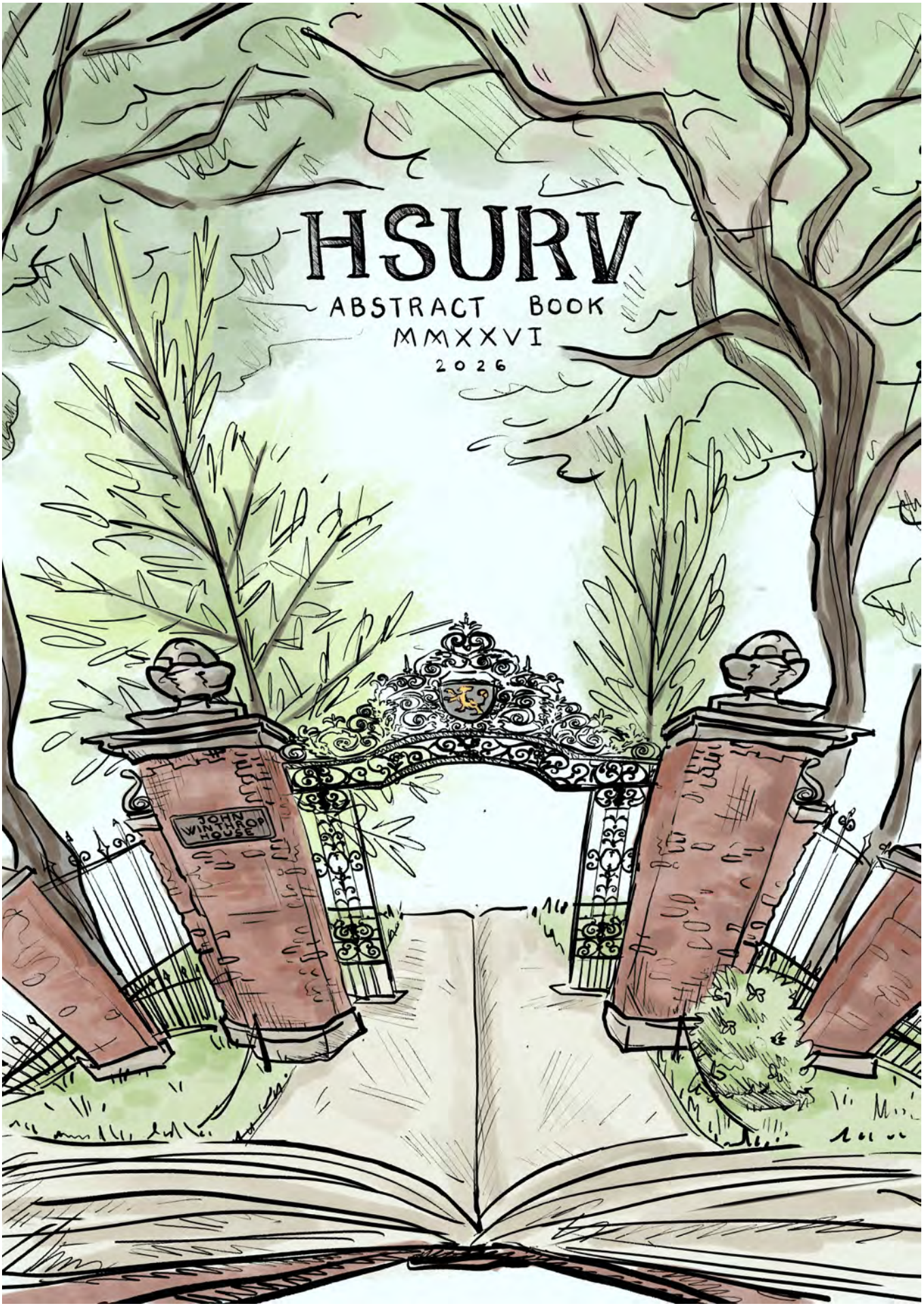
HSURV
ABSTRACT BOOK
MMXXVI
2026
JOHN WINTHROP HOUSE

Abstract Book

MM.XX.VI

Abstract Book

Harvard Summer Undergraduate Research Village

Edited by Isabelle Agarwal (Lead Editor), Nurayda Albeez, Bishwo Jeet Bista, Chance Bonfanti, Anthony Borrelli, Jolene Cao, Taylor Cross, Aditi Desai, Lucas Fang, Veronica Fleming, Alex Gao, Maya Gewurz, Tristam Hines, Grace Hur, Danielle Im, Aditi Joshi, Riddhem Kapoor, Dalevyon LJ Knight (Lead Editor), Joyce Kwack, Xin Lin, Audrey Lu, Kerry Nguyen, Yvette Nyamhere, Joanna Osaghae-Nosa, Sarah Park, Akshaya Ravi, Karolina Spiewak, Bill Tang, Caitlyn Thompson, Anthony Wei, Iris Xue, Hanah Youn, and Emma Zhang.

Designed by Emily Kuang, Katherine Lam, Julia Wu (Lead Artist), Lena Xie, Amy Zhang, and Selina Zhang.

From the comforts of Winthrop House, 32 Mill St, Cambridge, MA 02138,

During the Harvard Summer Undergraduate Research Village, June 8th–August 6th, 2026.

HARVARD COLLEGE

Office of Undergraduate Research and Fellowships

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Acknowledgments

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Program Descriptions

The Harvard Amgen Scholars Program (Amgen) is a summer undergraduate research program in biotechnology and biomedical sciences funded by the Amgen Foundation. Harvard Amgen Scholars, who are current sophomores and juniors, are matched with host laboratories at Harvard and its affiliates to conduct summer research. In addition to research, students participate in scholarly and pre-professional development sessions, advising, and social activities with their cohort and attend the North American Amgen Scholars Symposium.

The Build Learning through Inquiry in the Social Sciences (BLISS) program 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 and lives in one of the Harvard College houses with the other fellows in the Summer Undergraduate Research Village. In addition to conducting full-time research, BLISS Fellows participate in a rich variety of programming, including both social and academic activities.

The Du Bois Scholars Program (DBSP) was launched by Harvard and the Legacy of Slavery Initiative in 2024 as a fully funded summer research internship at Harvard College for scholars from select R2 and research-focused Historically Black Colleges and Universities. Scholars receive dedicated hands-on mentorship and gain access to a rigorous research and learning environment that fosters intellectual growth and personal development. Scholars live in the Harvard residential community and participate in programming with scholars from the Harvard Summer Undergraduate Research Village, creating relationships and experiences that will last a lifetime.

