However, there is no definitive evidence illustrating why some companies succeed and others fail. To further investigate this problem, fifteen successful and fifteen failing online marketplace startups from 2013-2015 will be analyzed for their marketplace design, market attributes, market failure addresses, and strategies for growth and preventing disintermediation. After recording each piece of information using a Likert scale, a statistical analysis will be run to determine if successful marketplaces have significantly different aspects of their marketplace design than failing ones. The findings may suggest new ways for startups to operate their marketplaces in order to increase their chances of succeeding, enabling the growth of innovation in today's world.

Case Study: The Fuji-Xerox Merger

Annie Zhao
PRIMO Fellow
Economics, 2021

Harvard Business School
Advisor: Guhan Subramanian

Business deals may be commonplace, but not all deals resemble the transaction that Xerox, a well-known American digital document firm, announced on January 31, 2018. In one of the most irregular attempted mergers in recent years, the Japanese company Fujifilm would have taken control of Xerox in a $6.1 billion structured acquisition had activist Xerox shareholders not sued to halt the transaction. The documents unearthed during the subsequent discovery process revealed that the deal was both negotiated by a conflicted CEO and approved by a conflicted Board of Directors. This case study draws upon unsealed court records as well as contemporary evidence to provide an example of corporate governance gone wrong. Several individuals, including Xerox directors, had raised strong concerns about the deal. Nevertheless, the Xerox Board voted unanimously in favor of the transaction. By analyzing the year-long negotiation process from the perspective of the Board, this case aims to shed light on some potential pitfalls of the dealmaking process. Students and executives alike must be vigilant for conflicts of interests, mindful of incremental thinking, and confident enough to raise their hands when things have gone awry.

Innovation Races and Race Cars: Analyzing the Interplay of Regulation, Competition, and Innovation in the Formula 1 World Championship Series

George Hu
PRIMO Fellow
Economics, 2020

Harvard Business School
Advisor: Kyle Myers

Understanding the effect of market competition on innovation remains a primary concern for entrepreneurs, policymakers, and innovation economists alike. As economic theory notes both positive and negative effects of greater competition on firm-level innovation, empirical analysis in specific markets/sectors prove crucial to determining a quantifiable causal relationship between the two variables. Utilizing archival Federation Internationale de l'Automobile (FIA) data on Formula 1 (F1) race results, regulations, and constructor patents, our research empirically investigates the relationship between competition and innovation in F1 racing. Initial work has consisted of econometric analysis regarding the role of the F1 points system. Running fixed effect regressions, results suggest that the incentive effect of points on performance is substantial: drivers accruing fewer points earlier in a season perform worse in upcoming races independent of individual driver quality, team ability, and past results. This finding demonstrates the sizable role of effort in race performance on the part of the drivers and their teams, even in a setting often claimed to be characterized by the inherent ability of participants. Looking forward, we aim to leverage this point system effect to understand how policy changes and their effects on competition influence performance and innovation in F1 racing. Further conclusions on the interplay between regulation, competition, and innovation in the F1 context may eventually help not only to guide FIA sporting regulations but also to better inform optimal firm antitrust and competition policy in various sectors of the economy.

How Full-Time Employment Impacts Human Judgement and Decision-Making: The Case of Officials in the National Football League

Natalie Sherman Jollis
PRIMO Fellow
Economics, 2021

Harvard Business School
Advisor: Ethan Rouen
Mentor: Patrick Fergusen

There is an established trend of racial bias among rule-enforcing officials (i.e., referees) in professional sports. The bias exists despite career incentives for officials to be neutral, suggesting the officials' bias is implicit rather than intentional. Our study examines whether it is possible to mitigate implicit racial bias among sports officials by more closely aligning individual incentives with those of the governing sports organization. Until the 2017 season, all officials in the National Football League were part-time employees. During that season, 21 of the 124 officials were made full-time employees. We use a difference-in-difference model to compare penalty trends between full-time and part-time officials during the 2016 and 2017 seasons to examine whether this shift in employment reduced racial bias in penalty calls. In addition, during the 2017 season several players and teams protested unequal treatment of minorities by kneeling during the national anthem. We consider the kneeling protests as another potential reason for bias among officials and examine differences in penalty calling against protesting and non-protesting players. Preliminary analysis shows a positive correlation between kneeling and number of penalties called, suggesting bias among officials against protesting players. If our hypothesis is correct, both this bias and racial bias should be less prevalent in full-time officials. These results would support policies that increase interdependence between individuals and neutral organizations as a potential method for reducing individuals' implicit biases. The results may also have broader implications because sports officials often serve as a model for others who must make high-pressure decisions with limited context, for example military and police personnel.

Healthcare Provider Incentives to Invest in Housing

Kaya Bos
PRIMO Fellow
Economics and Integrative Biology, 2020

Harvard Business School
Advisor: Susanna Gallani

Focusing on value in healthcare delivery requires organizations to rethink many aspects of the design of their services. Minimizing costs while maintaining or improving outcomes for patients often goes beyond the boundaries of the direct interaction between patient and provider. Recent initiatives, such as BMC's Innovative Stable Housing Initiative, have extended the scope of healthcare services to include the social determinants of health. The Innovative Stable Housing Initiative invests directly in housing projects and housing support services for underserved neighborhoods. Our research seeks to examine whether investments in housing are an effective way to reduce healthcare costs while maintaining or improving outcomes for underserved, high-cost populations, who represent a significant portion of the population served through safety-net hospitals similar to BMC. We will conduct a case study as well as field research on BMC's housing investments and its housing support service investments. We will track healthcare costs for residents before and after BMC's involvement, and supplement the data with resident interviews reflecting on the impact these actions have had on their healthcare experience and outcomes. As a largely unexplored topic of healthcare research, this is a new method of improving value in healthcare and could represent an opportunity to implement policy that incentivizes partnerships between affordable housing and safety-net providers to increase patient value.

Incentives in Biopharmaceutical Innovation

Leopold Bottinger
PRIMO Fellow
Statistics, 2020

Harvard Business School
Advisor: Ariel Dora Stern

In recent decades, the American health care industry has been transformed through innovations including gene therapy and digitization. A variety of incentives, primarily from the government, affect these innovations and the progress of the healthcare industry. Along with faculty and doctoral students, we are investigating the history of venture capital (VC) investments in both the gene therapy and Health IT sectors to look at specific trends in investments over recent years. Both contexts display a drop in VC investment surrounding the 2008 financial crisis, followed by a recovery of investment activity and then a significant uptick from 2015 through 2017. VC investments in these industries have grown as a proportion of total VC dollars invested in healthcare. Changes in the legislative landscape which provided greater financial incentives for value-based care and the digitization of electronic health record systems likely buoyed these investments. Furthermore, technological advancements have been improving the value propositions of many young, technology-driven firms. These combined trends demonstrate the importance of incentives on innovation in biotechnology and Health IT.

Reverse Innovation in IQIC Sites: Bringing Evidence-Based Best Practices for Congenital Heart Disease from Lower- and Middle-Income Countries to Boston Children's Hospital

Kathleen A. Young
SURGH Fellow
Human Evolutionary Biology, 2019

Boston Children's Hospital, HMS
Advisor: Kate Doherty

The International Quality Improvement Collaborative for Congenital Heart Disease(IQIC) started through Boston Children's Hospital in 2008 to facilitate quality improvement practices for children with congenital heart disease in low- and middle-income countries by providing benchmarking data to 66 sites in 25 countries around the world. Throughout the year, the IQIC provides benchmarking reports, including both aggregate data for all sites and individual site reports. Additionally, the collaborative supports the implementation of evidence-based best practices through webinar series, online courses, and site visits.

At the same time, Boston Children's Hospital learns from these international sites. Reverse innovation involves evaluating what is being done well in resource-limited settings and applying these practices to more resource-rich settings such as Boston Children's. Often, developing hospitals generate numerous creative innovations to overcome resource barriers and decrease costs. To identify these innovations, we will first run analyses on the 2017 Annual Benchmarking Reports to find sites with low mortality and infection rates. Next, we will interview members of the BCH team who have visited these sites and conduct a survey of innovations they noticed there. As a possible next step, we will reach out to members of a few sites and conduct a survey of what innovations they believe are working well. The rising costs of healthcare worldwide make this research incredibly important, and we hope to find practices that can be used to improve the quality of patient care for lower cost.

How Power Differences Drive the Laughter Gap Between Men and Women

Sophie Edouard
PRIMO Fellow
Applied Mathematics, 2021

Harvard Business School
Advisor: Alison Wood Brooks
Mentor: Trevor Spelman

Across several diverse data sets, we find that women laugh significantly more than men. However, women report higher negative affect (NA), suggesting that their laughter in conversation may not reflect authentic feelings of happiness. We found robust correlational evidence between gender and the propensity to laugh—across 2000 real speed-dating conversations and in a 2013 Gallup poll of over 175,000 Americans, women laughed much more frequently than men, but increased laughter did not predict enjoyment of the conversation or life satisfaction. Now, we seek causal evidence to understand the gender gaps in laughter and happiness, and to mitigate these differences by manipulating power. We focus on power as an independent variable because prior research has shown that low-power individuals experience greater NA and, separately, that women tend to hold lower-power roles than men. In a novel experimental songwriting paradigm, participants were assigned to mixed-sex dyads and tasked with creating an original song. One participant was randomly assigned the role of the producer (high-power) while the other the singer (low-power). Following the experiment, participants were surveyed on their experience, and their interactions were coded for laughter. If our hypotheses are supported, then women assigned to the producer role will have a lower rate of laughter and lower negative affect than women assigned to the singer role. This work makes important contributions to the research on gender, laughter, and power—it's not only the first research to empirically link gender, laughter, and happiness, but also to identify a mechanism for the gender-laughter gap.

Babylon Check Chatbot

Uriel fza Gutierrez
PRIMO Fellow
Economics, 2019

Harvard Business School
Advisor: Karen Huang

The popularity, availability, and ease of using mobile connected devices has caused an increasing amount of people to use these devices to seek real-time medical advice. The UK's National Health Service (NHS) partnered with Babylon Health to launch *Babylon Check*, an automated triage symptom checker. This chatbot does not provide medical diagnosis, but instead directs the patient to the most appropriate source of care. It is possible that patient satisfaction and trust in the chatbot will increase if the chatbot is programmed to prompt users with more follow-up questions. To test this hypothesis, an initial experiment was conducted via Amazon Mechanical Turk. A control group of users were prompted with the normal amount of follow-up questions that the commercially deployed *Babylon Check* would ask. The treatment group of users were prompted with more follow-up questions. Users with the same symptoms would be given the same triage advice, regardless of the amount of follow-up questions asked. The users were then asked a series of follow-up questions to measure their satisfaction with using the chatbot. Preliminary results showed that the users who were asked more follow-up questions reported having a better experience and were more likely to use the chatbot again. It is important that users are satisfied with their chatbot experience and trust the triage advice for individuals to avoid unnecessary emergency or urgent medical care. This could potentially alleviate the current strain on NHS services and help allocate medical resources and time more efficiently.

The Influence of Tools and Automated Managerial Cognition on Innovation

Jia Yi Lim
PRIMO Fellow
Applied Mathematics and Economics, 2021

Harvard Business School
Advisor: Andy Wu
Mentor: Sourobh Ghosh

With recent advances in cognitive information technology, numerous meaningful implications in information technology have been implemented to improve management decisions. Companies such as Optimizely have commercialized the process of A/B testing to enable more accurate and objective strategic decision making. This brings forth the question: how should managers invest in A/B testing to improve company cognitive capabilities? Our group looks into the startup Optimizely, to analyze the effectiveness of A/B testing for its customers and to research how A/B testing can be generalized as a concept into other fields to improve management strategic testing across the board.

Hedge Fund Activist Investing

Alex Yu
PRIMO Fellow
Statistics, 2020

Harvard Business School
Advisor: Suraj Srinivasan

Hedge fund driven shareholder activism is presently one of the most important and controversial developments in the US business world. In the last few years hedge fund managers like Bill Ackman (Pershing Square), Carl Icahn (Icahn Enterprises), Daniel Loeb (Third Point) among others have become a powerful force in US corporate governance. Because of the increasing prominence of hedge fund shareholder activism and the often hostile tactics they use, its effectiveness and whether it effects positive and long-term company growth has come into question. We investigated the effectiveness of activist-led spin-offs, which activist hedge funds might advocate for in order to increase a company's value. We looked through databases on Capital IQ and CRSP to find all the spin-offs in the past ten years. We then identified the spin-offs led by activist hedge funds. Finally, we calculated the returns for each spin-off transaction and compared the average returns for transactions influenced by activist hedge funds with those not influenced by them. Our findings show that spin-offs led by activist hedge funds, on average, lead to higher company returns. But while this speaks for the average, there are two stories to tell here—one where activist hedge funds are held as triumphant aggressors that bring positive change, and one where their hostility amounts to failure. Going forward, we want to investigate the key drivers of activist-led spin-off success and failure.

Charitable Giving, Gender, and Behavioral Economics

Bella Ganthier
PRIMO Fellow
Sociology, 2020

Harvard Business School
Advisor: Christine Exley

In the realm of gender bias studies, there exists a plethora of research on gender-based discrimination and how gender stereotypes influence men and women. This study focuses on the impact of subjective information on people's perception of a woman's performance given perfect objective information. The study was split into two phases. Phase one involved compiling a list of damaging things women say or do that prevent them from being hired or promoted within their chosen career area using a randomized Qualtrics survey. Phase two involved a survey in which we tested the impact of these subjective, damaging things on people's perceptions of a woman's performance when they were also provided with objective information, in the form of the women's Armed Services Vocational Aptitude Battery (ASVAB) test score. Preliminary findings suggest that when women bring up topics that are strongly associated with female stereotypes, such as family or child care obligations, there may be deleterious effects on their chances of success in the workplace. Following further data collection, this study could have implications for how women should conduct themselves in professional settings, and how we can lessen the effect of gender stereotypes.

New Firm Pricing Strategy

Alex Wu
PRIMO Fellow
Economics, 2020

Harvard Business School
Advisor: Alexander MacKay

We study the dynamics of firm pricing strategy by analyzing a dataset of new entrants in the Illinois energy market. More specifically, we consider how fringe firms price in response to a dominant firm. Compared to 1-year energy futures prices, the price of the dominant firm explains over three times more of the variation in fringe firm prices. We find that fringe firms are forward-looking, since they price in response to the dominant firm's average future prices as opposed to its monthly sticker price. For 1-year contracts, a $1 increase in the dominant firm's one-year price corresponds to a $1.016 increase in the fringe firm's price compared to a $0.217 response to the price in the current month. The same increase in the dominant firm's two-year price corresponds to a $0.119 decrease in the fringe firm's price. This suggests that firms are forward looking up to about one year. Lastly, fringe firm prices are 13.2% higher than dominant firm prices. This is largely driven by products that are marketed as renewable energy sources.

ENGINEERING SCIENCES

Motion of Water Droplets on Oil-Infused Slippery Surfaces

Lilian Magermans
PRISE Fellow
Mechanical Engineering, 2019

School of Engineering and Applied Sciences
Advisor: Joanna Aizenberg
Mentor: Solomon Adera

Inspired by the *Nepenthes* pitcher plant, slippery liquid-infused porous surfaces (SLIPS) are micro/nanostructured superhydrophobic surfaces impregnated with lubrication oil. SLIPS have received significant attention since their invention few years ago due to their ability to enable remarkable droplet mobility. They do so by significantly reducing solid-liquid contact between the droplet and the underlying substrate. SLIPS are useful in various engineering applications, ranging from power generation and heat transfer to hydrodynamic drag reduction. However, the motion of water droplets on SLIPS is not well-understood. This work focused on understanding the motion of millimeter-size water droplets on SLIPS. We fabricated SLIPS samples from a transparent thin film of nanostructured boehmite on glass. Boehmite was formed from alumina sol-gel by immersing the spin-coated and cured glass slide in hot water at 95°C for 15 minutes. The samples were then functionalized by placing them in a jar containing cured PDMS at 235°C for 2 hours. Finally, the samples were infused with silicon oil to create SLIPS. We studied the motion of water droplets on these SLIPS using high-speed imaging. Our preliminary results show that the coalescence velocity of water droplets on SLIPS is a function of the viscosity, thickness of the lubrication oil, and size of the droplet. This work provides new insight into the coalescence mechanism of water droplets on SLIPS, which may open up new application areas for SLIPS.

A New Electrochemical Method of CO_2 Capture

James Salvador Niffenegger
PRISE Fellow
Mechanical Engineering, 2019

School of Engineering and Applied Sciences
Advisor: Michael Aziz
Mentor: David Kwabi

As carbon dioxide (CO_2) emissions continue to increase, climate change threatens to severely damage communities and biodiversity. One strategy to reduce this harm is carbon capture and sequestration, a process in which CO_2 is separated from a point source or ambient air before being compressed and sequestered from the atmosphere. A common method involves converting CO_2 to carbonate/bicarbonate in strongly basic solution and separating pure CO_2 from the capture solution though highly energy intensive heating. Whereas CO_2 is very soluble in base, it is insoluble in acid; therefore the energetic cost of removing CO_2 from the capture solution can be significantly reduced using an electrochemical system that can reversibly change the acidity of an electrolyte.

This research project seeks to create an electrochemical system that can cyclically capture CO_2 in base and acidify that solution, releasing the pure gas for sequestration. The electrochemical flow cell comprises an electrolyte containing organic redox-active molecules that change acidity by releasing/taking up protons during oxidation/reduction. The cell will connect to an air-liquid contactor that will capture CO_2, and sensors will measure CO_2 levels going into and out of the contactor. The pH change of multiple compounds upon charge and discharge will be determined. Preliminary tests show that ADQS can swing within a pH range from 3 to 12, which is appropriate for certain capture solutions, and the contactor can potentially capture between 42%-74.5% CO_2. If successful this system could reduce the cost of CO_2 capture.

Dielectric Elastomers: A New Method to Delay the Electro-Mechanical Instability

Chet C. Johal
PRISE-Emmanuel Fellow
Physical Natural Sciences, 2019

School of Engineering and Applied Sciences
Advisor: David R. Clarke
Mentor: Ehsan Hajiesmaili

Dielectric elastomers are rubbers which deform when a voltage is applied. Potential uses include muscles for soft robots and lenses which deform to focus. This research deals with how microscopic structural changes may affect their macroscopic electrical and mechanical properties.

Dielectric elastomers provide ideal soft actuators due to their fast reactions and large strains. Optimizing their properties with the addition of plasticizer and additional crosslinker can improve electrical characteristics and aid understanding of plasticization mechanisms. The optimum crosslink density is explored for CN9018, an acrylic, (manufacturer: Sartomer) by mechanical testing of dog-bone shapes fitted to the Gent Model (minimising shear modulus for Imax $\sim$7), revising a previous estimate based on rectangular shaped samples. The addition of plasticizer (Benzyl Butyl Phthalate) is investigated with mechanical testing. Data are interpreted through the Gent Model, allowing for an estimation of the degree of plasticizer which produced the greatest delay of the electromechanical instability; the onset of failure for compliant elastomers. A dielectric elastomer actuator (DEA) is fabricated from this discovered ideal composition to demonstrate the (larger) deformation possible. An increased crosslink density is required to prevent a decrease in the modulus. The tunable crosslinker used was 1,6 – Hexanediol diacrylate (HDDA). The plasticizer particles cause local polymer chain stretching, increasing strain hardening, thereby retarding the electromechanical instability, and hence are expected to delay electrical breakdown. This research may improve the operational range of dielectric elastomers and further elucidate the mechanism of plasticization, in lieu of its ability to cause local chain stretching.

A Bayesian Inference Framework for Two-Color Holography

Yasemin Kiriscioglu
PRISE Fellow
Mathematics and Physics, 2020

School of Engineering and Applied Sciences
Advisor: Vinothan Manoharan
Mentor: Solomon Barkley

Digital holographic microscopy is an imaging technique that produces holograms, which can show the interference pattern of light shining through a particle. With light scattering theory and the fringes that the interference pattern creates, we can infer a particle's three dimensional position from the hologram, parameters which are not extracted to the same degree of precision in other imaging techniques. This study uses red and green lasers on colloidal particles (diameter 0.1-1.0μm) to create holograms, and compares the data extracted from them, varying the color of the laser, the size of the particle and the statistical inference method. Previous work in imaging colloidal particles by the Manoharan group has shown that using Bayesian inference to analyze holograms yields better results than least squares fitting which is traditionally used. The present study extends the Bayesian approach by investigating two-color holograms instead of single color holograms. The use of two different wavelengths provides additional information, including the ranges of uncertainty, to measurements of particle position, size and refractive index. Preliminary results suggest that fitting converges in reduced time and parameters are more accurate in the two-color system. These two improvements could be conducive to resolving holograms of complex assemblies of colloids, since their three-dimensional configurations cannot be detected with most digital imaging techniques.

Estimating Drinking Water Contamination by Poly- and Perfluoroalkyl Substances among Domestic-Well Users in New Hampshire

Beverly Ge
PRISE Fellow
Environmental Science and Engineering, 2020

School of Engineering and Applied Sciences
Advisor: Elsie Sunderland
Mentor: Cindy Hu

Poly- and perfluoroalkyl substances (PFAS) are a class of anthropogenic substances that have been used in a variety of industrial and consumer products since the 1950s. Human exposure through pathways such as drinking water has been linked to numerous adverse health impacts ranging from cancer and immunotoxicity to endocrine system disruption. New Hampshire's Department of Environmental Services (NHDES) has been conducting an ongoing investigation of PFAS in the state's drinking water supplies, resulting in a large database of PFAS concentrations. Our goal is to build a predictive model for propensity of PFAS contamination in private wells using the NHDES data based on proximity to point sources (i.e. industrial sites, wastewater treatment plants, airports, and military bases) as well as other natural variables (e.g. soil geochemistry, groundwater recharge, and precipitation). After the data for relevant natural factors and point sources have been collected, a logistic regression will first be applied, followed by the testing of different machine learning methods (e.g. boosted regression trees, artificial neural networks). The machine learning method with the best predictive performance will then be applied to estimate drinking water contamination by PFAS among private wells in New Hampshire from which measurements were not initially taken. This approach will help fill gaps in the existing sampling data and enable the identification of hot spots of contamination to protect New Hampshire residents from exposure and mitigate public health impacts.

Sensing Garment to Combat Infant Mortality in the Developing World

Charles L. Colt-Simonds
PRISE Fellow
Electrical Engineering, 2020

School of Engineering and Applied Sciences
Advisor: Conor Walsh
Mentor: Yichu Jin

Outside the developed world, child mortality remains a prevalent issue, with most child deaths occurring within the first few weeks of life. There is very little data available on the causes of infant mortality, but previous research has largely attributed it to hypothermia and apnea. We propose a low-cost, non-intrusive method of monitoring infants during the first week of life, alerting caretakers to potential health risks such as rapid drops in temperature, while also collecting data on respiration rates and temperature swings. We hope to promote the use of "Kangaroo Care," in which a baby spends most of its time swaddled against the caretaker, making skin-to-skin contact. This method of care has been shown to improve a baby's odds of surviving the first week of life by reducing its risk of hypothermia and apnea. The proposed device will be textile-based, taking the form of either a pair of garments (one for the infant and one for the caretaker) or a single patch to be sewn onto a garment of the caretaker's choice. As currently envisioned, this device will incorporate a resistive strain sensor to measure breathing rate, and a thermistor or temperature sensitive fabric to measure body temperature. Future expansions may include an EKG-based heart rate sensor using fabric electrodes. Preliminary results suggest it should be possible to accurately monitor temperature and breathing for at least a week using these sensors, as they are both sensitive and low-power enough for this application.

ENGLISH

Paper Slips: Natural Science and Poetry in the Eighteenth and Nineteenth Centuries

Norah Murphy
SHARP Fellow
English, 2020

English
Advisor: Deidre Lynch

In the eighteenth and nineteenth centuries, blank books were not simply diaries, as the layperson may think. Rather, they were repositories for poetry, personal notes, newspaper clippings, and more, reflecting their owner's reading (and writing) practices. Utilizing the Houghton and Schlesinger Libraries' collection of albums, scrapbooks, and commonplace books, my project partner and I took stock of Harvard's resources in this field. Concurrently, we looked for themes within the books' contents to represent with ten images of book pages, to be published with captions as exhibits on the Romantic Circles Gallery, a peer-reviewed academic website devoted to the study of Romantic period art and literature. Together, we examined over 100 manuscripts in the Houghton and Schlesinger libraries, using various search terms and strategies to navigate irregular catalogue systems. This project helped us amass data about the nature of Harvard's collections, and also led me to specific books unified by the theme of natural science. One such book, an autograph album compiled by Nancy Jane Park in the early nineteenth century, hosts not only traditional sentimental verses and illustrations, but a series of three poems handwritten alongside illustrations of the Earth and planets. Astronomy and Lord Byron's poetry intersect in this album. Though this is but a handful of pages in one book within a much larger collection, it speaks to the breadth and depth of information that future researchers could draw from Harvard's collections of scrapbooks.

Paper Slips: Remembrance of Things Past in Blank Books of the Eighteenth and Nineteenth Centuries

Faith Ahhyeon Pak
SHARP Fellow
Comparative Literature, 2019

English
Advisor: Deidre Lynch

The Romantic period (1750-1850) marked a cultural movement towards sentimentality, nostalgia, and appreciation for nature that stemmed from a general sense of losing old ways of life from the technological advancements of the Industrial Revolution. It became common practice for young women to preserve mementoes of love, friendship, and nature in blank books, such as autographed poems usually brooding on the brevity of life and beauty, and pressed flowers and locks of hair. The friendship album, or "album amicorum," became increasingly standardized as the practice grew more and more popular towards the mid 19th century, and almanacs, magazines, or "ladies' cabinets" regularly featured sentimental poems specifically written to be transcribed into these albums. These scrapbooks and albums may be seen as an early form of social media, as people would draw from a shared pool of circulating media, cutting and pasting favorite items of popular art and literature into blank books that would be passed around among friends. Trawling through Houghton and Schlesinger libraries' vast collection, my partner and I took notes and pictures that will be featured on the Romantic Circles website, an online gallery dedicated to the study of the Romantic period. Interesting finds include a woman's hairwork album filled with braided locks of hair from her friends from the Schlesinger library, and a pocket-book from the Houghton library containing dried leaves, flowers, and strands of hair inserted in the beak of a tiny silver bird on a slip of paper. Our research reveals a strong urge in Romantic culture for collecting and preserving the ephemeral in a time of revolutionary social change, as well as giving insight into the possible roots of modern social media in the Internet age.

Digital Learning in Poetry in America

Frank Cahill
SHARP Fellow
English and Statistics, 2019

English
Advisor: Elisa New
Advisor: Leah Reis-Dennis

Deviating from the classroom-based pedagogical model, Poetry in America (PIA) is a digital platform designed to engage learners without pre-existing interest in poetry. HarvardX, the platform hosting PIA's courseware, offers data-based insight into the efficacy of its unique multimedia approach. One method of analysis on this data quantifies replays. Each video is divided into five-second segments; at the beginning of each segment, the number of unique viewers and the total number of times that segment is viewed is measured. A proxy for the percentage of viewers replaying a given segment is constructed and used to find local maxima and minima in these replay-percentage values. These maxima and minima point to segments of high- and low-viewer engagement, respectively. In longer videos simulating seminar discussion, viewers have been found to "track" arguments: replay rates increase as an argument unfolds and peak with an argumentative climax. Rates then decrease as the argument concludes, only to increase as it pivots in a new direction. Thus, online viewers are acutely aware of argumentative development and respond with replays. This suggests that the classroom learning experience, where viewers are actively driving discussion, can to an extent be replicated on online platforms. However, the digital medium enables not only the reproduction of the classroom experience but also provides an opportunity to improve upon it. For example, videos can be repackaged to support viewer replays without sacrificing viewer retention. When used smartly, the online platform provides the flexibility to support viewers' learning curves in ways that the physical classroom cannot.

Producing Poetry in America

KeeHup Arie Yong
SHARP Fellow
Psychology, 2019

English
Advisors: Elisa New, Leah Reis-Dennis

Poetry analysis is a discipline often misunderstood by many. The use of seemingly random commas, lines broken in the middle of words, and obscure metaphors and allusions are often enough to push people away from delving deeper into poetry. "Poetry in America" strives to globalize poetry analysis for a larger audience.

Production at the "Poetry in America" team consists of two branches of content creation: educational course material and a television show. The former allows for exploration in script writing, course creation, and close analysis of literature with educators. Online course material fosters a community of learners, and the job of production is to bridge the gap between the audience and the poems through creative media. The television show is a more entertainment-specific endeavor; filming centers around interesting poems and fascinating guests, all grouped together by their passion for the subject matter in the poems. A special focus on social media campaigns for the television show is ongoing, with the creation of art pieces, television show stills, and clips furthering the show and its relationship with viewers. This approach to poetry serves to make poetry more engaging to both classrooms and in-home viewers.

Both paths of the production focused on demystifying poetry for people interested in learning, and to make poetry fun for those opposed. "Poetry in America" aims to make poetry an experience that creates a fun relationship between education and entertainment.

FOLKLORE AND MYTHOLOGY

'Forgetful of Their True Selves': Women Warriors in Old Norse History and the Contemporary Imagination

Noah Houghton
SHARP Fellow
History and Literature, 2020

Folklore and Mythology
Advisor: Stephen Mitchell

The image of the Viking woman warrior is ingrained in modern culture: from Valkyrie in the 2017 Marvel film *Thor: Ragnarok* to Lagertha in History Channel's popular television series *Vikings*, something about the Norse woman warrior has remarkable cultural staying power. My project examines the historicity of these figures, and re-examines the extant academic consensus by emphasizing new anthropological findings and the questionable authorship of surviving Norse texts. I began my project by reading core Old Norse literature such as Snorri Sturlusson's *Prose Edda* and the Norse sagas and romances, as well as a wide variety of modern scholarship on the Vikings and specifically on Viking women. In particular, the September 2017 article "A female viking warrior confirmed by genomics" by Dr. Charlotte Hedenstierna-Jonson, a researcher at Uppsala University, was a core inspiration and lodestone for my ongoing research. By examining the different ways in which medieval and Norse texts treated women warriors, it becomes clear that the original Viking stories were more accepting of women warriors than their European retellings, which may indicate a corresponding difference in cultural attitudes. This provides some textual evidence to support Dr. Hedenstierna-Jonson's argument that women warriors played a larger role in the historical Viking culture than is currently believed by modern scholars. By continuing to interrogate the modern understanding of these stories and continuing to advance gender-conscious research in Norse anthropology, the historical image of the Viking woman as little more than homemaker may be rehabilitated into the complex and nuanced role she plays on television.

GLOBAL HEALTH AND HEALTH POLICY

Innovation and Digital Health Accelerator Internship

Emily Dahl
SURGH Fellow
Electrical Engineering, 2019

Boston Children's Hospital, HMS
Advisor: Tim Driscoll

This summer I am interning at the Boston Children's Hospital Innovation and Digital Health Accelerator (IDHA), working to bring creative pediatric digital health solutions into clinical practice. The accelerator evaluates applications from Boston Children's employees, as well as external digital health startups. Throughout the application process, IDHA screens for projects that are innovative, fulfill an unmet market need and will enhance the standard of pediatric care. IDHA leverages unique expertise in the digital health field to support promising startups, providing technical assistance as well as access to clinician leaders and the potential to validate technology in clinical settings. Alongside with assisting in reviewing applications, I am working on a team revising the accelerator grant application process, revitalizing our application and adapting our marketing content including our online portfolio and written recommendations for innovators.

I am also acting as project manager and analyst on a clinical data platform development team aiming to create a standardized system to aggregate, process, visualize and integrate different types of data into clinical databases. We are creating an adaptive platform to support a variety of projects we are accelerating, including projects in diabetes management, autism diagnosis, and concussion detection. I am involved in these projects from a strategic perspective, analyzing market opportunities, organizing resources and learning about contract and stakeholder negotiations.

GOVERNMENT

The Politics of Genomics

Ryan Zhang
BLISS Fellow
Social Studies, 2021

Government
Advisor: Jennifer Hochschild

Genomic science is revolutionizing our world, offering pioneering applications in fields ranging from medicine and genealogy, to abortion and criminal justice. However, the rise of genomics is controversial; while some embrace new genomic technologies, others voice concerns about morality, privacy, and discrimination. Our project investigates the politics of genomics, adopting disputes over four genomic technologies as case studies: BiDil (a heart medication for African-Americans), DNA ancestry testing, forensic biobanks, and prenatal genetic testing. Specifically, my work uses empirical methods, including aggregating survey data, conducting literature reviews, analyzing interviews with genomics experts, and tracking positions of elected officials regarding genomics, to show that even in today's era of hyperpolarization, genomics disputes are fought neither along partisan lines nor between liberal and conservative ideological camps. Instead, our evidence indicates that one's stances in genomics disputes depend on two dimensions. The first dimension, called "genetic penetrance," measures whether an individual believes human characteristics are caused by genetics or the environment. The second dimension measures "technology optimism/pessimism," or whether an individual believes that technological advancements are generally beneficial or harmful to society. Given that conventional frameworks of partisanship or ideology are inappropriate, these two dimensions constitute a new model for examining the nature of public opinion on genomic science. Ultimately, our research empowers the public, policymakers, and scholars to truly understand how the genomics revolution is transforming our politics, our society, and our lives.

Neighborhood Density and Political Orientation in Greater Boston

Simon Eder
BLISS Fellow
Linguistics and Anthropology, 2020

Government
Advisor: Ryan Enos
Mentor: Riley Carney

The context in which people live affects their behavior. The political orientation of communities tends to vary with density, with urban areas leaning liberal and rural areas leaning conservative. Why this is the case, however, is not well established. This study investigates which, if any, characteristics of neighborhoods of different densities correlate with political orientation. To collect a data set, we observed a sample of 500-foot-long residential stretches (approximating city blocks) within a sample of census tracts (approximating neighborhoods) of varying densities in the Metro Boston area. We recorded a set of 20 characteristics for every block and for each building on the block. Analysis of the preliminary data suggests that neighborhoods of greater density are both less similar to each other and less uniform vis-à-vis the buildings they comprise than neighborhoods of lesser density on a number of measures. This could imply that residents of denser areas may have more liberal values because they are immersed in a more heterogeneous geographical context. By examining some of the correlations in neighborhood-level politics, this study may provide a clearer understanding of past and future electoral outcomes.

Turnout Buying and Public Good Provision

Archie Hall
BLISS Fellow
Social Studies, 2020

Government
Advisor: Horacio Larreguy

Turnout-buying, the practice of offering gifts or bribes to supporters of a political party in return for turning out on election day, is rife across Africa. This study aims to reveal the causal effect of turnout-buying on public good provision by exploiting high rainfall around election days to isolate the exogenous effect of turnout-buying. The logic underlying the use of rainfall is simple; high rainfall increases the difficulty of voting, by flooding roads for instance. This raised barrier to voting is more likely to deter those who were not given any sort of gift or bribe in return for turning out to vote, which amplifies the effect of turnout-buying on electoral results in areas of high election-day rainfall. Preliminary results indicate that the mechanism of connecting high rainfall to a strengthened impact of turnout buying is valid. Voters in areas of high election-day rainfall are more likely, by a statistically significant margin, to believe that turnout-buying is prevalent, but are no more likely to report experiencing it themselves. The next step for this project will be to connect this mechanism to outcomes related to public good provision. Observing a significant effect of turnout buying on outcomes related to public good provision – such as vaccination rates or years in school – would underscore the importance of action against turnout buying in developing democracies. A better understanding of which aspects of public good provision are most impacted by turnout buying can suggest potential solutions for mitigating the impact of turnout buying on the overall performance of government throughout Africa.

Vice Districts and the Social Geography of Illegality

Owen Torrey
BLISS Fellow
Undeclared, 2021

Government
Advisor: Ryan Enos
Mentor: Amy Lakeman

Vice districts (designated zones whose boundaries permit sex work and other historically outlawed vices) were popular tools of American social organization at the turn of the nineteenth century. Gilded age reformers believed these districts would siphon off disreputable but inevitable activity into concentrated zones, leaving other areas unaffected. To examine the geographic distribution of historic vice districts in urban environments, this study developed two original data sets: a) a mapping of evidence reports made by the Committee of Fifteen, a private group of religious leaders, activists, and businessmen that investigated vice in Chicago, and b) an inventory of vice districts within the United States that details district location, formation, and disbandment. Preliminary evidence suggests common social geographic trends across historic vice districts. Municipal policies prescribing minimum distances between brothels and social landmarks (e.g. churches, schools, and military bases) restricted locations available for segregated districts, affecting their demographic makeup. Factors like income and race appear to have been salient, as officials sought to keep affluent areas free from crime. The data from the Committee of Fifteen reports may further suggest whether designated regions were successful in restricting vice, through mapping areas where sex work occurred outside of officially sanctioned zones. Through quantitatively analyzing what is typically considered qualitatively, the study of vice regulation may point towards how social landscape, individual identity, and government policy work together in shaping the urban geography of illegality.

Anarchy in Zine

Nicole Angela Araya
SHARP Fellow
Visual and Environmental Studies, 2020

Mentors: Emilie Hardman, Alexis Waller

The purpose of this study is to investigate the methods used to promote anarchist sentiment in Houghton Library's Printernet Zine collection. We analyze the subversion of mass media norms, including the visual and literary aesthetics of political information. The zines were created largely independent of state, market, or social censorship, as they operated within local, not-for-profit networks. Anarchist zine creators made expressionist collages out of newspapers, magazines, and advertisements to demonstrate the folly of state politics and the capitalist illusions of freedom. Anarchists also expressed their dissent from the mainstream via other art forms, including comix, visual art, poetry, short fiction, personal essays, and academic analyses of political and social issues. Zines make the political personal by expressing larger political critiques and ideals through the lens of the psychological, personal, and abnormal. Anarchists conveyed their objective of free will by utilizing humorous, sexual, shocking, experimental, and playful expression to incite political activism. Zines are an effective medium to communicate not only anarchist politics, but also candid critique of government and capitalism, suspicion of the "normal," distaste of conformity and limits, conscious awakening of mass psychological control, and resistance against passive consumer mentality.

HISTORY

Harvard Art Museums

Katherine Alosi Okumu
SHARP Fellow
Anthropology and History, 2020

Harvard Art Museums
Advisor: David Odo
Mentor: Correna Cohen

Museums in the 21st century have to wrestle with the important question of how to best communicate and foster appreciation for art. My project at The Harvard Art Museums attempts to answer this question through in-depth research in Harvard University's Fine Arts Library and in the Busch-Reisinger, Fogg, and Arthur M. Sackler Museums. My research approach has two distinct components. The first phase of my research involves developing and implementing a weekly public tour called "Fictive Presence." By conducting in-depth research on the historical and theoretical contexts behind three specific objects, I explore ways to increase accessibility and engagement in a more expansive audience. For these tours, I have integrated information from walkthroughs and showcases from curatorial staff into my research. Weekly written reflections help me revise and improve my tour to better achieve its goals. The second phase of my research will entail applying the lessons learned through constructing my public tour to designing educational programming around a public art project by the renowned Teresita Fernández. This public art project, entitled *Autumn (...Nothing Personal)*, seeks to provide a physical space for unrecognized voices in Harvard Yard. The programming around *Autumn (...Nothing Personal)* will culminate in the creation of a teaching guide for student tour guides during the semester. Ultimately, this project will foster new programming at the Museums and explore the importance of inclusion in art spaces.

Waiting for Liberty: Suffrage Beyond Seneca Falls

Brooke Martin
SHARP Fellow
Social Studies and Women, Gender, and Sexuality, 2021

Radcliffe Institute
Advisor: Tamar Goren Brown

Plenty of history books give a simplistic overview of the history of the women's suffrage movement in America, claiming it began in 1848 with the Seneca Falls Convention and ended in 1920 with the ratification of the 19th Amendment. This narrative, though, is a heavily reduced account of a centuries-old movement that is still not truly finished. The Schlesinger Library's "The Long 19th Amendment" project seeks to expand this simplified version of events in part by exhibiting archival items in such a way that questions conventional understanding of the women's suffrage campaign. My research involved assessing the scope and content of the library's archives to help choose what items would be displayed. I used archival organization and search tools like HOLLIS and OASIS to both view materials digitally and work with them hands-on, with selected objects ranging from personal diaries to parade banners. The exhibit, which is planned for spring 2020 to coincide with the hundredth anniversary of the amendment, will attempt to draw attention to the contributions of women outside of this time frame, the complicated intra-movement politics of the American women's suffrage push within broader crusades for equality, and the failings of an amendment predicated on the rights of well-off white women. In examining the Schlesinger Library's archives to view what material they contain (and just as importantly, what they do *not* contain) regarding the American women's rights movement from the Revolution to the present, I hope to elevate stories and voices too often forgotten by history as we move toward the centennial anniversary of the 19th Amendment.

HUMAN DEVELOPMENTAL AND REGENERATIVE BIOLOGY

High-Throughput Screening for Compounds that Induce Maturation of Stem Cell-Derived Beta Cells

Arielle Rothman
PRISE Fellow
Engineering Sciences, 2021

Harvard Stem Cell Institute
Advisor: Douglas Melton
Mentor: Aharon Helman

Type 1 diabetes affects millions of people worldwide and is caused by autoimmune destruction of beta cells, the insulin-producing cells located in the pancreas. A promising cure for the disease is transplantation of stem cell-derived beta (SC-B) cells to replace the destroyed cells. Researchers have developed a protocol for *in vitro* differentiation of stem cells into insulin-secreting beta cells. This represents a significant advancement in the field of regenerative medicine as transplantation of the cells into diabetic rodents restores blood glucose regulation. While the transplanted cells function well, the SC-B cells are functionally immature before transplantation in that they lack adequate glucose responsiveness, as demonstrated through impaired glucose-stimulated insulin secretion (GSIS). Furthermore, SC-B cells express the maturation markers MafA and Ucn3 at significantly lower levels than functionally mature human islets. To identify compounds that induce SC-B cell maturation *in vitro*, we are running a fluorescence-based high-throughput screen using antibodies that detect the maturation markers MafA and Ucn3. This screen is fully automated through the use of robots for greater accuracy and efficiency. In preparation for the screen, we are running multiple technical tests to optimize MafA and Ucn3 antibody staining. Our initial tests suggest that the assay is accurate enough to identify compounds that increase MafA and Ucn3 expression. The addition of these compounds to the differentiation protocol may yield functionally mature SC-B cells with improved glucose responsiveness.

Anti-PD-L1 and Targeted Therapies as a Treatment Option for Triple-Negative Breast Cancer

Bethlehem Lulseged
PRISE Fellow
Human Developmental and Regenerative Biology, 2020

Dana-Farber Cancer Institute, HMS
Advisor: Kornelia Polyak
Mentor: Masa Aleckovic

Triple-negative breast cancer (TNBC) is difficult to treat because it lacks estrogen, progesterone and Her2 receptors which can be better targeted through hormonal therapies and anti-Her2 treatments. As a result, TNBC patients look to chemotherapy, radiation and surgery for treatment, even if these options are not always effective. However, due to the high levels of tumor-infiltrating lymphocytes (TILs) in TNBC, immunotherapy has been hypothesized to be an effective treatment option. Previous research has found that PD-L1, an immune response inhibitor, is overexpressed in a subset of TNBCs. When PD-L1 is repressed, patients have seen an increase in the response rate of cancer combatting immune cells. However, PD-L1 inhibition has only led to a 20% response rate, inciting interest in combining PD-L1 inhibition with other treatments. Previous experiments in our lab indicate that the combination of anti-PD-L1, targeted therapies and chemotherapy are effective in reducing breast cancer. In vivo models have been used to test the performance of various combinations of immunotherapies on the cancer cells. We used immunofluorescence, immunohistochemistry, and polychromatic flow cytometric analysis to characterize the tissues of the in vivo models to better understand how the immunotherapies, alone and in combination, affect the cancer and immune cell responses. Our preliminary results show a distinct difference in immune cell response rates between single and combination treatments. The triple treatment shows the greatest increase in the number of TILs. These results provide promise for greater use of immunotherapies in combination with targeted therapy and chemotherapy for TNBC patients.

Vitamin D Binding Protien Enhances Maturation of iPSC-Derived Cardiomyocytes

Gabriela O. Escalante
PRISE Fellow
Human Developmental and Regenerative Biology, 2021

Harvard Stem Cell Institute
Advisor: Richard T. Lee
Mentor: Jessica Garbern

Induced pluripotent stem cells (iPSCs) have the potential to regenerate injured cardiac tissue via transplantation. For use as a therapeutic treatment, iPSCs must first be differentiated into electrically mature cardiomyocytes. Using current protocols, iPSC-derived cardiomyocytes (iPSC-CMs) remain in an immature state similar to fetal cardiomyocytes, causing fatal arrhythmias in animal models. Given that previous studies have shown that the extracellular matrix (ECM) may promote maturation of iPSC-CMs, this study aimed to identify soluble factors in the cardiac ECM that promote cardiomyocyte maturation. High performance liquid chromatography was used to fractionate decellularized matrices of freshly harvested bovine hearts by molecular weight. iPSC-CMs were treated with decellularized fractions in culture for six days and then screened for expression of genes associated with maturation: CRYAB, ECHS, PDLIM5, and PYGM. Samples with the highest expression levels of these maturation genes were analyzed using mass spectrometry to identify possible proteins related to iPSC-CM maturation. Vitamin D binding protein (VDBP) was found to be associated with increased expression levels of maturation genes. Cultured iPSC-CMs were subsequently treated with VDBP for 6 days, with dosages ranging from 0.100 ng/mL to 10 ng/mL. Preliminary data revealed a dose-dependent increase in maturation gene expression following VDBP treatment, along with a 2.5-fold increase in cardiac troponin T (cTnT) and a 2-fold increase in myosin heavy chain 6 (MYH6) expression, both protein markers for contractile maturity. These data suggest that VDBP is a component of the cardiac ECM that enhances iPSC-CM maturation. This finding opens up the possibility to update current iPSC-CM protocols to include VDBP treatment, in order to produce more mature cardiomyocytes.