The Foundational Undergraduate Experiences in the Laboratory (FUEL) program, run by the Harvard Department of Chemistry and Chemical Biology, prepares students for real world research through guided research projects, workshops and field trips. The program trains participants in a variety of fundamental research techniques used in chemical and biotechnological research with a focus on environmental issues. Participants learn crucial skills needed for science communication, such as the creation of scientific posters, and connect with various Harvard faculty and labs through the Lab Match Challenge.

The Harvard Stem Cell Institute Summer Internship Program (HIP) for undergraduates is an summer experience dedicated to hands-on research in the laboratory of a stem cell institute faculty member. The program is an open door; an invitation to learn and do as much as you can to develop your interests within the overarching topic of stem cell science. Our interns arrive from a wide variety of colleges and universities worldwide, and this diversity is part of what makes our program rich and unique.

The Kempner Research in Artificial and Natural Intelligence for Undergraduates with Mentorship (KRANIUM) is a summer program launched in 2024, sponsored by the Kempner Institute for the Study of Natural and Artificial Intelligence as part of the Harvard Summer Undergraduate Research Village (HSURV). KRANIUM aims to provide a formative and substantive research experience for — and build community among — a small cohort of Harvard College undergraduates interested in the study of natural and/or artificial intelligence.

Laidlaw Scholars Leadership & Research Programme is a unique two-year opportunity for first-year undergraduates who want to become ethical, effective change-makers. In their first year, Laidlaw Scholars spend the summer after their first year completing a fully funded research project. During their second year, Scholars participate in cohort-based leadership training at Harvard and through Oxford University's Ethical Leadership Programme, ultimately earning a Leadership Certificate, and work with an international partner to apply their leadership and public service training.

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

The Program for Research in Science and Engineering (PRISE) seeks 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 within a diverse, vibrant intellectual and social community.