Identifying Pathways that Function in Connective Tissue Attachment Maintenance and Healing

Ozichi Osuoha
PRISE Fellow
Human Developmental and Regenerative Biology, 2019

Massachusetts General Hospital, HMS
Advisor: Jenna Galloway
Mentor: Marie-Therese Nödl

Tendon-bone attachment sites and ligament-bone attachment sites are known as entheses, which are unique structures that can withstand and efficiently transfer force from tendon to bone and bone to bone, respectively. Entheses are characterized by the type of tissue present at the skeletal attachment site: fibrous connective tissue or fibrocartilage. Fibrocartilaginous entheses comprise the majority of entheses found in the human body and are frequently injured. Studying attachment site repair in a regenerative and genetically manageable organism, such as the zebrafish, provides insight into how successful regeneration can be accomplished. The Galloway lab demonstrated that zebrafish tendons, such as the maxillary superficial tendon (MST), are analogous to mammalian tendons. Tenascin-C (tnc), an extracellular matrix protein with roles in cell proliferation, adhesion, and migration, is expressed and is thought to function in adaptation to compression at attachment sites. Previous experiments in this lab demonstrated that zebrafish *tnc*$^{hu3580-/-}$ mutants' MSTs fail to reattach to the maxillae after injury. However, upon further examination, it was shown that complete regeneration in *tnc*$^{hu3580-/-}$ mutants occurred. Accordingly, tnc does not play a role during enthesis healing and instead appears to affect the morphology of musculoskeletal connections. To test this, comparative injury assays and histological evaluations were performed to confirm that regeneration occurred and demonstrate that tnc is needed to establish tendon attachments. These findings improve the current fundamental understanding of enthesis biology, which is used to develop better regenerative medicine-based strategies to improve injury outcomes.

Function of Eya2 in Promoting Axolotl Limb Regeneration

Jose L. Martinez Fernandez
PRISE Fellow
Human Developmental and Regenerative Biology, 2020

Harvard Stem Cell Institute
Advisor: Jessica Whited
Mentor: Konstantinos Sousounis

More than two million Americans suffer from limb amputations due to injury or disease, and this number will double by 2050. However, approaches to therapeutic treatments could be found in the axolotl salamander's ability to regenerate complex body parts. Past experiments in which the axolotl was subjected to repeated amputations at the same plane have resulted in failed regeneration and the development of a stump, similar to a human amputee's. Downstream gene expression analysis revealed several pro-regenerative genes to be misexpressed including *eyes absent 2*, a phosphatase with known roles in promoting progenitor cell survival. The current hypothesis is that down-regulation of Eya2 induces a non-regenerate state by reducing the ability of limb cells to proliferate. To study its specific role during limb regeneration, *Eya2* expression was abolished by CRISPR Cas9-targeted genome editing. Animals confirmed not to express *Eya2* were subject to amputation and the effects on limb regeneration were studied using histological and biochemical methods. Further, visualization of *Eya2*-expressing cells was achieved by a CRISPR Cas9-targeted knock-in method whereby expression of the Cre recombinase was paired with *Eya2* in a lineage tracing-permitting genetic background. These animals would allow us to understand where and how Eya2 is expressed during homeostasis and regeneration. Collectively, these data will not only serve to clarify the previously unknown Eya2 genetic pathway within the axolotl salamander, but also to identify its function during appendage development and regeneration.

Asn297 Sequon Variation Effect on IgG Antibody Glycosylation

Marinna Okawa
SURGH Fellow
Human Developmental and Regenerative Biology, 2020

Ragon Institute
Advisor: Galit Alter
Mentor: Richard Lu

The hallmark of the adaptive immune system is its ability to produce millions of antibodies to recognise nearly any antigen. The antibody consists of two regions: Fab and Fc. The Fab works with the adaptive immune system to recognize the target antigen. The Fc region coordinates with the innate immune system as it recruits immune cells' Fc receptors and triggers an immune cascade. This Fc domain undergoes post-translational glycosylation, where a glycan (sugar) is attached to the Asn297 residue. The Asn297 sequon consists of Asn-X-Thr, where X is any amino acid except Proline. This project aimed to determine if the amino acid sequences surrounding the sequon affected which of the 30 different types of glycans would be added, since glycan identity affects the type of immune cell recruited.

59 IgG1 antibody plasmids were synthesized with variations in the amino acids surrounding the Asn297 sequon. These were grown in ampicillin-resistant bacteria. The DNA for each was isolated and put into a destination vector via Golden Gate Assembly, using a *Bsa1*-HF restriction enzyme to simultaneously insert the IgG variant, Variable Heavy, Variable Light, and Furin sequences into one plasmid. The resulting kanamycin-resistant plasmids were uptaken by bacteria via transformation. Transformants with the desired DNA sequence were cultured, and their DNA were isolated and transfected into mammalian cells. Antibodies produced were purified, and the identity of the glycans attached to the Asn297 residues were determined.

Successful completion of the proposed project could suggest that the amino acid pattern around the Asn297 sequon helps define glycosylation. Better understanding of these effects on antibody glycan identity could lead to the production of more efficient therapeutic antibodies able to recruit specific immune cells.

Effects of Aging and Tendon Anatomical Location on TSPCs

Ege Eskibozkurt
PRISE Fellow
Human Developmental and Regenerative Biology, 2019

Wyss Institute
Advisor: David Mooney
Mentor: Benjamin Freedman

Musculoskeletal injuries affect 33 million people in the United States per year, and 50% of these injuries involve tendons and ligaments. Although aging may contribute to tendon degeneration and injury, these effects depend on a particular tendon's type and its anatomical location in the body. However, the effects of aging on tendon stem/progenitor cells (TSPCs) from different anatomical locations (e.g., shoulder, knee, and ankle) has not been fully explored. The purpose of this study is thus to identify how aging and anatomical location affect TSPC properties. TSPCs are isolated from Fischer Brown Norway hybrid rats from young, middle, and old age (9, 18 and 28 months) and different anatomical locations (Achilles, patellar and flexor digitorum longus tendons). Isolated cells are cultured and prepared for flow cytometry to screen for markers of TSPCs (CD90, CD146 and CD44). A scratch assay is performed for assessing migratory abilities, and a β-galactosidase assay is used to evaluate senescence. Results of this study will show how ageing and anatomical locations affect TSPC behavior and provide insight into therapeutic applications of these TSPC populations in augment tendon healing.

Screening for Potential Mutations in *DLK1* associated with Central Precocious Puberty

Leo Garcia
PRISE Fellow
Undeclared, 2021

Brigham and Women's Hospital, HMS
Advisor: Ursula B. Kaiser
Mentor: Ana Paula Abreu

Puberty, or reproductive maturation, is regulated through the hypothalamic-pituitary-gonadal (HPG) axis, but the underlying pubertal regulation mechanisms within the HPG axis remain largely a mystery. People with altered pubertal timing face multiple health risks, including higher rates of obesity and cancer. The Laboratory of Reproductive Neuroendocrinology (LRN) has collected samples from patients with central precocious puberty (CPP), a type of early puberty, to identify genetic links to CPP. The LRN first identified mutations in *MKRN3* in this population. More recently, mutations in *DLK1* were identified in a family with CPP. In addition, *DLK1* has been shown to harbor single nucleotide polymorphisms linked with earlier menarche. We are now screening for mutations in our cohort of patients with CPP to find potential genetic links between *DLK1* and CPP. We first sequenced *MKRN3* in these subjects to confirm that there were no mutations in this gene, ruling it out as the cause of CPP in these subjects. Following this, *DLK1* was sequenced to screen for mutations which may lead to CPP. Preliminary data have not shown any significant variations; however, only 50% of the cohort has been sequenced and among these, the first exon has not yet been sequenced. There is a probability that a mutation may exist in the remaining samples or in the first exon. It is essential to continue to explore the mechanisms of pubertal timing to generate new or improve approaches for the diagnosis and treatment of CPP. Such treatments could prevent the negative long-term consequences of CPP, such as obesity, cancer, and psychological conditions.

Inhibiting Arginine Metabolism in Myelodysplastic Syndrome

Eliane Grace
PRISE Fellow
Human Developmental and Regenerative Biology, 2021

Harvard Stem Cell Institute
Advisor: David Scadden
Mentor: Nick Van Gastel

It has been demonstrated that arginase, an enzyme that breaks down arginine, has an immunosuppressive effect on cancers ranging from solid tumors to leukemia. Since T cells need arginine to proliferate, arginase can allow cancer to escape the immune system. Arginase inhibitors reduce tumor growth by preventing the depletion of arginine in the tumor microenvironment. We will investigate arginase protein levels in hematopoietic stem and progenitor cells (HSPCs) in wildtype and myelodysplastic syndrome (MDS) mouse models and test the effect of an arginase inhibitor on normal and MDS HSPCs. We used flow cytometry to determine arginase levels in the HSPCs of wildtype mice. We found clear levels of both Arginase 1 (ARG1) and ARG2 enzymes in HSCs, and the levels of both proteins are slightly higher in more committed multipotent and myeloid progenitors. We then investigated whether the levels of arginase differ in MDS and wildtype mice. Preliminary data suggest elevated protein levels of ARG1 and ARG2 in MDS HSPCs. We plan to repeat these experiments, increase the size of our experimental cohorts, and test different MDS models to confirm our preliminary findings. We will also determine arginase protein and arginine levels in the bone marrow plasma of wildtype and MDS mice using ELISA and mass spectrometry, respectively. If differences can be confirmed, we will target arginase activity using an arginase inhibitor and test whether this can impair MDS progression in an animal model. If we are successful, our findings could lead to the first metabolic treatment for patients with MDS.

Implications of Hormesis in PC9 Cancer Cells

Sophie Heritage
PRISE-Emmanuel Fellow
Medicine, 2019

Harvard Stem Cell Institute
Advisor: Lee Rubin
Mentor: Methodios Ximerakis

Hormesis is a biological phenomenon whereby a beneficial effect (e.g. stress tolerance, growth, longevity) results from exposure to low doses of an agent that is otherwise toxic or lethal when given at higher doses. The significance of hormesis on sensitivity of PC9 cells, a human non-small lung cancer cell line, to chemotoxic agents is largely unknown. We cultured PC9 cells under standard conditions and measured their viability upon exposure to different doses of two well-known chemotherapeutics agents: etoposide, a topoisomerase inhibitor, and gefitinib, an epidermal growth factor receptor inhibitor. Once a lethal dose had been determined, varying low doses were tested prior to lethal dose application of the chemotherapeutics to observe whether there were protective effects that prevent cell death and increase proliferation. Cell viability, toxicity, and proliferation were determined by immunocytochemistry and imaging. Cells were stained with calcein (metabolized by live cells), ethidium homodimer 1 (labels the nuclei of dead/dying cells), and a Ki-67 antibody that labels proliferating cells. Cell counting was performed using an Operetta automated microscope. If low drug doses confer PC9 resistance to normally lethal doses, further research would involve transcriptomic/proteomic studies on the resistant cancer cell lines to assess mechanisms of resistance. Therapeutically, improved understanding of chemotherapeutic resistance may improve drug regime efficacy and direct development of better drug targets.

The Effect of Smyd1 on Sarcomere Structure and Proliferation of Neonatal Cardiomyocytes

Karen Reyes
PRISE Fellow
Molecular and Cellular Biology, 2019

Harvard Stem Cell Institute
Advisor: Richard T. Lee
Mentor: Vinicius Bassaneze

Newborn mice and rats have been observed to have the capacity to regenerate heart tissue after injury, however, they lose this ability soon after birth. In neonatal mice, the primary mechanism of heart regeneration is via dedifferentiation and proliferation of existing cardiomyocytes.

This increased proliferation is accompanied by an observed disassembly of the sarcomere which is a key component of cell structure. Despite this observation,the direct regulators of the disassembly and re-entry into the cell cycle remain unsolved. The SMYD1 protein has been shown to be critical for cardiac development and sarcomere formation in cardiomyocytes.We hypothesize that SMYD1 modulation interferes with rodent cardiomyocyte proliferation. Lentiviral vectors for SMYD1 overexpression and downregulation with shRNA were employed in four different cell culture media conditions in order to test this hypothesis. Cell proliferation was measured by flow cytometry using cell cycle and DNA synthesis markers. Our data show that when either NRG1 protein or 10% FBS were present in cell culture media, around 20% of cells incorporated the DNA synthesis marker after 24h, however, in the presence of any lentivector, including a control vector driving mCherry fluorophore expression, about 5% of cells incorporate the DNA synthesis marker. Our results indicate that it is possible to modulate SMYD1, but an unknown factor causes an inhibitory effect on proliferation.

These steps toward developing a more complete understanding of the transcriptional factors and mechanisms that play a role in this observed regeneration have the potential to lead to therapeutic strategies to treat patients who have suffered heart failure.

Investigation into the Regulation of the Maternal to Zygotic Transition in Parhyale Hawainesis

Robert Appleby
PRISE-Emmanuel Fellow
Biochemistry, 2019

Organismic and Evolutionary Biology
Advisor: Cassandra Extavour
Mentor: Leo Blondel

The Maternal to Zygotic Transition (MZT) is a fundamental process in animal embryonic development. During MZT, the embryo is released from the maternal gene regulation program and the zygotic genome becomes activated and regulates the remainder of embryogenesis. There are a number of proposed molecular mechanisms that control the MZT, and current research suggests they work in conjunction. The amphipod crustacean Parhyale hawaiensis is a rising model organism used for research into limb regeneration, cell biology and embryogenesis. Cells of an animal embryo typically undergo the MZT in synchrony; we have chosen P.hawaiensis to study the MZT because our preliminary data suggests that, unusually, different cells of the embryo may undergo this transition at different times throughout development. When the genome becomes activated, RNA polymerase II (Pol II) switches from a transcriptionally inactive to active state through phosphorylation of the C-terminal domain (CTD). Observing the phosphorylation state of Pol II may therefore be a reliable proxy for following the progression of the MZT in different cells. The goal of this project is to determine the state of Pol II phosphorylation in the embryonic cells of P.hawaiensis throughout early development. I plan to compare these data with previously established cell lineage data, to try to identify properties that may regulate the activation of the zygotic genome. I aim to determine whether the MZT takes place in cells according to a recognizable pattern (for example, cell lineage or number of divisions), or whether the transition is a stochastic process. Research into the MZT expands current understanding of how genomes are regulated, which is vital not only for developmental biology but also benefits diverse fields of study such as cancer biology and biotechnology.

HUMAN EVOLUTIONARY BIOLOGY

The Role of IAP in The Observed Beneficial Effects of Exercise in Murine Models of Colitis

Matthew Z. Farber
PRISE Fellow
Human Evolutionary Biology, 2019

Massachusetts General Hospital, HMS
Advisor: Richard Hodin
Mentors: Robin Vasan, Fatemah Adiliagheam

Exercise has been linked to improved conditions in IBD patients, but published literature is inconsistent and nonspecific in regard to the mechanism and degree to which exercise is beneficial. Intestinal Alkaline Phosphatase (IAP) is a brush border enzyme shown to have beneficial effects in murine models of colitis. After 5 weeks of exercise (EX) or no exercise (NEX), mice were fed DSS in their drinking water to induce colitis. Preliminary findings indicate that EX mice were less susceptible to weight loss, an indicator of colitis, than NEX mice, suggesting that exercise helped diminish the symptoms of colitis. If further analysis of certain inflammatory cytokines such as TNF, IL6, and IL1b reveals greater inflammation in NEX mice, this will be strong evidence that exercise helps protects against colitis. Histological analysis of colon samples will show the degree to which exercise prevents inflammation in the colon. If stool samples in EX mice show higher levels of IAP expression than NEX mice, IAP might be the mechanism through which exercise is improving colitis condition. If further research studying the effects of exercise in colitis-induced IAP knockout mice showed no change between EX and NEX mice, IAP could be considered a critical component of the beneficial effects of exercise.

Cortisol, Testosterone, and Online Mating Rejection

Nicola Young
PRISE Fellow
Human Evolutionary Biology, 2019

Psychology
Advisor: Max Krasnow

Research indicates that human cortisol and testosterone levels increase in response to in-person, mating-relevant interactions. In the modern, social media-dominated dating culture, an important next step is to evaluate hormonal responses to online mating interactions, particularly in the face of rejection. This study examined the effect of feedback after an online dating simulation on salivary testosterone levels in males and salivary cortisol levels in both males and females. Groups of up to eight same-sex, heterosexual adults between the ages of 18 and 26 came to the laboratory, provided baseline saliva samples, completed questionnaires about predictors of cortisol reactivity, and created dating profiles, including an on-site photograph. Next, they rated profiles from members of the opposite sex, supposedly belonging to participants in a separate room who were simultaneously rating them. The subjects then received positive, negative, or no feedback at all on their own profiles and, after a brief waiting period, provided a second saliva sample. Data collection is currently active, but salivary hormone analysis (EIAs) will not be conducted until the study is complete (N=180). An increase in cortisol with online evaluative social interactions, regardless of feedback condition, could give insight into the role the HPA-axis plays in cyber-bullying induced mental illness. Alternatively, a lack of cortisol and testosterone reactivity in the face of rejection may help explain the cultural transition toward online dating.

Barefoot versus Shod: How Footwear Affects the Anatomy and Walking Biomechanics of the Longitudinal Arch

Lourdes Kaufman
PRISE Fellow
Human Evolutionary Biology, 2019

Human Evolutionary Biology
Advisor: Daniel Lieberman
Mentor: Nicholas Holowka

The longitudinal arch (LA) is a vital anatomical structure that stiffens the foot during walking. Approximately one-third of people in habitually shod (daily shoe-wearing) populations suffer from flat foot. Flat foot occurs when the LA is either absent or lacks the stiffness necessary to maintain its shape during propulsion, impairing gait and often causing pain. Previous studies have shown that habitually shod individuals are more likely to suffer from flat foot than minimally shod (unsupportive sandal-wearing) or barefoot individuals, but the relationship between muscle size and dynamic LA stiffness during propulsion are unknown, especially in barefoot individuals. In this study, we examined how being habitually barefoot versus shod affects the anatomy and walking biomechanics of the foot. We collected data in two distinct areas within a single Kalenjin-speaking population in Kenya: Eldoret, a habitually shod population, and Pemja, a habitually barefoot population. We are currently measuring changes in LA height during walking by tracking markers placed on 5 anatomical locations on the foot and leg in videos of participants walking using the DLTdv5 program in MatLab. We are also measuring the size of the Flexor Digitorum Brevis and Abductor Hallucis muscles by analyzing ultrasound images taken of participants' feet. We predict the barefoot group will have a higher LA that is dynamically stiffer during stance phase, as well as proportionally larger AH and FDB muscles. Testing this hypothesis has implications for the treatment and prevention of flat foot: if correct, strengthening the foot muscles rather than wearing arch support could be a more effective intervention, and wearing minimal shoes could prevent flat foot.

Examining the Relationship between the Gut Microbiota and the Total Phenolic Content of Wines

Brandi Moore
PRISE Fellow
Human Evolutionary Biology and Integrative Biology, 2019

Human Evolutionary Biology
Advisor: Rachel Carmody
Mentor: Katia Chadaideh

Polyphenols are abundant compounds found in plants, and there is increasing evidence for their anti-inflammatory, antioxidant, and anticarcinogenic potential. Red wine is documented to have high polyphenol levels and is associated with prevention against chronic health conditions. Polyphenols are poorly absorbed into circulation, raising the possibility that the link between the consumption of polyphenol-rich food and protection against chronic pathologies is mediated through the gut microbiota. This study explores this potential relationship by assessing total phenolic content (TPC) in several wines to identify a candidate for future *in vitro* and *in vivo* experimentation.

The Folin-Ciocalteu assay was used to quantify TPC in samples of white wine, rosé, and several red wines. Absorbance levels of samples were read using optical density measured at a wavelength of 726nm and TPC was determined using a calibrated, standard curve.

As predicted, red wine samples had higher TPC than white wine and rosé. The red wines with the highest TPC were an Italian blend, a Californian Pinot Noir, and a Madiran wine, each with TPC of approximately 137mg/100ml. Madiran wine was selected for further experimentation because it is produced from tannat grapes, a grape variety with high phenol content and a reputation for fortifying health. Future experiments will examine the relationship between Madiran wine and the growth of various microbial strains *in vitro*, and the impact of Madiran wine consumption on the mouse gut microbiota *in vivo*. From this, the connection between the gut microbiota, polyphenols, and red wine's therapeutic potential can be further understood.

INTEGRATIVE BIOLOGY

Changes to the Plant Microbiome During Pathogen Infection

Laura Jenny
PRISE Fellow
Integrative Biology, 2021

Integrative Biology
Advisor: Naomi Pierce
Mentor: Lori Shapiro

Plants serve as hosts to complex communities of microbes. These plant-associated microbial communities, the microbiome, can be used to understand how beneficial microbes contribute to host immunity and susceptibility to pathogens. To better understand the interaction between the microbiome and responses of hosts to pathogens, we performed a common garden experiment in which we inoculated cucumber (*Cucumis sativus*) and crookneck squash (*Cucurbita pepo*) with the bacterial plant pathogen, *Erwinia tracheiphila*, or *Et*, which causes bacterial wilt of cucurbits, which only infects squash, cucumber, and melon plants in eastern North America. We sampled microbial communities from the leaf, stem, root and blossoms of untouched control plants and *Et* inoculated plants at three times: (1) the time of inoculation, (2) when first wilt symptoms appeared, and (3) when the whole plant was symptomatic (immediately before plant death). We then used 16S barcode sequencing to investigate how microbial communities change during host disease. Through this project, we aim to discover whether single microbes or microbial communities are associated with resistance to *Et*. As one of the first studies of its kind, this research will provide a conceptual foundation for understanding the connection between the plant microbiome and plant health, which is be relevant for developing new methods of pathogen resistance in agriculture.

Long-Term Experimental Changes in Microbiota confers Non-Mendelian Inheritance in *Nasonia vitripennis*

Mushtaaq Ali
PRISE Fellow
Integrative Biology, 2021

Rowland Institute at Harvard
Advisor: Robert Brucker
Mentor: Guan-Hong Wang

Microbe symbionts play important roles in a host's life and previous experiments have studied host-microbiome interactions in response to environmental pressure. Previous hybridizations of different species of the jewel wasp, genus *Nasonia*, resulted in hybrid lethality, a biological speciation phenotype, due to host and gut bacteria incompatibilities. Currently, we are working to understand the role of the microbiome in speciation when a population of the *Nasonia vitripennis* is fed atrazine, an herbicide, for many generations. Several ongoing experiments will determine the phenotypic and genotypic results of this environmental pressure. So far, experiments indicated that hybridizations of the atrazine and control populations led to increased lethality for certain populations, specifically those with a hybridized genome but a control microbiome, demonstrating possible hybrid incompatibility. To determine the origin of this post-zygotic incompatibility in earlier generations, follow-up experiments involving the revival of "living fossils" of previously refrigerated generations will be conducted. Additionally, by genotyping the wasps and isolating bacteria in the microbiome that are found to degrade atrazine, we are trying to better understand the genomic basis for this divergence in the host genes as well as within the microbiome. Through these experiments we seek to understand the microbiome's role in the evolution of the host species.

A Population Genomic Analysis of Cryptic Speciation in Thrushes (Aves: Turdidae)

Johnathan Clark
PRISE Fellow
Integrative Biology, 2019

Integrative Biology
Advisor: Scott Edwards
Mentor: Flavia Termignoni Garcia

A cryptic species complex may evolve either if speciation occurred too recently for the accumulation of morphological differences between incipient species or if strong stabilizing selection is acting on the species to prevent the appearance of outward variation. The gray-cheeked thrush (*Catharus minimus*) and Bicknell's thrush (*Catharus bicknelli*) are two songbird species native to eastern North America that comprise a cryptic species pair, distinguishable in the field only by differences in song and interspecific differences in breeding habitat and wintering sites. While the gray-cheeked thrush nests in low-altitude inland taiga and winters in northern South America, Bicknell's thrush nests in temperate montane forest and winters in the mountains of Hispaniola. The species were considered conspecific until 1998 and biomolecular data suggests that they are each other's closest relatives. The *C. bicknelli – C. minimus* complex may therefore offer an opportunity to observe ongoing adaptation during speciation. We are currently sequencing whole genomes for each species using the Ilumina 10x platform and the ALLPATHS-LG assembler. These reference genomes will provide a foundation for a population resequencing study to identify genomic regions showing unusual patterns or degrees of divergence between the two species, with the goal of finding regions that show evidence of selection in only one of the species. Regions of particular interest include loci associated with hypoxia mitigation, cold tolerance and long-distance flight, given the extended open-ocean route that Bicknell's thrush follows during migration. Ultimately, this study may improve our understanding of speciation in the absence of strong morphological or plumage differences.

A High-Resolution Spatial Analysis of Microbes in Sediment

Isabella Colocci
PRISE Fellow
Integrative Biology, 2019

Organismic and Evolutionary Biology
Advisor: Peter Girguis
Mentor: Jeffrey Marlow

To fully understand the ecology of microbial sediment, it is necessary to preserve micro-scale spatial relationships because they may shape the microbial environment and dictate microbial metabolic activities. Interactions between microbes can allow more efficient use of resources, enable the development of new metabolisms, and drive evolutionary changes. Established microbiology techniques do not allow preservation of micro-scale spatial information. We combined the use of bioorthogonal non-canonical amino acid tagging (BONCAT) and fluorescent *in situ* hybridization (FISH) to identify active bacteria within sediment samples. Live cell imaging followed by sediment fixation and FISH allowed us to directly observe co-occurrence and movements of individual bacteria. Preliminary development and testing of these techniques in lab samples has been successful. We now plan to progress to *in situ* experiments at the Sippewissett salt marsh, Falmouth, MA. The results obtained will provide much-needed data about the ecology and potential interactions between microbes and offer a more realistic view of the microbial communities that modulate elemental fluxes on a global scale.

A Greater Resolution Analysis of Pfs47 in *Plasmodium falciparum* in Madagascar

Kevin Bao
PRISE Fellow
Integrative Biology, 2019

Integrative Biology
Advisor: Dan Hartl
Mentors: Ben Rice, Jenny Pham

Malaria is responsible for almost half a million deaths each year, predominantly in the Global South. Despite successful reduction in malaria incidence since 1950, progress has plateaued in many regions, and in Madagascar, prevalence has actually increased. Contemporary control techniques focus on targeting the vectors through genetic sterilization and improving drainage. However, there is still much to learn about the /textitPlasmodium parasite's evolutionary history. In particular, the Pfs47 gene codes for a 6-cysteine surface protein which is believed to be involved with mosquito immune system evasion. Previous studies have not only established this gene as an important candidate in parasite-focused control options, but also shown that it possesses broad and potentially adaptive polymorphism across global regions and mosquito vectors. This study aims to provide a higher resolution analysis of Pfs47 diversity and evolution by focusing on recently acquired genetic data from Madagascar, an island notable for its geological and anthrpological histories. By sequencing these samples and placing them into existing malaria phylogenies, we can begin to understand the significance of the diversity in Pfs47. At the confluence of these eclectic factors, we hope to discover what adaptations /textitP. falciparum possesses. With a greater understanding of the evolutionary and adaptive history of malaria, we hope to gain greater insight into further control methods for the disease.

The Biomechanics of Leg Extension in Jumping Spiders

Lincoln Sorscher
PRISE Fellow
Slavic Languages and Literatures, 2021

John Harvard Distinguished Science Fellowship
Advisor: Paul Shamble

There are more species of jumping spiders than any other arachnid family on the planet, and jumping is a fundamental aspect of their evolutionary success. Although jumping is the primary movement for hunting and general mobility in the salticid family of jumping spiders, the physics behind exactly how salticids maneuver their legs to power their jumps remains largely unaddressed. Through video analysis of spiders jumping, we aim not only to keenly observe these leg extensions, but also to model the spiders' trajectories through inverse dynamics. We specifically analyze the launch portion, the most predictive and physically concise aspect of the entire jump sequence and hope to use our results as inputs into the flight portion of the jump. Modeling solves a variety of overlooked biomechanical problems. Our data adds to discussion about spiders' unique use of a hydraulic mechanism to jump. With acceptable biomechanical assumptions and anatomical information from spider CT scans, musculature requirements reveal the degree to which salticids rely on hydraulics. Additionally, models provide a unique lens through which we can understand how these mechanisms compare to the resilin-based, elastomerically powered jump common among leaping insects. Interpreting the physics behind how jumping spiders launch themselves yields both a wealth of biomechanical and comparative zoological information and a pipeline for scanning and modeling locomotion in other exoskeletal organisms.

The Evolution of Visual Defensive Behavior in Ecologically-Diverged Deer Mice

Victoria Tong
PRISE Fellow
Neurobiology, 2020

Organismic and Evolutionary Biology
Advisor: Hopi Hoekstra
Mentor: Felix Baier

Deer mice (genus *Peromyscus*) are the most widespread mammalian genus in the United States and have colonised many diverse ecological habitats. Geographically closer species are more genetically related, however, selective pressures have forced closely-related species to adapt both physically and behaviorally to their different habitats, making *Peromyscus* an ideal model for studying evolution. Defensive behaviors are of particular interest, as well-developed defensive behaviors are critical to survival and are thus under strong selective pressure.

We investigated defensive behaviors across six forms of *Peromyscus*. Mice were exposed to a visual stimulus displayed on a screen above an arena with a shelter. The stimulus comprised a dark circle moving from a corner (sweeping) and then rapidly expanding in the center of the screen (looming), to imitate a bird cruising and then diving on the mouse. Four subspecies were forest-prairie pairs: one pair from the East Coast, and another from Oregon. Eastern prairie mice exhibited the most robust response: they froze during sweeping and fled to the hut during looming. Western prairie mice exhibited a similar but less robust response. Both forest subspecies mostly froze for sweeping and did not flee for looming. These results are consistent with expectations as aerial predators are a larger threat for prairie mice. While tests on the two beach mice forms are ongoing, preliminary results and existing literature suggest that they will behave similarly to the forest mice.

Future studies will aim to further understand the evolution of these defensive behaviors and elucidate the molecular, genetic, and neural mechanisms governing them.

MATHEMATICS

Representations of $\mathrm{SL}_2\,\mathbb{C}$

Serina Hu
PRISE Fellow
Mathematics, 2021

Mathematics
Advisor: Joseph Harris

Representation theory is a branch of mathematics that can connect many fields within mathematics as well as describe concretely certain symmetries of a system in physics and chemistry because of its ability to express an abstract symmetry group in terms of linear maps on certain vector spaces. One such symmetry group that can be considered is the special linear group $\mathrm{SL}_2\,\mathbb{C}$, which is the set of maps that preserve volume and orientation in $\mathbb{C}^2$. All representations of $\mathrm{SL}_2\,\mathbb{C}$ can be decomposed into so-called "irreducible" representations (just as every integer can be written as a product of primes). These irreducible representations can all be identified by considering the local structure of $\mathrm{SL}_2\,\mathbb{C}$, which is its Lie algebra $\mathfrak{sl}_2\mathbb{C}$. The Lie algebra itself has representations that we can classify by first considering only the action of the diagonal matrices of $\mathfrak{sl}_2\mathbb{C}$, then the actions of the remaining components. These representations were discovered to have a particularly elegant classification as symmetric powers of the standard representation of $\mathrm{SL}_2\,\mathbb{C}$. The techniques used can generalize to the semisimple Lie groups, which include the matrix symmetry groups that appear in other parts of math and the physical sciences.

On Distributions Corresponding to Seifert Matrices of Genus 1 Knots

Filippos Ilarion Sytilidis
PRISE Fellow
Mathematics and Physics, 2020

Mathematics
Advisor: Alison Miller

Classical knot theory, the study of smooth embeddings of S^1 in S^3, has found remarkable connections to many fields of mathematics and physics. These connections arise from knot invariants, mathematical objects that distinguish knots and thus constitute a vital part of knot theory. We will examine connections between knot theory and number theory by studying the Alexander invariants and the Seifert matrix of a knot. Albeit not a knot invariant itself, the Seifert matrix contains rich topological and arithmetic data. In particular, there exists a correspondence between equivalence classes of Seifert matrices of genus 1 knots and equivalence classes of binary quadratic forms. This correspondence, by elementary results from the reduction theory of binary quadratic forms, induces a map between Seifert matrices and points in the fundamental domain of the upper-half complex plane and, therefore, associates families of genus 1 knots to distributions of points in the complex plane. Moreover, the Seifert matrix completely determines the Alexander module and the Blanchfield pairing of a knot, thus giving rise to a distribution of points for each pair of those invariants. We present and analyze such distributions associated to families of genus 1 knots and to pairs of Alexander module with Blanchfield pairing corresponding to Alexander polynomial of the form $mx^2 + (1 - 2m)x + m$. These distributions might, upon successful completion of the project, suggest conjectures regarding characteristics of the considered knot families and the Blanchfield pairing that could give more insight in the connections between the topological and the arithmetic approach to knot theory.

Toward the K-Theoretic Classification of Topological Materials

Cameron Krulewski
PRISE Fellow
Mathematics and Physics, 2019

Mathematics
Advisor: Michael Hopkins

In algebraic topology, we are interested in properties of spaces that are preserved by continuous deformation. Intuitively, two spaces are topologically equivalent if they can be squished into each other's shapes. However, for complicated, higher-dimensional spaces, this intuition does not get us very far. A more powerful method of distinguishing topological spaces and discerning their properties is to assign algebraic invariants to them.

This project focuses on a particular invariant known as K-theory and its connections to analysis via index theory. My goal is to understand the constructions linking K-theory with operator analysis and to elucidate their physical interpretations. Roughly speaking, one forms the K-theory of a space X, denoted $K(X)$, by considering what kinds of continuously-varying vector spaces can be formed over X. Considered as subspaces transformed by operators parameterized by X, these vector spaces can tell us about the properties of the operators. For example, they depend on the symmetries of a Hamiltonian operator associated to the surface of a topological material, and thus convey physical information about its topological phase. In materials physics, this correspondence is beginning to be applied to study topological insulators and superconductors, allowing researchers to describe their material properties using K-theory.As mathematicians and physicists make this K-theoretic classification more comprehensive and rigorous, it may become a tool for improving the design of topological materials.

MOLECULAR AND CELLULAR BIOLOGY

Toward a Scalable Strategy for Human Genome Recoding

Stephen Casper
PRISE Fellow
Integrative Biology, 2021

Harvard Medical School
Advisor: George Church
Mentor: Eriona Hysolli

Cellular recoding refers to the editing of a cell's coding DNA and translational machinery to alter its codon use and genetic code without modifying the proteome. It has been a significant goal in synthetic biology for its applications in viral resistance, biocontainment, and the creation of cellular chassis for reengineering the genetic code. Despite this potential, recoding has proven challenging, principally due to the scale of editing required and complications from large-scale codon substitution, and while previously demonstrated in *E. coli*, recoding has never been undertaken on a genome level in Eukarya. We aim to investigate methods for recoding human cells toward the goal of creating a fully-recoded cell line. We are designing a feasible set of codons to replace and experimenting with recoding several genes in the Y chromosome toward a better understanding of effective recoding strategies involving base-editors, TALENs, CRISPR-Cas9, recombineering, and multiplexed automated genome engineering. As has been observed in *E. coli*, we expect human cells to be generally, though not completely, robust to codon substitution. We anticipate significant challenges from the scalability of current editing technologies, incompletely characterized human genes and tRNAs, and the challenge of verifying correct protein translation from recoded genes.

Exploring SREBP Inhibitors' Therapeutic Potential via Fluorescence Polarization and Protein Structure Determination

Weimer Macuri-Espinoza
PRISE Fellow
Molecular and Cellular Biology, 2020

Dana-Farber Cancer Institute, HMS
Advisor: Haribabu Arthanari
Mentor: Andras Boeszoermenyi

As efforts to develop effective treatments for cancer continue, one promising solution lies within mammalian cell metabolic pathways. In these pathways, the sterol regulatory element binding protein (SREBP) family is a group of transcription activators that regulate cholesterol and fatty acid homeostasis. If these regulatory proteins are properly inhibited, then faster growing cells, such as those in tumors, can be targeted by using these inhibitors as a treatment method. Furthermore, because the SREBP family is involved in regulating lipid homeostasis, finding effective SREBP inhibitors seems to be a promising source for treating lipid-related and metabolism-related diseases. In order to find effective drug candidates, over 300 candidates went through fluorescence polarization (FP) assays. Ten to twenty candidates that properly inhibited a certain domain of a type of SREBP in the FP assays were then chosen for additional characterization. This characterization was performed via nuclear magnetic resonance (NMR) spectroscopy and X-ray crystallography. Preliminary results indicated that the ten to twenty selected drug candidates inhibited SREBP binding activity *in vitro*. Findings from NMR spectroscopy and X-ray crystallography served to further inform protein structure and the efficacy and potency of SREBP inhibition *in vitro* caused by the drug candidates. Further work remains to determine the effect of these inhibitors *in vivo*, but with an ever increasing body of knowledge, SREBP inhibitors have promising potential in the realm of drug discovery.

Bacterial Colonization of the Maternal Reproductive Tract

Courtney Lewis
PRISE Fellow
Molecular and Cellular Biology, 2019

School of Public Health
Advisor: Grace Chan
Mentor: Oludare Odumade

Neonatal sepsis is a significant cause of infant mortality in developing countries. Bacterial colonization of the maternal reproductive tract is associated with sepsis in newborn infants. The goal of this study is to explore the prevalence of reproductive tract bacterial colonization among pregnant women in Ethiopia and describe the distribution of bacterial species among colonized women. Data collectors utilized cotton swabs to collect vaginal samples from pregnant women prior to delivery. Vaginal swabs were cultured on agar, and isolated bacteria were identified. The frequency of maternal colonization by different species of bacteria was calculated using STATA 15. Preliminary results indicate that 83.9% of women in the study were colonized. The most common pathogens were *Escherichia coli* (33.25%), Coagulase-Negative Staphylococci (14.43%), and *Staphylococcus aureus* (8.68%). Further investigation of the association between bacterial colonization and neonatal sepsis is needed to understand the risk of colonization on sepsis.

Using Population Genetics to Track the Spread of *Plasmodium falciparum* in Two Regions of Senegal

Ruth Hailu
SURGH Fellow
Human Developmental and Regenerative Biology, 2021

School of Public Health
Advisor: Dyann Wirth
Mentor: Rachel Daniels

Over 3.2 billion people live in areas with high risk of malaria transmission. In 2016, malaria caused about 216 million clinical episodes and 445,000 deaths in 106 different countries, an increase from previous years of dramatic declines. With a shifting focus in countries approaching pre-elimination status to tracking regional transmission of malaria, genetic signals can be used to map transmission across specified areas and populations. These methods were used to compare transmission characteristics in two regions of Senegal, Thies and Kedougou, areas of low and high transmission, respectively. A total of 251 dried blood spots containing parasites collected from patients seeking treatment for suspected malaria infection in these two regions were genotyped using a 24-single nucleotide polymorphism molecular barcode. These barcodes were compared to analyses of previous samples in these clinic sites between 2006-2015. Previously, from 2006-2010, the epidemiological model based on the genetic data strongly suggested a reduction in transmission. However, in 2012 the data suggested the occurrence of a rebound in transmission. The rebound was not found to be reversing until 2014. Our study builds on these pre-existing observations and explores dynamic changes in parasite populations during 2017 by assessing three different population characteristics: polygenomic and monogenomic proportions, clonal clusters, and longitudinal persistence. Based on our results, national malaria control programs will be able to identify dominating populations of parasites in specific regions and make programmatic changes to target therapies for at-risk populations.

Examining Cardiomyocyte Signaling Pathways and Myofibril-Associated Regulators using *in vivo* Proximity Labeling

Rachelle Ambroise
PRISE Fellow
Chemical and Physical Biology, 2021

Boston Children's Hospital, HMS
Advisor: William T. Pu
Mentors: Yuxuan Guo, Blake Jardin

Contractile dysfunction of cardiomyocytes (CMs) causes dilated cardiomyopathy. In some inherited forms of dilated cardiomyopathy, mutations in myofibrillar and sarcomeric genes impair the function of essential components of myofibrils, elongated filaments responsible for CM contraction. However, the exact mechanisms by which these mutations cause dilated cardiomyopathies are largely unknown. One such sarcomeric gene, *ACTN2*, encodes α -actinin 2 protein, which anchors myofibril actin filaments to the sarcomere Z-line to organize the sarcomeric structure. To examine the contributions of ACTN2 to CM contractile performance, we inactivated *ACTN2* in a low fraction of cardiomyocytes in the neonatal mouse heart. *ACTN2* ablation caused myofibrillar disorder and broadly dysregulated cardiomyocyte gene transcription. This observation led us to hypothesize that ACTN2 participates in signal transduction pathways that regulate gene expression. To investigate this hypothesis, we ventured to identify proteins located in close proximity to ACTN2 using the BioID2 proximity labeling apparatus, which localizes a promiscuous biotin ligase (BirA*) to the region of interest by fusing it to a target protein to thus biotinylate proteins within 10 nm. We fused BirA* to ACTN2 and verified that the fusion protein mediates *in vivo* biotinylation of proximal proteins through western blot analysis of heart lysates. In the future, biotinylated proteins will be purified by streptavidin pull-down and mass spectrometry-based protein identification. Successful completion of this project may enhance our understanding of myofibrillar signaling and the pathogenesis of dilated cardiomyopathy.

Homophilic Specificity of Clustered Protocadherin Interactions

Brenda Chiang
PRISE Fellow
Molecular and Cellular Biology, 2019

Molecular and Cellular Biology
Advisor: Rachelle Gaudet
Mentor: Elizabeth May

Neuronal development includes a process of dendritic self-avoidance mediated by a family of membrane proteins called clustered protocadherins. Each neuron expresses a unique subset of the more than 50 clustered protocadherin variants, or isoforms, in the human genome. Highly specific homophilic interactions between clustered protocadherins of the same isoform allow neurons to recognize interactions between dendrites from the same cell. The homophilic specificity of clustered protocadherin interactions, combined with the stochastic expression of a unique set of isoforms in each individual neuron, is critical for the proper development of neuronal networks. Previous work by the Gaudet Lab used molecular dynamics simulations to identify pairs of interacting residues at the homophilic binding interface and statistical energy models to predict residue pairs with higher interaction energies, and therefore higher energy contributions to homophilic specificity. By mutating residues involved in higher energy pairs, we hypothesize that a given isoform, isoform 1, can be engineered to stop binding to itself and instead bind to a different isoform, isoform 2, forming a heterodimer. We are currently performing cell aggregation assays, in which we expect cells expressing the mutant isoform to aggregate with cells expressing isoform 2 – through cell-surface protocadherin interactions – but not with cells expressing isoform 1. This result would confirm our model's ability to predict the interaction energies of specific residues in protocadherin isoforms, as well as deepen the understanding of molecular level interactions that contribute to protein-protein interaction specificity.

Role of c-type Natriuretic Peptide in Suppressing VEGF-Mediated Angiogenesis in Diabetic Retinopathy

Brandon Duffy
PRISE Fellow
Integrative Biology, 2020

Schepens Eye Research Institute
Advisor: Leo Kim
Mentor: Angie Sanchez

Diabetic retinopathy (DR), a diabetes-induced medical condition that damages blood vessels in the retina, is the leading cause of blindness in adults in the United States. Vascular endothelial growth factor (VEGF) experiences elevated levels in the eyes of diabetic patients and is responsible for the aberrant blood vessel growth and blood retina barrier leakage seen in DR. DR is commonly treated with anti-VEGF agents; however, these drugs have questionable effectiveness and may have severe side effects. Natriuretic peptides are a family of hormones that regulate vascular tone and fluid balance. Studies have shown that atrial natriuretic peptide (ANP) can reverse the adverse effects of VEGF on the retina. However, studies have also suggested that C-type natriuretic peptide (CNP) may be a more potent treatment than ANP. This study investigates the role of CNP on reducing the effects of VEGF in diabetic retinopathy both *in vitro* and *in vivo*. In preliminary tests of the effect of CNP *in vitro*, human retinal endothelial cells were treated with CNP and VEGF. Proliferation and scratch-wound migration assays were used to determine the effect of CNP on blood vessel formation in tissue culture. Preliminary data from these assays suggest that CNP may reduce cell growth in the presence of VEGF. While these results are not statistically significant, they demonstrate the potential of CNP as a treatment for diabetic retinopathy.