The Research Experience for Undergraduates Programs (REU) at the School of Engineering and Applied Sciences (SEAS) welcome students from colleges across the country to perform cutting-edge research in world-class laboratories in several exciting branches of science and engineering, including biomaterials, materials science, nanotechnology, robotics, computer science, and energy and the environment.

The Molecular and Cellular Biology (MCB) Summer Connectomics Internship for Outreach Neuroscience (SCION) allows students to engage in independent neuroscience research under the mentorship of graduate students or postdoctoral fellows. They focus on understanding the neural basis of zebrafish behavior by reconstructing neurons from electron microscopy images. Participants contribute to original research, practice scientific communication through workshops and presentations, and attend an invited speaker series.

The Summer Humanities and Arts Research Program (SHARP) strives to build community and stimulate creative thought among a small cohort of Harvard undergraduate researchers in the humanities and arts. Students work on pre-designed 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 with social and academic activities.

The Summer Program for Undergraduates in Data Science (SPUDS) aims to provide a formative and substantive data science research experience and to promote community, creativity, and scholarship amongst Harvard College students. SPUDS supports Fellows with interests in computer science, mathematics, and statistics, including those who are interested in data science applications across the arts, humanities, sciences, and more. As part of SPUDS, fellows participate in rich evening programming, including both social and academic activities, and become members of a vibrant intellectual and social summer community.

The Salata Summer Undergraduate Research Fund (SURF) program supports undergraduate students who undertake research work in climate, sustainability, or the environment more broadly. The Fund offers two types of research experiences for Harvard students: one for faculty-advised independent research typically in support of senior thesis projects (with a preference given to rising seniors), and one for research assistantships to encourage undergraduates to participate in summer research experiences alongside Harvard faculty.

The Summer Undergraduate Research in Global Health (SURGH) program endeavors to build community and stimulate creativity among a small cohort of Harvard undergraduate researchers in global health. SURGH fellows work on pre-designed research projects with Harvard-affiliated faculty and researchers. Students live together in one of the Harvard College houses and participate in rich evening programming, including both social and academic activities.

Letter from the Editors

Dear Research Village,

Congratulations on successfully completing an incredible summer of research!

This summer, HSURV once again brought together 300+ fellows from 50+ universities to form a special community, exploring beyond our known boundaries into questions at the intersections of science, social sciences, humanities, arts, engineering, and more. Throughout the highs and lows of our research journeys, our curiosity and love for research bonded us all together.

Whether in the lab or the library, students dedicated themselves to a summer of hard work, new collaborations, and unwavering curiosity to learn not only about the world around them, but also about one another.

From cheering for the World Cup to watching the July 4th fireworks, we shared a spectacular and GOOAL-orious ten weeks that flew by so fast. We also bonded through exciting fellow-led activities, whether it was attending the Red Sox games, going whale watching, or exploring Boston's hidden gems. We are so thankful for our many friendships that will last far beyond this one summer with HSURV.

Our research journeys would not be possible without the continuous support, guidance, and inspiration from our mentors and faculty.

Our research community is very grateful for Dr. Elizabeth Perten for her help with creating this abstract book. Additionally, a huge thank you to Dr. Jonna Iacono, Tom Hamel, Ariel Lepito, and the rest of the URAF team for their endless support throughout the entire summer. Thank you also to all the house staff who made Winthrop a second home for us.

To the fellows: thank you for creating such a welcoming and collaborative HSURV community. These abstracts truly reflect your hard work and passion, along with the breadth and depth of your research. We hope you will treasure all of your HSURV memories and that these abstracts continue to spark new ideas and discussions.

Sincerely,

The Abstract Editing Team

Letter from the Artists

Dear Research Village,

We did it! Congratulations on putting in the long hours into your research and coming out the other side stronger, brighter, and all the more wiser.

Our design this year speaks to the ideas of collage, collision, and collaboration. Our work is inspired by both conceptual science art—reminiscent of scientific publication covers—and contour drawing—a delightful series of abstractions capturing the mass and movement of the real world.