The Effect of Compound X on Wild-type and P23H Mutant Opsin Cells

Esther Elonga
PRISE Fellow
Chemistry, 2021

Broad Institute
Advisor: Anna Greka
Mentor: Moran Dvela

Retinitis pigmentosa (RP) is the most common inherited retinal degenerative disease characterized by loss night vision in adolescence, side vision in young adulthood and central vision later in life. More than 50 genes contributing to this disease have been identified; however, the most common autosomal dominant mutation in North America is a P23H mutation in rhodopsin, the light sensitive protein of rod photoreceptors. This mutation-inducing substitution of proline with histidine leads to a misfolding of opsin that accumulates in the endoplasmic reticulum (ER), and acquires a toxic gain of function leading to photoreceptor cell death. We are studying the effects of an identified compound X in cells expressing either wild-type (WT) or P23H mutant opsin, tagged with a C-terminal green fluorescent protein (GFP). The effect of the compound is studied by following GFP fluorescence over time. After treatment with the compound, we detected no change in the levels of the WT protein. However, cells expressing P23H mutant opsin showed a significant decrease in GFP at 72 hrs. Future studies will address the precise mechanisms by which the compound removes mutant opsin from cells, offering hope for the development of a treatment for this currently untreatable condition.

Automatic Behavior in Musicians

Erin Kim
PRISE Fellow
Molecular and Cellular Biology, 2019

Brigham and Women's Hospital
Advisor: Jeanne Duffy
Mentor: Kirsi-Marja Zitting

Automatic behavior syndrome (ABS) describes the continuation of action through periods of mind wandering as if one is operating on "auto-pilot." Drivers commonly experience the phenomenon as they drive down highways and belatedly realize they missed the exit they had intended to take. While anecdotally common with highly-learned behaviors such as driving, ABS remains poorly understood. The study aims to investigate ABS in musicians, specifically pianists and string instrumentalists. Highly trained musicians must practice the same pieces of music over and over until the music is learned by heart. Many report that they have ABS-like experiences while practicing or performing. Musicians are accustomed to long recording sessions which allows for greater opportunities to capture episodes of ABS. By tracking ABS with specific parts of the musical piece, it is possible to approximate durations of "auto-pilot." Musicians will be asked to participate in two-hour long recording sessions consisting of audio, visual, and high density EEG measurements. Questionnaires will also be administered to record self-reported instances of ABS. It is hypothesized that ABS occurs due to localized regions of the brain entering states of sleep, or "local sleep." Increased theta waves, which occur during initial stages of sleep, are predicted to be found in the regions of the prefrontal cortex associated with working memory. This may explain the periods of amnesia that occur with ABS. Based on self-reported data, the fine motor functions of musicians can also be affected, leading to more mistakes. The results of this study will contribute to the general understanding of ABS and the behavioral impacts of sleepy individuals performing safety-sensitive activities such as driving a motor vehicle.

Investigating the Role of Glutathione Synthesis in Organ Homeostasis of Adult Mice

Michelle Koh
PRISE Fellow
Molecular and Cellular Biology, 2021

Harvard Medical School
Advisor: Joan Brugge
Mentor: Isaac Harris

Contrary to the popular belief that antioxidant supplementation prevents cancer, clinical studies have shown that antioxidants instead promote tumor incidence. In concordance, researchers have found that reducing the synthesis of the most abundant antioxidant in the cell, glutathione (GSH), prevents tumor onset in mice by impairing their ability to buffer oxidative stress. Compared to such tumor-related studies, less is known about the role of GSH in non-cancerous cells. While GSH synthesis has been shown to be essential for mouse embryogenesis, its function in maintaining organ homeostasis in adult mice is unknown. In our study, we are investigating the effects of whole-body ablation of the rate-limiting enzyme in GSH synthesis (GCLC), using a genetic mouse model. We generated *GCLC$^{f/f}$;Cre-ERT2* mice that possess an enzyme that can be activated through tamoxifen treatment to specifically excise the GCLC gene. After several days of tamoxifen treatment, Cre recombinase activity was induced, leading to the deletion of GCLC across multiple organs (Gclc$^{-/-}$ mice). Overall, Gclc$^{-/-}$ mice underwent rapid weight loss and curvature of the spine (kyphosis). Our analyses focus on the liver, as it is the highest producer of GSH in the body. In addition to confirming GCLC deletion at the mRNA and protein level, we observed increased transcription of target genes for Nrf2, a transcription factor that responds to oxidative stress. Despite these changes at the transcriptional level indicating oxidative stress, histological analyses revealed no damage to the liver. Thus, preliminary results suggest that the requirement of GSH synthesis for adult organ homeostasis differs greatly from the requirement for embryogenesis. We anticipate that understanding the roles of GSH in organ homeostasis will aid us in better understanding how to therapeutically target this process in cancer patients.

Investigating the Role of T3SS Slippage Sites in Secretion of Therapeutic Proteins by a T3SS Competent Strain of *E. coli* Nissle 1917

Truelian Lee
SURGH Fellow
Undeclared, 2021

Massachusetts General Hospital, HMS
Advisor: Cammie Lesser
Mentors: Jason Lynch, Coral González-Prieto

Probiotic bacteria such as *Escherichia coli* Nissle 1917 (EcN) represent a self-replicating and versatile drug-delivery platform. However, EcN secretes few proteins into its surroundings. In contrast, many Gram-negative pathogens use type III secretion systems (T3SSs) to directly inject virulence proteins into human cells. Using a synthetic biology-based approach, the Lesser lab introduced into EcN the operons encoding for a T3SS modified to secrete proteins into the extracellular environment. It is unknown whether the levels of secretion observed in this strain (known as T3EcN) are the maximum possible. *Spa13*, *Spa33*, and *MxiA* encode proteins vital to T3SS structure. Interestingly, these genes have translational slippage sites, sequences of nine repeated adenines that cause RNA polymerase to integrate additional nucleotides not encoded by DNA. In *Shigella*, slippage at these sites results in decreased T3SS expression and thus lower protein production. We hypothesized a similar phenomenon occurs with T3EcN and that modifying the DNA sequence to prevent slippage would increase secretion.

To test this, I will knockout *Spa13*, *Spa33* and *MxiA* in T3EcN and complement with expression plasmids encoding genes where the RNA slippage site has been repaired to prevent slippage. Complementation with plasmids encoding the wildtype genes will serve as a control. I will then compare secretion of each strain using liquid secretion assays followed by western blot. I anticipate that strains complemented with repaired genes will exhibit increased secretion over the wildtype control. This work will inform the process of generating an optimized T3EcN that better secretes therapeutic payloads.

Assessing the Role of *SKA2* in Stress-related Psychiatric Disorders

Katelyn Li
PRISE Fellow
Neurobiology, 2021

McLean Hospital, HMS
Advisor: Kerry J. Ressler
Mentor: Jakob Hartmann

It is well-established that dysfunctions of the hypothalamic-pituitary-adrenal (HPA) axis are observed in many stress-related psychiatric disorders, including major depression and post-traumatic stress disorder (PTSD). The main modulator of HPA axis activity is the glucocorticoid receptor (GR), a nuclear receptor and transcription factor that is activated by glucocorticoids (GCs). The spindle and kinetochore-associated complex subunit 2 (*SKA2*) protein has been identified as a putative GR interaction partner. Notably, epigenetic and genetic variation within the *SKA2* gene, and alterations in its level of expression, have been associated with risk of PTSD and suicide. Our objective was to investigate the role of *SKA2* in the central nervous system and validate it as a potential candidate gene in stress-related psychiatric disorders. To analyze expression pattern of *SKA2* in the human brain, we performed immunohistochemistry (IHC) on post-mortem hippocampal and amygdalar tissue. We then utilized RNAScope *in situ* hybridization technology to investigate the expression pattern of *SKA2* and *Nr3c1* (GR) mRNA in the hippocampus and amygdala of three adult C57BL/6J male mice that were sacrificed under baseline conditions. Preliminary analysis suggests that *SKA2* is prominently expressed in pyramidal neurons of the hippocampus and basolateral amygdala. RNAscope images reveal that *SKA2* is primarily neuronal and is co-expressed with GR in the mouse brain. Our findings may be important in elucidating the underappreciated role of *SKA2* in stress-related psychiatric disorders.

Testing for Causal SNPs of Type II Diabetes

Emily Lopez
PRISE Fellow
Molecular and Cellular Biology, 2021

Brigham and Women's Hospital, HMS
Advisor: Alexander Banks

Type II diabetes is a disease where a person's cells are unresponsive to insulin, resulting in decreased glucose uptake. A variety of factors cause type II diabetes, such as dysfunctional beta cells, extra weight, and genes such as CDKAL1. In this study, we are focusing on a specific single nucleotide polymorphism (SNP) to see how a risk allele affects cell function relative to a reference allele.

To do this, we created a pair of matched tissue culture cell lines differing in the expression of a risk or reference SNP within CDKAL1. We edit the SNP using CRISPR-Cas9 with single guide RNAs and a template to change the G risk allele to the A reference allele using homology directed repair. To edit the gene, 293T cells were transfected with the machinery to edit the part of the cell's DNA with the risk allele to the reference allele. Once transfected, the cells were split into 96-well plates, one cell per well. Once the mutated cells were successfully selected, we observed the effects of changing the allele from risk to reference on CDKAL1 and neighboring genes. Our hypothesis is that changing this specific SNP will affect the mRNA levels of CDKAL1. If successful, we will have a better understanding of the genetic effects of CDKAL1 on type II diabetes. Our future tests of other SNPs on the CDKAL1 gene following the same protocol will allow us to better understand the effects of CDKAL1 on type II diabetes.

Maternal Vaccination to Boost Neonatal Immunity

Francesca J. Noelette
PRISE Fellow
Molecular and Cellular Biology, 2019

Ragon Institute
Advisor: Galit Alter
Mentor: Madeleine F. Jennewein

The placenta is crucial to the health of a growing fetus. All necessary nutrients, even antibodies, travel across the placenta from mother to child. This project seeks to determine the viability of vaccinating pregnant mothers to boost immunity in neonates. Our goal requires an understanding of antibody transfer across the placenta and vaccine response in pregnant women. Knowing that cytotoxic antibodies cross the placenta to the fetus in higher quantities than other types of antibodies, immunofluorescence was conducted on placenta samples to determine the mechanism of this crossing by identifying the receptor that could transfer highly functional cytotoxic antibodies and was most abundant on the maternal side of the placenta. We also sought to know whether vaccine response in pregnant women led to production of antibodies that could bind the abundant receptors. Otherwise, the antibodies would not transfer at high enough quantities to provide the neonate with immunity. Therefore, plasma from pregnant women vaccinated for influenza was analyzed to determine the reactivity and type of their antibodies. Preliminary results indicate that FcgRIII receptors allow for the high transfer of cytotoxic antibodies, but research on the effect of the influenza vaccine on antibody production in pregnant women is still incomplete. Nonetheless, if vaccines that encourage the production of cytotoxic antibodies or antibodies that bind FcgRIII in pregnant women can be developed, it would be possible to provide greater immunity to neonates, making them less vulnerable to infectious disease during the first year of life.

Mapping Proviral Landscape in HIV Elite Controllers

Ben S. Rhee
PRISE Fellow
Molecular and Cellular Biology, 2021

Ragon Institute
Advisor: Xu Yu
Mentor: Kevin Einkauf

While a sterilizing cure of HIV-1 infection has only been reported in a single patient after a stem-cell transplant with CCR5Δ32-homozygous cells, a spontaneous functional cure of HIV-1 occurs in 0.3-0.5% of infected persons. These individuals, termed elite controllers (EC), maintain undetectable levels of HIV-1 replication without treatment. In this way, these individuals provide living evidence that immune-mediated control of HIV-1 infection is possible. The identification of effective viral control mechanisms active in these patients holds promise for inducing a functional cure of HIV-1 infection in a broader HIV-1 patient population. In previous investigations, the analysis of HIV-1 immune defense has mostly been focused on HIV-1-specific CD8 T cells restricted by so-called "protective" HLA alleles, while viral RNA sequencing studies have failed to identify specific viral defects in EC, relative to HIV progressors. Much less is currently known about the size, structure and composition of proviral reservoirs in EC. To address this, we have conducted full-length viral sequencing studies on proviral DNA in peripheral blood mononuclear cells (PBMCs) from 61 EC and 7 HAART-treated patients. Single-genome sequencing of individual HIV-1 DNA carried out by nested PCR with primers spanning the entire HIV-1 genome (∼9kb) and Illumina deep-sequencing were used to identify intact HIV proviral sequences from defective sequences. The preliminary analysis of this dataset indicated that despite an overall lower level of intact proviruses in EC compared to HAART-treated patients, a subgroup of ECs has larger, more clonally-expanded intact proviruses compared to what we have observed in ART-treated HIV infected patients. This discovery not only highlights the key differences among HIV-1 patient groups, but also brings potential for finding a definitive cure for the virus.

Parathyroid Hormone Induces *CYP27B1* Gene Expression in Human Renal Proximal Tubule Epithelial Cells

Trang Truong
PRISE Fellow
Molecular and Cellular Biology, 2021

Massachusetts General Hospital, HMS
Advisor: Marc Wein
Mentor: Tadatoshi Sato

Parathyroid hormone (PTH) is a key regulator of calcium levels and bone homeostasis. In bone cells, PTH increases intracellular cAMP levels and leads to protein kinase A-mediated phosphorylation of salt-induced kinase 2 (SIK2). Phosphorylated SIK2 is inactive. Therefore PTH signaling reduces phosphorylation of SIK2 substrates such as class IIa HDACs and CRTC proteins which translocate to the nucleus to regulate gene expression when dephosphorylated. In kidneys, PTH signaling stimulates vitamin D activation by inducing *CYP27B1* expression. The intracellular signaling events required for this renal phenomenon are unknown. We investigated whether a similar SIK-dependent mechanism operates in human kidney cells. Human renal proximal tubule epithelial cells (hRPTECs) were exposed to different concentrations of PTH for 30 minutes and intracellular cAMP levels were measured. Western blots were performed to detect the presence of downstream substrates (e.g. pSIK 2/3, pCRTC2) after 60 minute PTH treatment. Total RNA was isolated from PTH-exposed RPTECs (4 hour treatment duration), and *CYP27B1* mRNA levels were measured by RT-qPCR. Though we found that PTH increases intracellular cAMP levels in a dose-dependent manner, western blots have not revealed clear PTH-induced changes in SIK substrate phosphorylation. Initial *CYP27B1* gene expression data from the RT-qPCRs have also been indeterminate to date. We plan to use a time-course approach in future experiments as the effects of PTH exposure in RPTECs may be more transient than previously thought. If we can decode the mechanism in which vitamin D is activated with PTH in humans, novel treatments for afflictions caused by vitamin D deficiencies (osteomalacia, Rickets, etc.) can potentially be developed by targeting this pathway.

A Genome-Scale CRISPR-Cas9 Sensitivity Screen for Combinations with CDK4/6 Inhibitors in Ewing Sarcoma and Neuroblastoma

Caroline Wechsler
PRISE Fellow
History and Science, 2019

Dana-Farber Cancer Institute, HMS
Advisor: Kimberly Stegmaier
Mentor: Lillian Guenther

Ewing sarcoma and neuroblastoma are aggressive pediatric solid tumors, harboring quiet genomes with few recurrent somatic mutations, and with few targeted therapies available. Drugs that inhibit CDK4 and CDK6, enzymes involved in cell-cycle regulation, have shown effectiveness in Ewing sarcoma and neuroblastoma models. However, prior studies suggest that this inhibitor class is maximally effective in combination with other drugs. CRISPR-Cas9 technology allows systematic knockout of genes to examine the effects of a specific genetic perturbation. I am optimizing a genome-scale CRISPR-Cas9 sensitivity screen to discover targets to be combined with CDK4/6 inhibitors in Ewing sarcoma and neuroblastoma, testing two cell lines in each. I tested several cell line models, examining drug effects on viability using in vitro ATP measurements, and examining target protein inhibition in various cell contexts using Western immunoblotting. Based on these results, I have selected candidate cell lines for screening and am measuring cell growth dynamics across a variety of drug concentrations for several weeks, performing serial assessments of viability and target inhibition to determine the optimal CDK4/6 inhibitor dose. The results, which we hope to obtain this fall, will lead to a follow-up project where I will validate targetable combination therapies for these two diseases. I am also following up on previous Ewing sarcoma screening results that identified IGF1R, a protein involved in cell growth, as a strongly synergistic target with CDK4/6 inhibitors, in neuroblastoma. Through both genome-wide and drug-specific methods, we hope to discover effective combinations that will lead to treatments for children suffering from these malignancies.

Investigation of the Role of srrA in eDNA Release and Biofilm Formation in *Staphylococcus aureus*

Carolyn Wong
PRISE Fellow
Applied Mathematics, 2021

Molecular and Cellular Biology
Advisor: Richard Losick
Mentor: Adnan K. Syed

Staphylococcus aureus is a common cause of hospital-acquired infections and is of particular interest because of its ability to form biofilms, a collection of cells adhered together and to a surface. Biofilm formation enhances antibiotic resistance of *S. aureus*, increasing the likelihood of transmission through contaminated surfaces. Biofilms are formed when bacterial cells lyse, releasing cytoplasmic components to form a sticky matrix composed of proteins and extracellular DNA (eDNA). Additionally, during biofilm formation the pH of the environment decreases, causing the proteins and eDNA to form an electrostatic net that adheres the cells together. Biofilm formation is also preceded by a decrease in the small molecule cyclic-di-adenosine monophosphate (c-di-AMP). We hypothesize that cell lysis and eDNA release are controlled by changes in c-di-AMP, which regulates cell-wall integrity. A decrease in cell-wall integrity could cause cells to lyse and release cytoplasmic components to form the biofilm matrix. Previous research from our lab suggests that the response regulator *srrAB* contributes to eDNA release during biofilm formation. This project investigates the role of *srrAB* in the molecular signaling pathway that leads to *S. aureus* eDNA release and biofilm formation. Further evaluation of cell-wall stability in the Δ*srrAB* mutant will help to elucidate the signaling network controlling *S. aureus* biofilm formation, which will assist in the future development of therapeutic treatments for *S. aureus* biofilm infections.

NEAR EASTERN LANGUAGES AND CIVILIZATIONS

The Unknown Archives of the Harvard Semitic Museum

Julia Englebert
SHARP Fellow
Near Eastern Languages and Civilizations, 2020

Near Eastern Languages and Civilizations
Advisor: Peter Der Manuelian

The Harvard Semitic Museum's vast collection of artifacts includes a trove of largely unstudied materials, such as the letters, invoices, and other documents preserved by the Museum's founder and first director Professor David Gordon Lyon. We aim to gain a better understanding of the Museum's beginnings through the organization, digitization, and analysis of these correspondence files, which cover Professor Lyon's travels throughout the Middle East, the University's early archaeological expeditions and accession of artifacts, as well as administrative operations at home. The organization of archival material will make previously unknown documents more easily accessible to future researchers, assisting with projects such as Professor Peter Der Manuelian's ongoing biography of George A. Reisner, a student of Professor Lyon. Eventually, our efforts will also contribute to the creation of a volume on the highlights and history of the Harvard Semitic Museum, which will disseminate Museum history to a wider audience. We hope to reinvigorate the enthusiasm that the Harvard Semitic Museum once inspired and transform it into an exciting destination for students, visitors, and researchers on Harvard campus.

NEUROBIOLOGY

Use of Magnetic Resonance Spectroscopic Imaging as a Predictor of Anti-angiogenic Drug Efficacy

Wesley Shin
PRISE Fellow
Neurobiology, 2021

Martinos Center
Advisor: Eva Ratai
Mentor: Daniel Kim

Glioblastomas (GBM) are one of the most lethal and intractable forms of cancer. Although many novel treatments are being developed, anti-angiogenic drugs continue to be commonly used. Glioblastomas typically exhibit neoangiogenesis, the formation of new blood vessels. As a result, anti-angiogenic drugs that inhibit the formation of blood vessels have potential to extend a patient's progression-free survival. In particular, this study focuses on the efficacy of a monoclonal antibody known as bevacizumab in treating GBMs. However, not all patients benefit from the drug. The use of bevacizumab is typically associated with a reduction in contrast on T1-weighted magnetic resonance imaging (MRI). As a result, it can be difficult to determine whether a patient responds to bevacizumab using conventional MRI data. Preliminary data suggests that magnetic resonance spectroscopic imaging (MRSI) can be used instead to predict the efficacy of bevacizumab-based treatment. MRSI data provides information on the concentration of various metabolites in various regions of the brain. Since healthy tissue and neoplastic tissue have different metabolite compositions, MRSI data provides insight into how patients respond to bevacizumab. In particular, tracking levels of choline, N-acetylaspartate, creatine, and lactate can be helpful in determining the efficacy of bevacizumab treatment, which has implications for improving patient management.

Neuronal Cell-Type Classification: Methods and Application to the Retina

Allison Kao
PRISE Fellow
Computer Science and Neurobiology, 2020

Molecular and Cellular Biology
Advisor: Joshua Sanes
Mentors: Karthik Shekhar, Irene Whitney, Wenjun Yan

Building a comprehensive catalogue of cell types is not only prerequisite to interrogating cellular identity, development, and evolution, but also crucial to experimental design of cell-level exploration of health and disease. The importance of a census is reflected in the growing push toward cell taxonomy studies, namely the Human Cell Atlas project and, for neuronal cells, the BRAIN initiative. Neuronal classification presents a unique challenge, as functional criteria traditionally assigned at the circuit level cannot easily be discerned in individual neurons. Thus, classification is based on three alternative properties: morphology, physiology, and molecular expression. The molecular description enables resolution of both intrinsic and transient cellular features.

We are generating a cell atlas of the murine retina, an accessible and well-studied part of the mammalian central nervous system. Retinal neurons are collected and profiled using single-cell RNA sequencing (scRNA-seq), a high throughput method that quantifies the mRNA makeup in individual cells. An unsupervised clustering analysis is then performed on the dataset to map cells to classes and types based on their transcriptomes. Cluster-specific markers determined by the computational method are applied to fluorescence in situ hybridization (FISH), a molecular visualization technique in which fluorescent RNA probes are bound directly to retinal tissue to label individual cells, thereby matching molecular to morphological classes.

With datasets in hand, I am contributing to the bioinformatics and morphological analyses. Looking ahead, this pipeline can be adapted to investigate lesser known cell populations in the brain, and on a broader scale, cell diversity of any kind.

Identifying Modifiers of Alpha-Synuclein Toxicity in Parkinson's Disease

Anahita Iyer
PRISE Fellow
Neurobiology, 2019

Brigham and Women's Hospital, HMS
Advisor: Dennis J. Selkoe
Mentor: Saranna Fanning

Parkinson's disease (PD) is a neurodegenerative disorder that causes severe motor deficits, and while current therapies treat symptoms, they do not provide cures. A key feature of PD neuropathology is the presence of Lewy bodies: abnormal cytoplasmic inclusions in the brain composed of insoluble aggregates of the protein alpha-synuclein. Elucidating the underlying causes of inclusion formation may lead to the identification of new targets for PD treatment. It has been found that the monomeric form of alpha-synuclein is more prone to aggregation and binds membranes more strongly than the native tetrameric form. Since specific membrane lipids may directly influence the amount of alpha-synuclein present in its monomeric or tetrameric state, we investigated whether genes that alter membrane composition influence the extent of alpha-synuclein–membrane interaction and resulting toxicity. We selected genes involved in lipid pathways that interconvert between different membrane phospholipids as candidates and designed constructs to overexpress these genes in neuronal cell types. We then investigated the effects of protein overexpression in inducible neuroblastoma cell lines expressing a toxic form of alpha-synuclein prone to aggregation by evaluating parameters such as inclusion formation, alpha-synuclein localization, phosphorylation states, and tetramer:monomer ratios. We will follow up promising targets in rat cortical neurons and human iPSC-derived neural stem cell lines. Consistent effects observed across multiple assays will implicate a candidate gene in regulating alpha-synuclein neurotoxicity. This research will allow us to identify components of lipid pathways that may contribute to the initiation of PD by altering membrane composition and better understand the molecular mechanisms by which alpha-synuclein misfolding and aggregation cause disease.

Lipid Dysregulation is a Significant Player in Parkinson's Disease Etiology

Jonathan R. Honey
PRISE-Emmanuel Fellow
Medical & Veterinary Sciences, 2019

McLean Hospital, HMS
Advisor: Penelope Hallett
Mentor: Oeystein Brekk

Aging is the primary risk factor for developing Parkinson's disease (PD), and lipid metabolism is significantly reduced in aging. The mechanistic basis for the degeneration of dopaminergic neurons in the substantia nigra (SN) pars compacta remains elusive to this day. For a long time, the progression of PD has been considered a "prion-like spread" of alpha-synuclein aggregates, proposed by Braak staging. Recently, a more holistic theory suggests PD is a result of age-related lipid metabolism dysregulation – id est, if we lived indefinitely, we would all succumb to lipid dysregulation and neurodegeneration. Genetic and environmental predispositions simply move the threshold into younger ages.

To investigate the validity of both theories, we stained human and murine brains for neutral lipids, alpha-synuclein protein and dense core vesicles. Using confocal laser scanning microscopy and automated image analysis, we investigated the lipid content and distribution of Lewy bodies alpha-synuclein containing aggregates) to find a putative chronological etiology for Parkinson's disease on a cellular level. Our preliminary results show a significant accumulation of lipid conglomerates within neuromelanin-positive neurons versus healthy control, qualitatively of higher abundance than expected for alpha-synuclein aggregates. Current analyses will also quantify neutral lipid aggregates within glia.

These findings differ from the classical view of proteinopathy by illuminating the interplay between age-associated changes in lipid homeostasis and the risk for neurodegenerative disease. This could significantly change how we view, treat and prevent Parkinson's disease, the world's second most prevalent neurodegenerative disease.

Altruism and Autism in Mice

Pauline Gabrieli
PRISE Fellow
Molecular and Cellular Biology, 2019

Massachusetts General Hospital, HMS
Advisor: Ziv Williams
Mentor: William Li

Though more than 1% of the children in the US suffer from autism spectrum disorders (ASDs), we still have a minimal understanding of the neural encoding behind such disorders. Though sSeveral murine models of ASDs existhave been developed, but there have been few studies on the differential neuronal activity of these mice's differential neuronal activity. To address this dearth of dataThus, we developed an assay of "helping behavior" in mice, in which one mouse could move into another chamber to turn off an aversive experience of electric shock on another mouse. We intend to use this assay on several models of ASDs in miceouse, including the widely used *SHANK3*-knockout model causing a deficiencywith mice deficient in the key synaptic scaffolding protein SHANK3, to examine differences in helping behavior between wild-type and autistic mice. We will then then plan to take single-neuron recordings from mice during this assay to examine key neuronal activity that underlies helping behavior between the different types of mice. Our results demonstrate that wild-type mice show a significant movement towards the zone that turns off shock during the assay. - i In other words, they demonstrate helping behavior, a social behavior which has never before been recorded in mice. Ultimately, studying the differences between the behavior and neuronal encoding of wild-type and autistic mice may provide key information forin the path to understanding the root causes of ASDs as a whole. Moreover, examining helping behavior in mice may be a step forwards towards unlocking on the complex neural mechanisms behind higher-order human behaviors like altruism and empathy.

SCD1 as a Novel Therapeutic Vulnerability in Glioma Stem Cells

Mohamed El-Abtah
PRISE Fellow
Neurobiology, 2021

Massachusetts General Hospital, HMS
Advisor: Christian E. Badr
Mentor: David J. Park

Glioblastoma multiforme (GBM) is the most aggressive form of primary central nervous system (CNS) tumors with a high mortality rate and adaptive resistance to chemotherapy and radiation. Several lines of evidence show that in conjunction with glucose, brain tumors utilize sources such as acetate and fatty acids to sustain their growth, hence increased lipid synthesis is a hallmark of GBM. A screening of several compounds on Glioma stem cells (GSCs) suggested that targeting Stearoyl CoA Desaturase 1 (SCD1), a pathway that converts saturated fatty acids (FA) to unsaturated FA, could be a promising therapeutic approach to abrogating tumor formation. We showed that upon differentiation of GSCs into mature GSCs, expression of SCD1 decreased, indicating that this enzyme is crucial for maintaining the survival and tumor-initiating properties of GSCs as well as maintaining the stem cell signature. A short-hairpin (shRNA) knockdown of SCD1 resulted in a significant decrease in cell viability *in vitro* and in an orthotopic glioma mouse model, SCD1 knockdown reduced tumor formation while increasing mean survival. It is possible to replicate this phenomenon using pharmacological inhibition by use of Molecule X. Nude mice with implanted 83 GSCs-Fluc tumors received a daily intranasal dose of Molecule X for 14 days and bioluminescence imaging (IVIS Live Animal Imaging System) showed a significant decrease in the Fluc signal, corresponding to an improved prognosis, abrogated tumor formation, and improved mean survival rate. These preliminary results suggest that lipid biosynthesis is a keystone property of GBM tumors and exploiting this dependency can improve patient prognosis.

Investigating the Generation of Behavioral Bias through Neural Morphology in *Drosophila melanogaster*

Pablo Reimers
PRISE Fellow
Neurobiology, 2019

Organismic and Evolutionary Biology
Advisor: Ben de Bivort
Mentor: Kyobi Skutt-Kakaria

The study of individuality has long interested humans as a means to understand themselves. However, the origin of these differences has been difficult to uncover. Here, we use *Drosophila melanogaster* as a means to study the neurobiological underpinnings of idiosyncratic behavior in genetically identical animals. Utilizing the Gal4/UAS system, we target outputs of the Central Complex (CC), a highly convergent premotor area, as a likely locus of behavioral bias generation where left-right asymmetries in the cellular properties of the few outputs would introduce left-right asymmetries in locomotor behavior. We aim to correlate behavioral bias in walking behavior to asymmetries in presynaptic volumes of a specific neuronal class. To accomplish this, individual flies were tracked as they walked freely in a three-armed chamber to measure locomotor bias. Presynaptic markers were expressed in a desired class of CC output cells, such that immunohistochemistry and confocal microscopy could capture fluorescence in the bilaterally symmetric arborations projecting from the CC. Volumes for these arborations were quantified, and the asymmetry between the left and right side of the brain was correlated to the behavioral bias of each fly. This study failed to reject the null hypothesis that volumetric asymmetries in these neurons does not predict behavioral bias, as no significant correlation was found. These results advocate for further investigation, either with functional calcium imaging or higher resolution to identify more subtle asymmetries that were imperceptible in this experiment, in order to further address the neurobiological basis for individuality.

Maltreatment and Postpartum Depression

Orgilmaa Munkhbaatar
PRISE Fellow
Neurobiology, 2019

McLean Hospital, HMS
Advisor: Martin Teicher

Extensive research has shown the enduring effects of childhood maltreatment on the brain as well as the connection between childhood maltreatment and postpartum depression symptoms. The primary goal of this project is to explore the impact of childhood maltreatment as a risk factor for postpartum depression by gathering behavioral and neuroimaging data of individuals clinically diagnosed with depression and identified to have been exposed to maltreatment through the Maltreatment and Abuse Chronology Exposure survey, and controls. Analysis of the acquired data permits identification of differences in brain architecture and functional connectivity that distinguish maltreated mothers with depression from maltreated and non-maltreated mothers without psychopathology. The study used a 2x2 factorial research design to evaluate brain structure and connectivity to investigate the relationship between the extent of maltreatment exposure and postpartum depression. Neuroimaging analysis was performed with the FMRIB Software Library and Independent Component Analysis to study the whole brain files of subjects in resting state. Results from this project may assist in the recognition of a more distinct and empirically-based neural characterization of postpartum depression which is critical for refining diagnosis and developing targeted methods of intervention.

Investigating the Relationship Between Dopamine Ramping and Spatial Awareness

Aleeza Shakeel
PRISE Fellow
Neurobiology, 2020

Molecular and Cellular Biology
Advisor: Naoshige Uchida
Mentor: HyungGoo Kim

The neurotransmitter dopamine facilitates learning, motivation, and decision making. To prevent and treat disorders that result from abnormalities in dopamine (e.g., depression, Alzheimer's, schizophrenia), researchers are trying to understand how dopamine functions in healthy individuals. Prior research shows that dopaminergic neurons respond with a short burst of activation when rewards are received. Interestingly, an expectation of reward diminishes the overall dopamine response. Recent studies show that dopamine gradually ramps up as the animal approaches a reward location. This project investigates the mechanisms that cause dopamine ramping. Since dopamine ramps occur when the animal moves to obtain rewards, we hypothesized that the hippocampus generates dopamine ramping during spatial navigation. The hippocampus is a region in the brain involved in recognition and memory. Place cells in the hippocampus fire when an animal occupies a specific location, creating a cognitive map in the brain. To see if there is a relationship between the hippocampus and dopamine ramping, we examine how brains function with an inactive hippocampus.

In this experiment, we placed 12 mice in a virtual reality maze that releases water at a specific location. A genetically-encoded calcium indicator is expressed in the dopamine neurons in the VTA and the SNc. The activity of the dopamine neurons is monitored through optical fibers implanted in the DLS and the VS. We will try two methods hippocampal inactivation: DREADD and JAWS. Six mice will have DREADD bilaterally injected in the CA1 area of the hippocampus while the other six have JAWS bilaterally injected. After training the mice, we will examine whether a hippocampal inactivation eliminates dopamine ramping.

Slit-Robo GTPase Activating Protein (SRGAP2)'s Role in Regulating Critical Period Timing

Yanni Cho
PRISE Fellow
Neurobiology, 2020

Molecular and Cellular Biology
Advisor: Takao Hensch
Mentor: Geoffrey Vargish

Critical periods (CPs) are windows of brain maturation characterized by enhanced neural plasticity enabling experience to extensively shape function. Accelerated or delayed CPs are observed in neurodevelopmental disorders, such as autism spectrum disorders (ASD), indicating that proper CP timing is important for normal brain development. Convergent evidence reveals CP timing to be dictated by local circuit changes in the balance of excitation (E) and inhibition (I). However, the mechanisms governing these dynamic changes remain poorly understood. To date, Slit-robo GTPase activating protein (SRGAP2) is the only protein known to impact the synaptic maturation of both E and I, suggesting SRGAP2 may influence CP timing. Evidence from our lab shows that global deletion of SRGAP2 delays parvalbumin-expressing interneuron (PV) maturation and perineuronal net (PNN) formation, indicating delayed CP trajectory. In this study, we explored the cell-type specificity of SRGAP2 function, using PV- and cortical pyramidal (TLCN) cell-selective conditional deletion of SRGAP2. We performed immunohistochemistry to examine PV-cell maturation and PNN formation in each line of mice. Further, to probe how SRGAP2 influences E/I balance, we used selective markers to quantify the number of E and I axonal boutons innervating cortical pyramidal and PV cells in both global and conditional knockout animals. Preliminary evidence after PV-specific deletion shows reduced PV intensity but normal PNN development during the CP. This study may elucidate principles of brain development that underlie the etiology of developmental disorders such as ASD.

Optimizing Fluorescent Immunocytochemistry Results of Voltage-Gated Potassium Channel Expression using Methanol Freeze-Substitution

Jonathan V. Garzon
PRISE Fellow
Undeclared, 2021

Boston Children's Hospital, HMS
Advisor: Paul Rosenberg
Mentor: Rheanna M. Sand

Fluorescent immunocytochemistry utilizes specific antigens which bind to proteins of interest and allow for these proteins to be seen under different wavelengths of light through fluorescent dyes. We aim to visualize voltage-gated potassium channels (Kv) 1.1, 3.1b, and 7.2 after optic nerve injury with greater anatomical preservation through the methanol freeze-substitution method, a fixation method which bathes the substance tested in methanol to remove all water. This method may be used in future experiments to unravel the pathway through which neurons may survive and axons may regenerate after optic nerve injury. Three days after stimulating injury through optic nerve crush, wild-type C57BL/6J mice eyeballs will be harvested under various fixation and post-fixation methods including methanol freeze-substitution. After maintaining mouse eyes treated with methanol in -80°C temperatures for two days, the retinas are removed and sliced onto various slides for staining and imaging. Considering how previous use of methanol freeze-substitution in autometallography has shown greater preservation of anatomical structure in the retina, the same should occur through immunocytochemistry. These experiments would provide evidence of the methanol freeze-substitution method as an optimal choice for immunocytochemistry of the mouse retina. This would give validity to this choice of method for future ICC experiments, which could help in understanding where Kv channels are expressed in the retina. Such knowledge could lead to treatments of optic nerve injury in humans targeting Kv channels to induce neuronal survival and regeneration.

Investigating Visual Evoked Potentials as a Potential Biomarker for Autism Spectrum Disorder in Tuberous Sclerosis Complex

Chinaza Ochi
PRISE Fellow
Neurobiology, 2019

Boston Children's Hospital, HMS
Advisor: Charles Nelson III
Mentor: Cora Mukerji

Children with Tuberous Sclerosis Complex (TSC), a rare genetic disorder, are at an elevated risk for developing autism spectrum disorder (ASD), a developmental disorder that leads to impairments in social interaction and communication skills. Research suggests that early interventions for ASD may be most effective in remediating these impairments, but it is difficult to predict which infants will go on to develop ASD. TSC can be diagnosed *in utero* and may provide unique insight into the neural mechanisms that give rise to ASD later in development. In this study, we will use visual evoked potentials (VEP) and behavioral measures to evaluate the mechanisms underlying elevated risk for ASD in infants with TSC. VEPs are event-related electrical potentials induced by a visual stimulus that can be measured with electroencephalography (EEG). This neural marker reflects basic cortical processing and is not dependent on language, motor coordination, or auditory abilities, making it a useful measure to utilize for infants. Through growth curve modeling, we can look at how the VEP changes over time in different clinical groups in comparison to the control. Our hypothesis is that children who later develop ASD will have a characteristic difference in their VEP trajectories. If our hypothesis is supported, we expect to find a potential marker of risk for developing ASD. This information, in combination with other measures, could be used to help predict which kids will go on to develop ASD, thereby allowing for early identification of kids who would benefit most greatly from intervention services.

Identifying Downstream Targets of Presenilin

Michelle Onyekaba
PRISE Fellow
Undeclared, 2021

Brigham and Women's Hospital, HMS
Advisor: Jie Shen
Mentor: Jongkyun Kang

Familial Alzheimer's Disease (FAD) is a heritable neurodegenerative condition that affects hundreds of thousands worldwide. Mutations in Presenilin (PSEN) genes are responsible for approximately 90% of the mutations leading to an FAD pathogenesis. In my research, I am using conditional mutant flies that have their Presenilin ortholog (Psn) knocked down from their neurons by shRNA. These mutant flies will then be used to identify and validate possible substrates of g-secretase and targets of Presenilin that support neuronal survival. The focus of my ongoing research is to identify these genes in the drosophila model that are necessary for age-dependent neuronal survival, as age-related neurodegeneration is the principle cause of Alzheimer's disease. I crossed two independent ShRNA lines of each of the 10 candidate genes to a neuron specific driver in order to knock down these genes selectively in neurons. I have already obtained these conditional mutant flies, and will perform histological analysis of the brain once they reach 15 and 30 days of age. I will assess the severity of neurodegeneration by quantifying the number of vacuoles in the brain. By identifying and comparing neurodegeneration in these conditional mutant flies, I will be able to identify genes that play significant roles in age-dependent neuronal survival. We will then test whether these genes interact with Psn in the support of neuronal survival, and our findings may bring us closer to a potential treatment for Alzheimer's in the future.

Targeting OPN and Qa-1 to Modulate Microglia Function in Alzheimer's Disease Model

Leon Yang
PRISE Fellow
Applied Mathematics and Neurobiology, 2021

Dana-Farber Cancer Institute, HMS
Advisor: Harvey Cantor
Mentors: Vivian Qiu, Xianli Shen

Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by neuronal death, amyloid-beta plaque accumulation, inflammation, cognitive dysfunction, and memory loss. To date, there is no effective treatment for the disease. Immunology is a budding field, especially in cancer research, and presents a promising avenue for future treatment. More specifically, microglia, resident immune cells in the central nervous system, are integral to the immunotherapeutic potential of the brain because they clear the amyloid-beta plaques that accumulate during the disease's progression. Because brain inflammation is a key feature of AD, we focused on genes that may regulate the inflammatory response of microglia in the context of AD. The *OPN* gene encodes osteopontin, a protein that is upregulated during inflammation. The *Qa-1* gene encodes a nonclassical class I histocompatibility molecule that is highly expressed by stressed immune cells, including activated CD4 T cells, macrophages, and dendritic cells. Using *OPN* knockout and knock-in as well as *Qa-1* knockout mice, we utilized a novel organotypic hippocampal slice culture (OHSC) model, which is a viable *in vivo* system to study the contribution of *OPN* and *Qa-1* to the function of microglia under both homeostatic and disease conditions. We also conducted co-culture experiments to study the underlying interactions between T cells, microglia, and neurons. Our preliminary results suggest that knocking out *OPN* and *Qa-1* could increase the ability of microglia to clear amyloid-beta plaques, although more extensive studies will continued to be conducted to solidify these findings. The implications of an immunological approach to solving Alzheimer's disease could be the first step towards effective therapies, a monumental step for an aging population.

Identification of Healthy and Pathological Behaviors Using Machine Learning

Joanna M. Tao
PRISE Fellow
Neurobiology, 2021

McLean Hospital, HMS
Advisor: Justin T. Baker

Smartphones and wearables (e.g., Fitbits) are popularly used, including in those with mental health conditions, allowing studies of both healthy and abnormal human behavior to use objective, continuous, unobtrusive measurement in natural settings. The present study employs wrist-worn devices that track accelerometry in conjunction with smartphone data, daily surveys and audio recordings, monthly on-site clinical interviews, and bimonthly brain scans to identify behavior states in outpatients with schizophrenia and bipolar disorders. Participants enroll in the study for one year, with the option of re-enrolling at the end of this time, allowing for the longitudinal collection of large amounts of data in a population known for profound changes in brain state, mood, and behavior, including pathological episodes. Computational techniques like machine learning then use these data to link changes in mood, cognition, and everyday behavior to the collected biological dynamics, and further understand, identify, and predict changes in behavior and brain state. Over 122 months' worth of data have been collected over 12 participants, with most months capturing changes in pathological state according to at least one of four clinical symptom scales. Preliminary analysis has found periodic changes in activity, which correspond with common sleep/wake schedules and qualitatively match the daily schedules reported by participants during the on-site interviews, including when changes in sleep behavior has been reported. This study deepens understanding of pathology's effect on behavior, and improves identification and prediction of pathological behavior and brain states, helping patients and caregivers avoid behaviors that result in episodes or hospitalizations.

ORGANIZATIONAL BEHAVIOR

Existential Thinking

Lilly Scherban
PRIMO Fellow
Social Studies, 2020

Harvard Business School
Advisor: Jeff Steiner

We seek to understand how existential thinking – which we define as the intrapsychic process involved in contemplating the fundamental questions of one's existence, such as what constitutes a good life – relates to an individual's orientation and attitudes towards work and perceptions of meaning and satisfaction with life. We show evidence that heightened existential thinking can spur changes in life philosophy, life orientation, and life priorities, and that it can alter the content of and satisfaction with one's life narrative. As a byproduct of existential thinking, individuals are also likely to cite increased existential wisdom and personal growth. Using longitudinal, qualitative interviews of 12 retiring individuals, we explore how existential thinking affects career decision-making and satisfaction with work and life activities.

Scaling Startups

Jack Li
PRIMO Fellow
Economics, 2021

Harvard Business School
Advisor: Ranjay Gulati

Scaling, or growing a venture beyond its founding team, requires more than just a great idea or access to funding. We explored the key challenges of growth, including employee connection with the business' purpose and culture, the employee's experience at work, and the employee's connection with others. We also considered the interventions that founders and venture capitalists must make in order to satisfy customers and investors and to establish sustainable work environments. Extensive online and archival research was conducted at Baker Library to identify ventures, like Spotify and Uber, whose successes or failures were tied to their ability to grow. This project will help lay the groundwork for writing future case studies.

PHYSICS

Selective Etching of (111)-oriented $SrTiO_3$

Miro Furtado
PRISE Fellow
Applied Mathematics, 2018

Physics
Advisor: Jenny Hoffman
Mentor: Jason Hoffman

Epitaxial growth of thin crystalline films has enabled the exploration of the unique electronic and magnetic properties of new and exotic materials. Recently, novel electronic properties have been discovered in complex oxides grown on $SrTiO_3$. The lack of simple techniques to prepare atomically well-defined (111)-oriented $SrTiO_3$ surfaces, however, has posed an obstacle in their exploration. With this project, we develop a procedure for the chemical etching and thermal annealing of $SrTiO_3$ (111) in order to produce an atomically-smooth and singly-terminated surface that is ideal for epitaxial growth. We exposed mechanically polished $SrTiO_3$ to successive stages of deionized water and hydrochloric acid in order to selectively etch the charged SrO_34-, followed by a thermal annealing process to facilitate atomic diffusion. Etched $SrTiO_3$ substrates were imaged using atomic force microscopy to determine their topographical properties. Thus far, we have succeeded in etching surfaces with promising step-sizes, but have yet to create ordered terrace structures. If our technique is successful, it may serve as a faster and safer alternative to traditional methods of etching $SrTiO_3$ (111) that rely on buffered hydrofluoric acid.