Inquiry and research are non-linear processes, and many of the research directions represented in this year's abstract book leverage the combination of two or more fields. Our illustration team brainstormed several diverging ideas, but through the creation of this book, synthesized them into a cohesive work. Lines of thought and hues and gradients weave our lived experiences into organic snapshots of passion and creation.

Our covers display handmade illustrations, representing how the pursuit of research is an art form demanding time, precision, and a greater sense of composition. This summer has been a wonderful confluence of research, learning, student-led activities, and many more experiences that words alone cannot convey.

Throughout these covers, we highlight hands in motion. Every pipetted microliter, every turned page, every inked note is a microcosm of the thinking and problem solving process, and how we work through our projected fields of inquiry. These hands also serve as a testament to the summer of connection and networks of peers that we've built alongside our research journey: friends we've made that have begun with the shake of a hand, reaching out to form new bonds. We hope our illustrations may offer a vicarious retelling of our wonderful journeys on and off campus, and serve as a bookmark for one of many valuable experiences as students, researchers, and uplifting community members over this summer.

We are very lucky to have the opportunity to spend a wonderful summer residing in the research village on campus. At its core, research is more than a single journal article, lab notebook, or digital schematic. It is a community, dedicated to robust inquiry and the dynamic exchange of ideas. Throughout long weekdays, packed evenings, and endless World Cup watch-parties, are beyond fortunate to be able to call the HSURV family home.

We are also deeply grateful to our mentors and research groups for supporting us in our growth–for giving us the space to make mistakes, ask questions, and grow into more proactive learners. It is through their time and mentorship, that we have developed as confident investigators and curious citizens.

We must thank Isabelle Agarwal and Dalevyon LJ Knight, our wonderful PAs for helping organize the entire abstract team. Additionally, we are endlessly grateful to Dr. Jonna Iacono, Tom Hamel, Ariel Lepito, and everyone in the URAF team for making this summer of research possible (and their abilities to work like locomotives!). Thank you to the Winthrop house staff for making this house a home away from home for everyone!

As the saying goes, it takes a village to raise a researcher. To our HSURV fellows, thank you for being incredible peers to grow alongside with. Signing off with a flourish,

Sincerely,

The Abstract Art Team

Letter from the Director

Dear Harvard Summer Undergraduate Research Fellows:

During the summer of 2026, we marked two significant anniversaries: the 250th anniversary of the founding of the United States of America and the twentieth anniversary of the Harvard Summer Undergraduate Research Village, which began with the founding of the *Program for Research in Science and Engineering (PRISE)*.

Anniversaries invite us to reflect upon what has transpired, with both gratitude and joy for good hard work done well and mourning for opportunities missed, our moral failures, and fellow travelers lost. They also invite us to contemplate what comes next. In the case of these two experiments in democracy — one with a big D and one with a small d — our ancestors, both intellectual and institutional, made a wager on the future. Building things, after all, is work measured in both moments and in generations, a step into a future you won't inhabit. With trust in a tomorrow they could neither see nor predict, they committed that future to others, believing that the more people who shared in the work of imagining, authoring, and building it, the richer, more beautiful, and more enduring it would become.

The abstracts that follow are one measure of what our predecessors made possible. They are the work of hundreds of students who arrived at the Research Village with different experiences and different ambitions, but with a shared commitment to asking and seeking to answer important questions. At lab benches and computer terminals, in libraries and archives, over microscopes and manuscripts, they entered into conversations that began long before they arrived and whose conclusions they may never see.

This summer, at the opening of the Research Village, I asked students to reflect upon Raymond Carver's poem, "What You Need for Painting." Borrowing from a letter by Renoir, Carver begins with a list of tools — pigments and palette knives and brushes (both "Flat hog-hair" and "pointed marten-hair") — and ends with:

Indifference to everything except your canvas.
The ability to work like a locomotive.
An iron will.

The poem begins with the tangible things one might need to paint and ends by reminding us that the most important tools cannot be bought; what is necessary is not sufficient.

The booklet in your hands is the product of many ordinary things: microscopes and MRI machines, pipettes and particle accelerators, libraries and archives, datasets and spreadsheets, notebooks and whiteboards. But these pages are also evidence of something less visible: attention sustained over time, important questions pursued with discipline, the generosity of mentors and collaborators, and the quiet courage required to remain with a problem until it yields something new.