Investigation of Neutrino Physics Reconstruction in a Pixel Readout of a Large LArTPC

Madeline Bernstein
PRISE Fellow
Physics, 2019

Physics
Advisor: Roxanne Guenette
Mentor: Corey Adams

Neutrinos present a unique opportunity to search for physics beyond the Standard Model. The liquid argon time projection chamber (LArTPC) is widely used to detect neutrino interactions. DUNE proposes a 40 kiloton LArTPC, projected to start collecting data in 2024. The current readout design for DUNE uses three wire planes, each of which reads out 2D images. However, using 2D images to reconstruct a 3D interaction introduces many challenges. An alternate readout system replaces the three planes of wires with a single plane of pixels, which can directly capture the three dimensional information of the particle interactions. Two residual neural networks were used to compare the wire and pixel models. The networks were trained to classify each event by the neutrino flavor and the number of pions & protons, using training data that simulates readout for wire and pixel detectors. Once fully trained, the two networks ran over test data sets, and the classification accuracy and misidentification rates were compared. In the preliminary tests, which were based on perfect detectors with no noise, the pixel model outperformed the wire model for all classification categories. The pixel model was significantly better than the wire model at classifying particle showers, although both models struggle to distinguish electron showers from neutral pion showers. This result indicates that pixel readouts could have clear advantages over wire readouts. Progress can still be made in particle showers classification, and future work will need to assess the impact of noise or defective channels.

Towards Stable Ohmic Contacts for $MoSe_2$

Sabrina Chern
PRISE Fellow
Chemistry and Physics, 2020

Physics
Advisor: Philip Kim
Mentor: Andrew Joe

Molybdenum diselenide ($MoSe_2$) is a semiconducting transition-metal dichalcogenide (TMD), a class of layered materials that can be exfoliated to the two-dimensional (2D) limit. 2D materials can be stacked in different combinations to make arbitrary heterostructures, which has led to new fields in each of the materials and their junctions. Currently, determining the quality of $MoSe_2$ crystals with electrical transport at cryogenic, or very low, temperatures is limited due to unreliable contact methods. Recently, Movva et al. 2015 in "High-Mobility Holes in Dual-Gated WSe_2 Field-Effect Transistors" demonstrated that prepatterned chromium/platinum (Cr/Pt) contacts produced stable ohmic contacts for tungsten diselenide (WSe_2) down to cryogenic temperatures, which has opened up the study of the intrinsic properties of this material. The contacts are patterned using e-beam lithography and the metal is deposited on the hexagonal boron nitride (hBN) substrate before the TMD is placed on top. As in Larentis et al.'s 2018 paper "Large effective mass and interaction-enhanced Zeeman splitting of *K*-valley electrons in $MoSe_2$," a similar methodology for $MoSe_2$ using Cr/Pd could lead to reliable Ohmic contacts at low temperatures. An Ohmic contact is the interface between a metal and semiconductor that demonstrates a linear current-voltage relationship. Reliable Ohmic contacts at cryogenic temperatures are necessary to make Hall measurements, which would yield electron mobility and thus a sense of the $MoSe_2$ monolayer quality. Four-probe and two-probe resistance measurements can be used to determine the contact resistance. This result could lead to better studies of the intrinsic electrical properties of the material, which has potential in devices that require a high mobility and current on/current off ratio.

Frequency Stabilization of an 841 nm laser for an Erbium Quantum Gas Microscope

Sambuddha Chattopadhyay
PRISE Fellow
Physics, 2021

School of Engineering and Applied Sciences
Advisor: Markus Greiner
Mentor: Sepehr Ebadi

Understanding emergent phenomena such as high-temperature superconductivity, topological phases, and localization at the microscopic scale is central to a more complete picture of condensed matter physics, yet an impossible task using the current methods in the field. Quantum simulation, achieved through quantum gas microscopy of ultracold atomic realizations of condensed matter systems, has shown promise as a tool to understand emergent phenomena in the many-body systems. Theoretical results suggest that a quantum gas microscope of highly dipolar erbium atoms can be used to probe lattice models beyond simple nearest-neighbor interactions. In order to simulate quantum dynamics in the ultracold regime, erbium atoms must be trapped and cooled to quantum degeneracy. The first step in the cooling process is laser cooling which typically achieves 20 micro-Kelvin. To accelerate the cooling process we will use a much narrower transition of Erbium atoms as the last stage of laser cooling to achieve sub micro-Kelvin temperatures. For the laser cooling of the narrow transition to be reliable the frequency of the 841 nm laser must be stabilized to better than 1 kHz, and not drift on a daily basis. This project aims to design and eventually engineer a laser frequency stabilization setup that locks the frequency of the laser to a high finesse, stable reference cavity by implementing the Pound-Drever-Hall frequency stabilization technique on an 841 nm diode laser.

Oscillatory Modes of a Two-Dimensional Monolayer of Spheres in a Rotating Drum

Pierre-Emmanuel Grimm
PRISE-Emmanuel Fellow
Aerospace Engineering, 2020

School of Engineering and Applied Sciences
Advisor: Shmuel Rubinstein
Mentor: Lisa Lee

Granular materials are collections of small, solid particles. Examples include rice, coffee, and powders in pharmaceuticals. Granular materials are often mixed in rotating drums where the downward force of their weight competes with the upward force caused by the particle-particle and particle-drum interactions, resulting in overall oscillation. In this study, the oscillatory modes of a two-dimensional monolayer of spheres in a rotating drum were investigated. The effects of four factors were explored: the number of spheres, the rotating drum speed, the sphere roughness and the drum wall roughness. The centers of mass of the spheres were tracked in video recordings and oscillatory behavior of the spheres were analyzed. Preliminary results suggest that the behavior of the spheres is dictated by the sphere-sphere and sphere-drum friction, and exhibits a transition as the number of spheres is increased. At low spheres counts, the spheres roll commensurately with the drum and slip past each other. As more spheres are added, the sphere-sphere friction starts to dominate, causing the middle spheres' rotation to be frustrated and slip on the wall. At high sphere numbers, the spheres exhibit an anti-ferromagnetic-like behavior, with neighboring spheres rolling in opposite directions, resulting in non-sinusoidal oscillations. Increasing the sphere-sphere friction causes this transition to occur at lower sphere counts, while increasing the rotating drum speed results in higher oscillation frequencies.

Microfluidic Development for NMR Sample Delivery in NV-NMR Experiments

Liam R. Corrigan
PRISE Fellow
Astrophysics, 2019

Center for Astrophysics
Advisor: Ronald Walsworth
Mentor: Matt Turner

Nitrogen Vacancy - Nuclear Magnetic Resonance (NV-NMR) is a magnetic imaging technology that uses nitrogen vacancy deficiencies in a diamond's crystal lattice to align magnetic spins and detect magnetic fields. It has a broad range of applications in imaging magnetic fields of proteins, neurons, rocks, and the earth's magnetic field. However, current solvent delivery methods in NV-NMR experiments are inefficient and imprecise. This study seeks to improve solvent delivery to the experimental apparatus by incorporating microfluidic technology. The Center for Nanoscale Systems (CNS) facilities were used to fabricate microfluidic devices made from polydimethylsiloxane (PDMS). Both soft lithography and 3D-printing are used to make molds. PDMS is deposited on the mold to form well-controlled microfluidic structures.The NV sensing diamond is then bonded to the microfluidic device using a plasma cleaner and can be used to sense NMR signals in small volume samples. The implementation of microfluidics is expected to improve the sensitivity of detection by measuring a better constrained volume, making the magnetic signal more coherent and thereby minimizing uncertainties. It is also expected to improve the rate at which different solvents can be imaged by minimizing setup time in order to improve the overall efficiency of the experiment. The techniques developed in this work are likely to be used in future experimental and commercial setups for NV-NMR experiments, and image samples that are relevant for molecular biology, material physics, and geology.

Position-Specific Attachment of Nanoscale Samples

Kai Trepka
PRISE Fellow
Chemistry and Physics, 2020

Rowland Institute at Harvard
Advisor: Ye Tao

Seeing is believing. For decades, improvements in scanning probe microscopy (SPM), including magnetic force microscopy (MFM), has advanced with the development of ever more sensitive and powerful scanning probes. In particular, improvements in probe fabrication have improved measurement techniques in several applications, including DNA bending and complex magnetic semiconductors. Just as Galileo imaged the stars, SPM images nanoscale objects, investigating phenomena from animal navigation to energy generation.

There are two common MFM setups: probe-on-tip scanning, in which a magnetic-tipped cantilever is scanned over a fixed sample, and sample-on-tip scanning, in which a molecule or complex is attached to the tip of a cantilever and scanned. In both implementations, position-specific attachment of nanoscale objects is an outstanding challenge for application to very small samples, such as proteins and viruses. To achieve high spatial resolution in probe-on-tip scanning while avoiding tip convolution with the sample, continued miniaturization of the magnetic tip is necessary. To perform sample-on-tip scanning, a single sample must be attached to the tip.

Here, we combine chemical and physical methods to develop one-to-one attachment procedures that can connect both a small-diameter iron cobalt nanoparticle (FeCo NP) and a single biological particle to a gold nanoparticle substrate. This allows one to miniaturize probes and perform magnetic microscopy of single biological particles, improving spatial resolution into previously inaccessible regimes. This one-to-one attachment paradigm enables high spatial resolution scanning of nanoscale samples, advancing technology and applied research alike.

Superradiant Spin-Squeezed Atomic Ensembles as a Method for Producing Squeezed Light

Brian Warner
PRISE Fellow
Mathematics and Physics, 2020

Physics
Advisor: Susanne Yelin

Squeezed states are those minimum uncertainty quantum states for which one variable of a defining pair of variables has an exceptionally lower uncertainty at the expense of a higher uncertainty in the other. Superradiant emission is a macroscopic quantum effect wherein a number of entangled atoms emit light in an intense directed burst. This occurs because of coherent interactions between the atomic ensemble and the light field, altering the normal process of spontaneous or stimulated emission. Superradiance has been shown theoretically in the case of a driven spin squeezed atomic ensemble. The objective of the current research study is to provide theoretical prescriptions for the production of light that is in a squeezed state in the driven superradiant emission of an ensemble of spin-squeezed atoms. By using the optical Bloch equations and numerical methods to extend this model, we are showing that the light produced by a superradiant spin-squeezed ensemble is itself squeezed and also providing formulas determining what qualities the radiating ensemble needs in order to produce light with a desired type of squeezing. One of the benefits of producing squeezed light from a superradiant ensemble is that the light would occur in the far infrared or terahertz frequency ranges, where currently no methods of producing squeezed light exist. Viable production of squeezed light at a variety of frequency ranges promises technical advances in noise-sensitive fields such as metrology and quantum computing.

Characterizing Linewidth Differences Between the First-Order Raman Active Phonon Frequency of Annealed and Unannealed Diamonds

Daniel Fernandez
PRISE Fellow
Mathematics and Physics, 2020

Physics
Advisor: Isaac F. Silvera

In high pressure physics, diamond failure in diamond anvil cells has been a central constraint in achieving the extreme pressures needed for many experiments, such as for producing metallic hydrogen. The defects that occur on the surface of polished diamonds could be one factor contributing to their failure at lower than aimed for pressures. We believe that the process of annealing diamonds at high temperature can decrease their susceptibility to failure by removing these defects from their lattices. My work focuses on characterizing the differences between the linewidth of the first-order Raman active phonon frequency of annealed and unannealed diamonds. This phonon is three-fold degenerate due to the cubic structure of diamond, but strain and defects can partially lift the degeneracy and cause line broadening. By removing or reducing the internal strain and defects in the diamonds, annealing should result in a narrower line. To get the first-order Raman lines, a laser is focused on each sample and a spectrometer is used to measure the spectrum at the first-order phonon frequency. The linewidth of each spectrum is then measured as the full width at half maximum. Finding measurable differences in the linewidths of phonons before and after annealing could provide evidence that annealing is effective at improving the structure of the diamonds, and therefore their ability to achieve higher pressures.

Investigation of the Optical and Spin Properties of Tin-Vacancy (SnV^-) Quantum Emitters in Diamond

Arjun Mirani
PRISE Fellow
Physics and Mathematics, 2020

School of Engineering and Applied Sciences
Advisor: Marko Lončar
Mentor: Linbo Shao

Single-photon emitters in diamond are promising candidates for qubits in a coherent, scalable quantum network. These emitters, known as diamond color centers, consist of an atom (such as nitrogen or silicon) adjacent to one or more vacancies in the diamond crystal lattice. One of the most well-studied color centers, negatively charged silicon-vacancy (SiV^-), has robust optical properties due to a structural symmetry, but undesirably low spin coherence time due to phonon-induced decoherence, in which lattice vibrations drive transitions between the split energy levels of the SiV^- ground state. The current project focuses instead on negatively charged tin-vacancy (SnV^-) centers: they are less susceptible to phonon-induced decoherence, due to their energy level structure, while also being optically robust.

The first phase of this project involved building a precisely controllable laser system to resonantly excite SnV^- centers. This system is a sum frequency generator, which exploits the nonlinear optical properties of crystalline lithium niobate to combine the frequencies f_1 and f_2 of two laser beams, producing an output beam of frequency f_1+f_2. The output frequency is tunable, to allow resonant excitation of four zero-phonon emission lines of SnV^- at cryogenic temperatures. The second phase, currently in progress, involves configuring a confocal microscopy setup to work with the relevant wavelengths and using this system to investigate various properties of SnV^-, such as emission linewidth, spin coherence time, and spectral diffusion. The resulting characterization of these properties aims to improve our understanding of tin-vacancy's potential for solid-state quantum network applications.

Twisted 2-Dimensional Materials

Yunchao Zhang
PRISE Fellow
Mathematics and Physics, 2021

Physics
Advisor: Amir Yacoby
Mentor: Di Wei

The puzzling behavior of strongly correlated materials, which exhibit electronic and magnetic properties, has been closely studied by physicists for decades, and the theory behind many of these phenomena still remains an outstanding problem in condensed matter physics. These phenomena often emerge at the interfaces of stacked two-dimensional electronic systems. Motivated by recent developments in the field, including the discovery of superconductivity in twisted bilayer graphene, we investigated how a twist angle affects the electrical conductivity of tantalum disulfide, a transition metal dichalcogenide. Unlike graphene, tantalum disulfide is known to superconduct as a monolayer, so its twisted form may be even more robust and conductive than twisted graphene. We first mechanically cleaved and exfoliated tantalum disulfide on silicon dioxide wafers. The tantalum disulfide was subsequently encapsulated in hexagonal boron nitride. The entire stack was assembled into an electronic device using thermal evaporation and electron beam lithography techniques; electrical contact was made using gold. Because tantalum disulfide is oxygen-sensitive, the entire process is conducted in an argon glovebox. By introducing and adjusting the "magic" twist angle between two tantalum disulfide layers, we expect to see enhanced superconductivity, which will be reflected by the presence of zero-resistance states at an increased critical temperature when compared to tantalum disulfide monolayer. The observation of these effects could offer significant physical insight into the theory of superconductivity and strongly correlated phenomena. Furthermore, two-dimensional materials such as tantalum disulfide have enormous potential in contributing to the development of high quality, compact, and energy-efficient electronic devices and components.

Potential Energy Surfaces from Time-Dependent Density Functional Theory Calculations

Andrew Winnicki
PRISE Fellow
Computer Science and Physics, 2021

School of Engineering and Applied Sciences
Advisor: Prineha Narang
Mentor: Johannes Flick

Trapping a molecule inside an optical cavity changes its potential energy surface (PES), a function describing the relationship between a molecule's energy and its geometry. Modifying this relationship changes how energy wavelets traverse the PES, opening up new possibilities for more efficient energy transfer pathways and reactions. Understanding the PES is a critical first step in potentially cultivating new methods of more efficient energy production. However, current methods of energy production obtain the PES without considering the quantum nature of light and matter. Using quantum electrodynamical density functional theory (QEDFT) in calculations can address the nature of matter and light on the same quantized footing. Preliminary results show that QEDFT calculations of the potential energy surface of formaldehyde with time-dependent local density approximation calculations are consistent with experimental values obtained from absorption and transmission spectra. Upcoming/future steps to the project include harnessing QEDFT to describe the potential energy surface of small molecules strongly coupled to the light field in optical cavities. We hope to show how this strong-light matter coupling modifies the PES, then model the dynamical behavior of multi-particle systems in optical cavities. The successful completion of our project would prompt a better understanding of the excited-state dynamics under strong-light matter coupling, opening up the possibility for more efficient energy transfer pathways, reactions, and methods of energy production.

Quality Factor Enhancement by van der Waals Clamping

Anca Dragulescu
PRISE Fellow
Mathematics and Physics, 2021

Physics
Advisor: Hongkun Park
Mentor: Ryan Gelly

One element that has become increasingly important in the study of 2D materials is the Van der Waals (VdW) heterostructure. Comprised of atomically thin materials stacked on top of each other, vdW heterostructures have unique electronic, optical, and mechanical properties. By suspending these structures, they can function as 2D mechanical resonators when driven by an external sinusoidal force. The maximum amplitude of the oscillation is a measure of how good the resonator is. Because they experience more damping, resonators fashioned from vdW heterostructures typically have lower quality factors than those made from a single material.

This study investigates possible methods of improving the quality factor for vdW heterostructure resonators by clamping the heterostructure to the substrate that supports them. This project presents how the quality factor is affected by the shape and material of the clamping mechanism, both at room temperature and cryogenic temperatures. Upon successful completion of the project, we expect that clamping should improve the quality factor of 2D resonators.

The successful completion of this project will provide a way of improving and reducing the damping of such structures, which would allow researchers to make better resonators based on this class of materials.

Modulation Transfer Spectroscopy of Rubidium as a Stable Frequency Reference for Laser-Cooling Molecules

Yoo Kyung (Eunice) Lee
PRISE Fellow
Music and Physics, 2019

Physics
Advisor: John Doyle
Mentors: Ben Augenbraun, Yicheng Bao

Cold molecule research, which studies molecules well below 10 K, is interesting for its potential applications to quantum computing, tests of fundamental theories of physics, and the study of novel behaviors in matter. To demonstrate quantum computation, we plan to use laser-cooling to load individual molecules into an array of optical tweezers. This requires that we stabilize multiple lasers at the sub-MHz level, which is 10 times more precise than the frequency reference scheme currently being used. To address this, a Littrow configuration external-cavity diode laser was built to perform saturated-absorption spectroscopy of the rubidium D2 line. This laser can achieve the stability required for future stages of the experiment. By applying modulation transfer spectroscopy, we generate an error signal which is used as feedback to a PID control system which corrects and stabilizes the laser frequency. The laser was locked to 384.230406 THz with a 200 kHz uncertainty and will be a more stable frequency reference for the lasers that are cooling molecules. This will improve the stability of the lasers so they can be used in further applications such as quantum computing.

Multi-Terminal Josephson Junctions

Brian Marinelli
PRISE Fellow
Physics, 2019

Physics
Advisor: Philip Kim
Mentor: Katie Huang

Current in superconductors (characterized by zero resistance) is carried by Cooper pairs, which are bound pairs of electrons in the material. These Cooper pairs have a characteristic size, ξ, which is thought of as the typical separation between the electrons in a pair. Recently, extensive research has been conducted on Josephson junctions, which separate two superconducting (SC) materials by a normal material. When the length of the normal region is kept $\lesssim \xi$ it has been observed that super-current may tunnel across the normal region by the formation of Andreev Bound States. We are working to fabricate and test multi-terminal Josephson Junctions. Graphene, a single layer honeycomb lattice of carbon atoms, serves as the scattering region which separates four SC contacts. Graphene and hexagonal-boron nitride (h-BN) are mechanically exfoliated and stacked so the graphene is encapsulated by h-BN. E-beam lithography writes the pattern of leads and reactive ion etching allows exposure of the edge of the graphene. The graphene is contacted through the edge by aluminum leads deposited using e-beam evaporation. Different geometries of the leads and scattering region will be investigated. Certain geometries allow for control of the SC phase of one or more of the leads by varying the applied magnetic field. This control allows for probing of the full space of superconducting phases. Theoretical predictions anticipate that different regions of the phase space may be characterized by different quantized values of transconductance.

Strontium Titanate Surface Preparation for Thin-Film Iron Selenide Growth

Camille Bean
PRISE Fellow
Physics, 2020

Physics
Advisor: Jennifer Hoffman
Mentor: Tatiana Webb

A superconductor is a material that conducts electricity without any energy loss, since it has zero electrical resistivity. Superconductors could be useful across many technological fields; however, they only operate at impractically low temperatures. Iron selenide (FeSe) is a superconductor that operates at up to 65 K in its thin-film form. This temperature is unusually high, but still far too low for most practical applications. By studying the surface properties of FeSe, we seek to understand its relatively high operating temperature, so that superconductors that operate at even higher, more practical temperatures can potentially be discovered. In this experiment, molecular beam epitaxy (MBE) is used to grow thin-film FeSe on strontium titanate ($SrTiO_3$), which is then imaged using an attached scanning tunneling microscope (STM). The MBE sublimates iron and selenium in ultra-high vacuum, creating gaseous beams which condense and react on the $SrTiO_3$ surface. Developing the correct surface structure of $SrTiO_3$ is crucial to facilitating FeSe growth. Early research suggests that this is best done through a preparation process involving stages of heating and chemical etching. However, the parameters of the recipe must be adjusted frequently, as not all $SrTiO_3$ samples are identical. We have investigated $SrTiO_3$ surface preparation parameters, using atomic force microscopy (AFM) as well as STM to evaluate the parameters concerning successful FeSe film growth.

Determining the Configurations of Colloidal Particles Under Depletion Forces and Electric Fields

Jacquelyn Ho
PRISE Fellow
Physics, 2020

School of Engineering and Applied Sciences
Advisor: Vinothan Manoharan
Mentor: Ellen Klein

Self-assembly is a common biological and chemical process, but it is not understood well on a fundamental level. To probe the mechanisms of self-assembly, we study colloidal particles — insoluble, micrometer-scale particles that experience Brownian motion. The ability to view such particles via bright-field microscopy and their observable equilibration time-scale make these particles ideal for studying structural rearrangements. We are exploring the equilibrium configurations that clusters of six colloidal particles form under two competing interactions: short-range depletion forces and electric dipoles caused by an external electric field. We use polystyrene particles 1.3 μm in diameter suspended in a solution containing colloidal silica as the depletant, and we perfuse this dispersion into square capillary tubes with a metallic coating on two parallel faces, which function as parallel plate electrodes. After using optical tweezers to assemble two-dimensional clusters of six particles within the dispersion, we apply an alternating current voltage to the electrodes and record the clusters using digital micrographs. We anticipate that the resulting conformations and their probabilities will be a function of the depletant concentration and electric field strength, and accordingly lie on a spectrum between the compact structures formed by six particles subjected to depletion alone and the linear chains formed by particles subjected to an electric field alone. Understanding the behavior of this simple system under two interactions that individually lead to different equilibrium configurations provides a foundation for understanding the self-assembly of more complex systems, in which various forces may drive the system into differing states.

Investigation of a Successful Doppler Cooling Scheme for Molecules

Caleb Heuvel-Horwitz
PRISE Fellow
Physics, 2021

Physics
Advisor: Susanne Yelin

Doppler cooling, useful for preparing ultra-cold atoms for quantum experiment submits an atom to counter-propagating beams that are detuned slightly below atomic resonance to effectively reduce the atom's temperature to nearly zero K. This research focuses on the development of a successful Doppler cooling technique for molecules. However, Doppler cooling requires a transition that is cyclic, such that the atom always returns to the same ground state after an absorption-reemission event. Finding a cyclic transition in a molecule is virtually impossible due to its complex internal structure. One solution is to use vibrational, rather than electric, transitions in the molecule. Vibrational transitions are less energetic and occur too infrequently to be used to cool a molecule in a reasonable amount of time, so to effectively utilize them in a cooling scheme, this research investigates superradiance and counter-propagating Raman beams as a solution. Superradiance, the phenomenon in which molecules clustered together emit photons more quickly than they would alone, theoretically speeds up the cooling process despite the slow nature of vibrational transitions. Photons in a Raman beam have higher energy than those of a vibrational transition, also speeding up the cooling process.

Structural Color from Binary Colloidal Aggregates

Edmund Derby
PRISE-Emmanuel Fellow
Physics, 2019

School of Engineering and Applied Sciences
Advisor: Vinothan Manoharan
Mentor: Ming Xiao

Structural color is caused by the interference of light scattered from a microstructure. Compared to pigment color, structural color is much more resistant to fading, so shows promise for developing long-lasting dyes. However, natural structural color, such as the blue in peacock feathers, is often angle-dependent (iridescent) because it arises from light scattering from anisotropic microstructures in the material. This project explores packing of a binary mixture of colloidal particles to make isotropic structures which result in non-iridescent structural colors. As a model, we assembled packed structures using two sizes of silica colloids (1.8 μm and 0.4 μm). We infiltrated the assembled samples with a refractive index-matched water–glycerol mixture, then dyed them and took 3D images using a confocal microscope. From the images, we calculated the structure factor of the large particles using particle tracking software and applied multiple scattering theory to predict the structural color properties of the packed structures. We compared the theoretical results to measurements of the reflection spectrum to determine how the large particles affect color. As expected, the binary mixture of colloids forms an isotropic disordered structure. We expect that exploring different relative sizes and quantities of the two particles will lead to different aggregate structures and thus structural color properties. With enough control over particle size, it is possible that a range of non-iridescent structural colors could be formed using this method.

PSYCHOLOGY

How do Young Children Learn Numbers?

Haley McBride
BLISS Fellow
Psychology, 2020

Psychology
Advisor: Susan Carey
Mentor: Deborah Zaitchik-Samet

Children's early number proficiency has been found to predict their subsequent performance in school and their future life success. Executive function skills, centrally important for a wide array of mental processes, have also been found to predict these same facets of school and life success. The goal of the current study is to determine if children's executive function skills have an impact on their number understanding; their ability to comprehend and manipulate the cardinal values of numbers. In this study, children aged three to four complete games over the course of two separate sessions. The first session assesses children's executive function skills such as shifting, inhibitory control, and working memory. The second session assesses their number understanding through tasks, such as ordering cards with different numbers of fingers on them and being asked to give a certain number of toys from a bucket. If executive function skills have an impact on children's number ability, then their performance on the executive function measures should be associated with their performance on the number measures. If this predicted pattern of results are found this would be significant because improving executive function skills could help improve children's overall number understanding. This factor would be important to consider when designing school curricula to maximize young children's success in understanding numbers.

Examining Children's Use of Top-Down Information in Real-Time

Maribelle Dickins
BLISS Fellow
Psychology, 2020

Psychology
Advisor: Jesse Snedeker
Mentor: Anthony Yacovone

When listeners hear continuous speech, they begin building representations of the incoming sounds, structures, and meanings. Low-level representations (e.g. sounds, words) are used to construct those at higher levels (e.g. structures, meanings). Information from higher-levels may also be used to constrain processes at lower-levels (e.g. plausibility may constrain your interpretation of ambiguous words). These top-down processes are rational and efficient in adults, but poor and delayed in children. This study examines when children use top-down information to make predictions about upcoming material. Using electroencephalography (EEG), we monitored the (early) left anterior negativity ((E)LAN) component. (E)LAN indexes the precise moment when children recognize mismatches between their syntactic predictions and the sentence. We used a naturalistic listening paradigm, whereby children passively listen to a recording of a children's book. (E)LANs were elicited by swapping determiners with prepositions in **high** and low predictable environments, i.e., "Miss Honey went to **the** | for blackboard…". We quantified predictability using cloze probabilities, which measure the likelihood of a word given its preceding context. This study manipulated cloze probability (high vs. low) and syntactic prediction (correct vs. incorrect) by interchanging words systematically. Data collection is ongoing; however, we predict that adults will show (E)LANs in high and low conditions because adults make coarse syntactic predictions even when individual words are not highly predictable. Children, however, will only show (E)LANs in highly predictable contexts due to increased potential for prediction. This study will advance knowledge on real time children's use of top-down information.

Evidence-Based Psychotherapies vs. Usual Clinical Care

Katherine Venturo-Conerly
BLISS Fellow
Psychology, 2020

Psychology
Advisor: John Weisz
Mentors: Spencer Evans, Katherine Corteselli

The psychotherapy clinicians provide in everyday practice often includes a combination of procedures learned during training and procedures informed by the clinicians' intuition. In contrast, dozens of psychotherapies have been documented in written manuals and tested against control groups in randomized controlled trials (RCTs). Therapies that have performed better than control groups in multiple RCTs are designated "evidence-based psychotherapies" (EBPs). A primary goal across the hundreds of RCTs published to date has been to identify therapies that produce better clinical outcomes for patients than the typical clinical care, or "usual care," offered by mental health clinicians. Do EBPs actually outperform usual care? We seek to answer that question by performing a meta-analysis of RCTs that compare an EBP to usual care. Our analysis will include studies published between 2008 and 2018, in which treatment focused on any of five common mental health problems: anxiety, depression, substance use, aggression/antisocial behavior, and attention deficit/hyperactivity. The primary outcome measures will be reductions in symptoms of those problems. We will determine how effectively EBPs reduce symptoms of these mental health problems and test possible moderators of treatment effectiveness. For example, we will compare the effectiveness of different types of EBPs (e.g. cognitive therapy, mindfulness) and we will compare the effectiveness of EPBs across problem types (e.g. anxiety, depression). The findings of this study may help guide future psychotherapy research and help clinicians and clinical directors determine which current EBPs offer a sufficient advantage over usual care to warrant implementation with their clients.

Infants' Inferences about Insides

Yiping Li
BLISS Fellow
Psychology, 2019

Psychology
Advisor: Susan Carey
Mentor: Jonathan Kominsky

Imagine that an object (A) moves toward a stationary object (B); upon contact, A stops and B starts moving in the same speed and direction as A. Previous literature suggests that infants see this event as causal. In other words, infants see A as an agent that caused B's motion and B as an inert patient that receives the transferred motion from A. This series of experiments investigates if infants infer causal agents and patients have insides. The first experiment replicates Experiment 3 in a paper by Setoh *et al*. (2013). After familiarizing 9.5- to 11.5-months-old infants with two furry objects (one self-propelling and one inert), both objects are revealed to be hollow. If infants look longer at the hollow self-propelled object than the hollow inert object, it suggests that they are surprised to see a hollow self-propelled object, and the study is a successful replication. A second and third experiment extend the findings by showing infants a causal event and an event in which the B travels at 3 times the speed of A, a physically impossible speed if B is inert and A is a sole cause of B's motion. With the results of these three experiments, the study examines (1) whether causal role in itself is enough of a cue to suggest the capacity to self-propel and (2) whether agents and patients in a triggering event are viewed similarly or differently from those in a causal event.

Digital Exchanges and Feelings of Interpersonal Closeness

Rebecca You
PRIMO Fellow
Psychology, 2020

Harvard Business School Marketing Unit
Advisor: Anne Wilson

In recent years, exchanging digital goods has become increasingly commonplace, whether in the form of money, books, or movies. Despite its ease and convenience, however, research has shown that individuals experience a phenomenon known as the "mere-ownership effect," in which they have greater psychological ownership over physical goods as opposed to digital ones. This study evaluated whether this phenomenon affects feelings of interpersonal closeness between the giver and the receiver of the physical or digital good. We tested this by compensating participants for completing a survey with a $5 payment in either cash or Venmo, and recorded their self-reported levels of interpersonal closeness to the researcher the next day. Preliminary findings revealed that giving and receiving physical (versus digital goods) enhanced feelings of interpersonal closeness between the giver and the receiver, especially when there was a high degree of ownership between the giver and the good. In other words, the more the receiver felt that they were given something of high ownership, the closer they feel to the giver of the good. The costs of being constantly digitally connected, then, may work against our favor and minimize the degree of closeness we feel with one another. Future studies can benefit from learning how this phenomenon affects different types of relationships (e.g. friends, family members).

Adolescent Learning

Amma Ababio
BLISS Fellow
History and Science, 2019

Psychology
Advisor: Leah Somerville
Mentor: Juliet Davidow

Learning is integral to every stage of development. Previous studies have shown that adults are better at learning to press a button to gain rewards than learning not to press a button to avoid punishments. These studies, however, did not explore possible behavioral changes from adolescence to adulthood and how adolescents use previously learned information in novel situations. We investigated these topics using a two-part behavioral paradigm: Learning and Inhibitory Control tasks. In the first task, the Learning task (adapted from Guitart-Masip et al., 2012), 22 subjects between 12 and 17 years of age learned to associate pressing or not pressing a button to two neutral stimuli with a monetary reward and two with a monetary punishment. Specifically, they learned to press a button to gain a reward (Go-to-Win), press a button to avoid punishment (Go-to-Avoid), not press a button to gain a reward (No Go-to-Win) and not press a button to avoid punishment (No Go-to-Avoid). Unlike previous studies, in the second task, the Inhibitory Control Task, subjects used what they had learned in a novel situation by pressing a button when they saw 11 new stimuli and not press a button when they saw the four familiar stimuli from the previous task. Ongoing analyses will investigate patterns of action-reward interactions and possible asymmetries in learning in the first task, and the effects of learning in the first task on performance in the Inhibition task. Results from this study could contribute to the understanding of developmental trajectories of learning.

Testing Grey Parrot *Psittacus erithacus* on Sequences and the Preposition "In"

Stephanie Dufresne
PRISE Fellow
Integrative Biology, 2020

Psychology
Advisor: Irene Pepperberg

Sequencing skills are required for organizing thoughts, following instructions in order, and syntactic understanding. Prepositions, which relate multiple objects, can create sequences. Given that birds' song learning has been proposed as a model system for human language acquisition, might birds be models for studies of sequential learning? We attempted to teach two Grey parrots (*Psittacus erithacus*) the concept of order using the preposition "in". We presented Athena (5 years old) and Griffin (23 years old) two different stacks of colored cups that were randomized via Random.org and stated which order to select ("Pick *blue IN yellow*", ignore "*yellow IN blue*". Even if successful, they might not fully understand "in", but likely would have acquired some knowledge of order. If successful, could they then also succeed when presented with two stacks comprised of three different colored cups (e.g., yellow IN red IN blue and not other permutations)?

Our results are encouraging. Griffin succeeded on the first task (75%, $p < 0.05$), and transferred at the same level to different colors without training. Athena, however, is still at chance. On the second task, Griffin is still at chance but is improving: he went from 50% (pure chance) accuracy on his first 18 trials to 67% ($p=0.07$) on his second 18 trials. We have too few trials to determine whether he is indeed understanding the order, or is instead focusing on a segment of the stack (e.g., the top cups) rather than comprehending the relation between "in" and the full arrangement. The study is ongoing with both birds.

Receptiveness in Social Interaction

Peter Kim
BLISS Fellow
Neurobiology, 2020

Harvard Kennedy School
Advisor: Julia Minson
Mentor: Hanne Collins

People experience difficulty engaging with and evaluating opposing views in an unbiased manner. Such intolerance can many times create group boundaries that incite conflicts between those with differing beliefs. Receptiveness has been defined as a "willingness to psychologically engage with opposing views." In our study, we seek to first answer whether this "receptiveness" can be transmitted from person to person, then further analyze the linguistic landmarks that define "receptiveness." To do this, participants are recruited to the lab and paired with a conversation partner who is selected by maximizing disagreement based on pre-experiment survey responses. They are then asked to discuss a topic about which they disagree on. In the control group, both participants in a dyad are simply asked to discuss the topic; however, in the experimental group, one participant is told to be "receptive" to the other's views. After the discussion, participants complete the "Receptiveness to Opposing Views" scale for both themselves and their conversation partner. Finally, the participants' conversations are analyzed with a natural language processing program to detect linguistic markers of receptiveness. We hypothesize that our receptiveness intervention will increase the receptiveness of the manipulated partner and may potentially increase the receptiveness of their conversation partner. If our results find that a simple reminder to be receptive increases the receptiveness of both the self and the partner, this can be a simple intervention that could improve the state of discourse across the political aisle.

The Infinite Analogical Model: A Probabilistic Approach to Learning by Analogy

Jambay Kinley
PRISE Fellow
Computer Science, 2020

Psychology
Advisor: Sam Gershman
Mentor: Thomas Pouncy

A large subset of semantic knowledge is guided by relationships between concepts or objects. Previous studies have proposed probabilistic models that discover systems of related objects. We extend this approach to account for learning analogies by clustering relations along with objects. We propose a nonparametric Bayesian model that discovers clusters of relations and objects when given data about whether different relation(s) hold or not between several different objects . This allows for a form of analogy : certain relation-object sets can be isomorphic to one another if they share the same relation and object types, in the sense that the same underlying relational system applies even though the relations and objects are superficially dissimilar. Thus far, the model and inference algorithms have been implemented. Preliminary results with synthetic data show that our model is able to correctly discover systems of relation types and object types. Going forward, the model will be applied to real-world problems and its predictions will be compared to data collected in behavioral experiments. We expect the model's predictions to closely resemble those found in these experiments. If our hypothesis is supported, it would suggest that our model provides a good account of analogical learning and would allow for its use in studies of analogical mapping which is a core process in human cognition.

SOCIOLOGY

Curricle Narrative Project

Snow (Xue) Dong
SHARP Fellow
Sociology, 2020

Berkman Klein Center
Advisor: Jessica Yurkofsky
Mentor: Matthew Brattles

What Harvard University stands for as an educational institution is essentially represented by its curriculum. The Harvard curriculum, however, has changed dramatically over time. These changes not only show a shifting academic landscape, but also point to evolving intellectual commitments and societal values of the times. In today's context of higher education in America, when Harvard University faces pressing questions of diversity and inclusion, reflecting on our past is ever more valuable. The Curricle Narrative project reflects on the evolution of Harvard curriculum through time, specifically focusing on academic departments and programs that highlight moments of change. At metaLAB, I conducted research through the Harvard University Archive, online departmental websites, and interviews, the output of which is visualized and presented online as stories of individuals who shaped Harvard University from its classrooms. The stories follow three distinct academic areas at Harvard: the East Asian Studies Department, the Women, Gender and Sexuality Studies department, and the Engaged Scholarship program. As my research reveals, despite their apparent differences, these areas of studies share commonalities in their founding and their interaction with the students and educators of Harvard University. The final product will be featured on the Curricle website, a course navigation and exploration software designed for Harvard undergraduates to better navigate the numerous course offerings. These stories will give voice to members of the Harvard University community by celebrating their collective identity as Harvard students and scholars, which derives its strength from its diversity.

Assessing Ethics Education at Harvard University

Maclaine Fields
BLISS Fellow
Economics, 2020

Edmond J. Safra Center for Ethics
Advisor: Danielle Allen
Mentors: Jess Miner, Michael Blauw, David Kidd

As part of the National Ethics Project, the Edmond J. Safra Center for Ethics is analyzing where and how ethics instruction happens at Harvard. Researchers created a custom search algorithm using a weighted dictionary of ethics-related terms, that has identified approximately 500 courses per semester offered across the university. Researchers are now surveying instructors about their instructional goals and methodologies and are using qualitative data analysis methods created by the Humanities and Liberal Arts Assessment Team (HULA) to code syllabi and instructor surveys that illuminate instructors' implicit learning pathways. Quantitative and qualitative data analysis are revealing how instructors engage students, what resources they deploy, which skills they hope students will gain, and how the course contributes to human development.

From this data, the team is developing a student assessment tool informed by humanists' methods and goals. To support the development of a new ethics assessment tool, we have begun a literature review on ethics assessment methodologies and instruments. The qualitative data analysis allows us to investigate the heterogeneity of perceptual domains engaged, areas of intended intellectual and personality development, and psychological capacities deployed for each class. Our team has begun a review of complexity theory literature to foster the development of an educational wealth index that will capture the degree to which any given course activates the many, diverse learning pathways that support human development across the many dimensions captured by the multiple intelligences framework.

Ultimately, these methods and tools can be replicated at other schools and in other disciplines. The team also plans to create data visualizations that allow students to find ethics courses at Harvard University.

Assessing the Role of Innovation in HIV Advocacy for the Commonwealth

Alyssa Panton
SURGH Fellow
Integrative Biology, 2021

AIDS Action Committee - Fenway Health
Harvard Center for AIDS Research
Advisor: Christopher Brennan
Mentors: Bisola Ojikutu, Wanda Allen

Public concern about the HIV epidemic is far less present than it was even 10 years ago despite the state of the epidemic being more severe than people acknowledge. A very high cumulative total of individuals who have been diagnosed with HIV/AIDS in Massachusetts, and a recent outbreak among people who inject drugs (PWID) in the Northeast region of the state have public officials on edge. At the *HIV Innovations in Action 2018* conference, panelists attributed stagnating grassroots advocacy in part to a lack of workforce diversity in prevention and care organization. This project assesses the validity of these concerns and proposes innovative solutions to overcome these obstacles. Data for this assessment is collected through independent interviews of HIV/AIDS healthcare advocates. The interview questions were designed to model session topics of the conference by discussing the role of innovation in *Getting to Zero (GtZ)*. Due to improvements in antiretroviral therapy, early diagnosis, and treatment access the life expectancy of people living with HIV (PLWH) is increasing, meaning there are more lifelong advocates occupying positions of influence throughout the public health ecosystem. Evidence suggests representative groups are better suited to define meaningful innovations for their own cohort. Thus, we hypothesize it would be wise to incorporate a variety of ages at the executive tier to maximize the impact of advocacy efforts. This project will provide local advocates with ideas for cultivating representative leadership and optimizing opportunities for age diversification to have a positive influence on community engagement across cohorts. Ultimately, we hope that this research improves innovation in HIV advocacy for the Commonwealth.

Why "Failed" Movements Matter: Effects of Pro-Choice Movements on the Enforcement of Abortion Bans in Central America

Lucas Mitchell
BLISS Fellow
Sociology, 2020

Sociology
Advisor: Jocelyn Viterna

In El Salvador, the influence of a transnationally-funded pro-life movement led to the passage of a total abortion ban in 1997 (abortion had been allowed in certain circumstances previously). In 2006, similar patterns led to the same law being passed in Nicaragua. There are remarkable similarities in how the abortion debate evolved in each country; however, El Salvador is the only country that regularly imposes decades-long sentences on women convicted of "fetal homicide." Our research seeks to test the hypothesis that as opposed to Nicaragua, where the presence of a small but vocal pro-choice movement prevented the policy debate from becoming one about enforcement, the lack of opposition to the powerful pro-life movement in El Salvador led to a greater focus on enforcement of abortion laws.

We reviewed articles in prominent Salvadoran and Nicaraguan newspapers from 1989-2014 and conducted interviews with Salvadoran civilians, activists, doctors, and politicians, coding them for a variety of abortion-related themes. Preliminary results uphold the hypothesis that in El Salvador, lack of opposition to the pro-life movement was a primary cause that led to the current zealous enforcement of anti-abortion laws. The Nicaraguan pro-choice movement is widely regarded as a failure due to a lack of progress in the areas of policy and public opinion. However, the case of El Salvador suggests that social movements may still have value when they act as a target for opposing forces, by preventing other potential groups (i.e. pregnant mothers) from becoming targets.

WOMEN, GENDER, AND SEXUALITY

(Under)Reporting Violence: Gender, Race, and Firearms in Focus

Ekemini U. Ekpo
BLISS Fellow
Sociology, 2019

Women, Gender, and Sexuality
Advisor: Caroline Light

In the wake of tragedies such as Parkland High School shooting, a light has once again been cast upon the issue of gun violence in the United States. However, the United States' collective imagination conjures enduring images of black and brown men as perpetrators of violence, even as white men are overwhelmingly the perpetrators of mass shootings. Furthermore, selective outrage, however temporal it may be, largely favors white victims. This two-pronged project aims to illuminate the oft-obfuscated realities of gun-related homicides for women and people of color. The first prong of this project entails making open-records requests of justifiable homicide cases in the state of Texas, a state known for its lax gun laws, in hopes of observing the extent to which demographic qualities inform the dismissal rates of cases that invoke self-defense. These qualities include but are not limited to: the race of the victim(s) and perpetrators(s), the relationship(s) between the victim(s) and perpetrator(s), and the geographic location of the incident,. The second prong of the project analyzes data provided by the National Violent Death Reporting System regarding female-perpetrated homicides in the United States, in anticipation of both a descriptive public health paper and a more extensive analytical paper discussing any discernible correlations between female-perpetrated violence and state legislation regarding gun use. We anticipate that through these efforts, we will observe statistically significant results which substantiate prior claims that marginalized gender and race demographics experience gun violence in ways distinct from popular discourses.

Acknowledgements

Greg Llacer
Director of Harvard College PRISE
Director of the Office of Undergraduate Research and Fellowships (URAF)

Jennifer Shephard
Coordinator of BLISS
Special Initiatives Program Manager in the Office of the FAS Dean for Social Sciences

Daria Wright
Coordinator of PRIMO
Staff Assistant in the Doctoral Programs at Harvard Business School

Thomas Spencer
Coordinator of SHARP
Assistant Director in the Office of URAF

Christy Colburn
Coordinator of SURGH
Associate Director of the Global Health and Health Policy Undergraduate Program

Emily Maguire
Coordinator of SURGH
Senior Program Coordinator of the Global Health and Health Policy Undergraduate Program

Chris Kabacinski
Administrative Coordinator of Undergraduate Research in the Office of URAF

Britta Wierich
Winthrop House Building Manager

PROGRAM ASSISTANTS:

Sean Gibney, *Lead PA*
Emma Clerx, *Administrative PA*
Madeleine Granovetter
Calder Miller
Vaibhav Mohanty
Steffan Paul
Claire Rushin
Olivia Velasquez

PROCTORS:

Tez Clark, *Lead Proctor*
Niamh Mulholland, *Emmanuel Proctor*
Audrey Effenberger
Laura Kanji
Alex Kelser
Jessica Kim
Michael Liu
Jin Park

Index