May these pages remind you of all that was accomplished this summer, as well as the alchemy of people, place, process, and shared commitments that made it possible.

The Research Village is the work of many and I would like to take a moment to thank them.

> Thank you, Proctors and Program Assistants, for your work supporting the rich and robust slate of activities that make our community such a fun one.
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> Thank you to the volunteer editorial team that has generously brought this book to life, with particular gratitude for this year's lead editors, Isabelle Agarwal and Dalevyon "LJ" Knight.
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> Thank you to many devoted colleagues who have worked tirelessly throughout the past year to make our community possible: our faculty mentors, the program teams, those in Housing and Dining, Winthrop House faculty and staff, and my colleagues in the Office of Undergraduate Research and Fellowships.

And thank you to the leadership of our university.

> Alan M. Garber, President, Harvard University, Mallinckrodt Professor of Health Care Policy, Professor of Economics, Professor of Public Policy, Professor of Health Policy and Management

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David Deming, Danoff Dean of Harvard College, Isabelle and Scott Black Professor of Political Economy, Professor of Economics

Amanda Claybaugh, Dean of Undergraduate Education, Samuel Zemurray Jr. and Doris Zemurray Stone Professor of English

Best wishes,

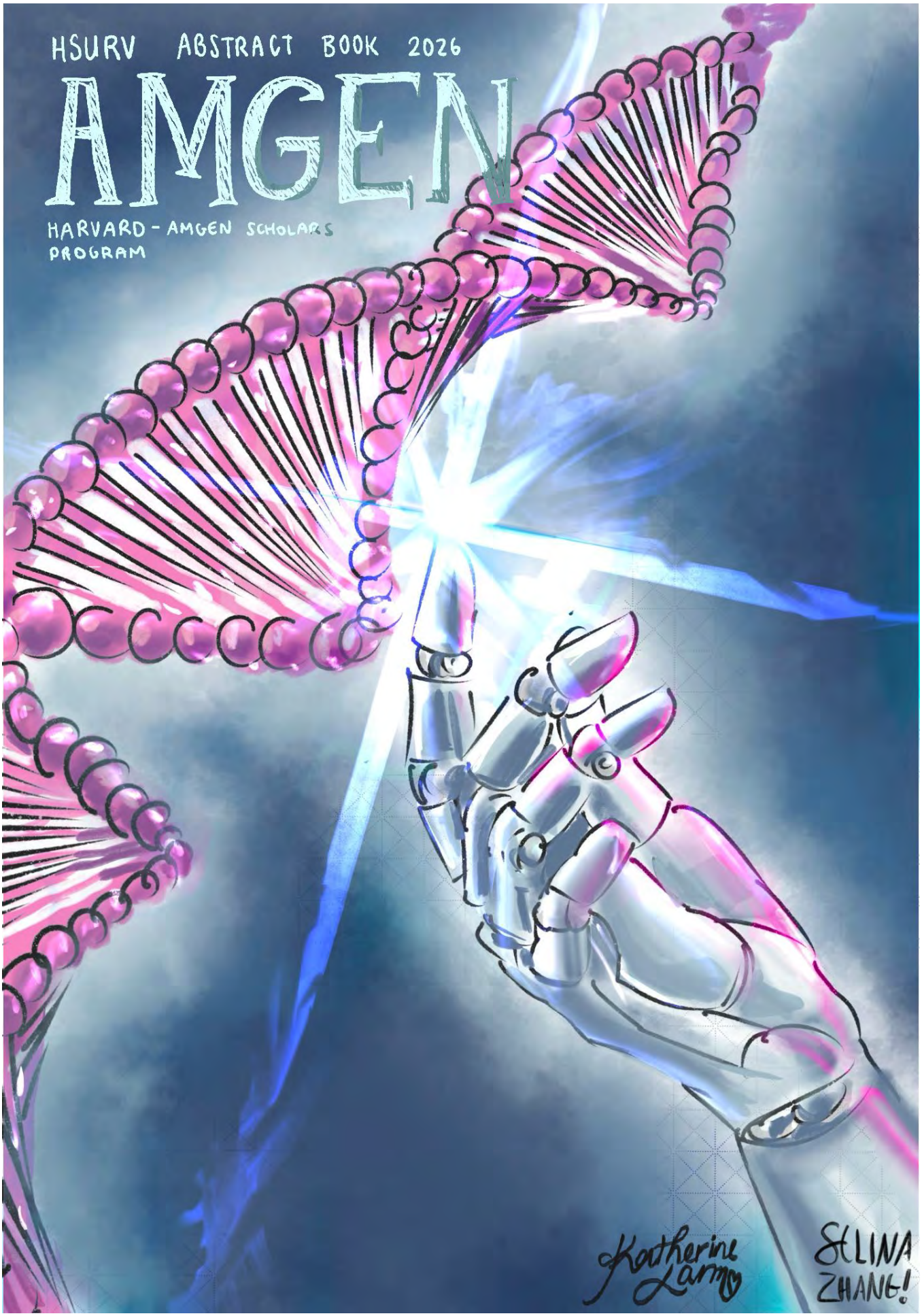
Jonna Iacono, PhD

Director, Office of Undergraduate Research and Fellowships

HSURV ABSTRACT BOOK 2026

AMGEN

HARVARD - AMGEN SCHOLARS PROGRAM



Structural Validation of a Partial Agonist Nanobody at the Melanocortin-1 Receptor

Student: Anushka Aggarwal
Mentor(s): Jeff Smith
Faculty Advisor(s): Andrew Kruse
Duke University | Molecular & Cellular Biology | 2028

The melanocortin receptors (MC1R–MC5R) are G protein-coupled receptors that regulate pigmentation, appetite, and immune responses, and are implicated in skin cancer, obesity, and inflammatory disease. MC1R is therapeutically important because activating it drives eumelanin production, a protective pigment that absorbs and scatters UV radiation, reducing DNA damage and skin cancer risk. Despite this clinical potential, few antibody-based therapeutics target the melanocortin family, largely because conventional antibody development methods are slow and rarely generate functional agonists. Nanobody353 (Nb353) is a computationally designed antibody fragment that functions as a partial agonist at MC1R. Structural modeling predicted a specific binding pose for Nb353 at MC1R, but the validity of this prediction has not yet been experimentally confirmed. To test the predicted binding pose, we identified residues critical for receptor engagement and designed four Nb353 variants, each targeting a different predicted contact point. These variants include point mutations to disrupt polar interactions essential for binding, a steric mutation that introduces a clash within the binding pocket, and a hydrophobic mutation to disrupt a proposed activation mechanism. We generated these mutants using Gibson assembly and expressed them in bacterial systems. Binding to MC1R will be assessed by flow cytometry, while functional signaling will be measured using a luminescence-based cAMP accumulation assay. We predict that mutations disrupting predicted contacts will reduce or eliminate Nb353's MC1R activity. Confirming this sequence-function relationship would validate our computational design pipeline and establish a rational framework for engineering improved antibody-based therapeutics for melanocortin-related diseases.

Targeting NDUFA10 Protein as a Possible Therapeutic Strategy

Student: Lalitha Appana
Mentor(s): Shan Jiang
Faculty Advisor(s): Liron Bar-Peled
University of Alabama, Birmingham | Molecular & Cellular Biology | 2027

Mitochondrial dysfunction contributes to a wide variety of diseases due to impairment of cellular energy metabolism, increased reactive oxygen species (ROS). This leads to damaged mtDNA and a disruption in inflammatory and quality-control pathways, thereby promoting neurodegenerative, metabolic, cardiovascular, and inherited mitochondrial disorders. This highlights the need for novel forms of therapeutics targeting mitochondrial processes. NADH:Ubiquinone Oxidoreductase Subunit A10 (NDUFA10) is an accessory and non-catalyzing subunit of the mitochondrial membrane respiratory chain NADH dehydrogenase (Complex I). NDUFA10 was initially considered for investigation when a patient with an inherited mitochondrial disorder presented with Leigh syndrome had a mutation in the NDUFA10 gene. Further investigation into the protein revealed that NDUFA10 plays a role in stabilizing Complex I function by maintaining the integrity of the mitochondrial membrane domain and electron transfer. It has also been implicated in regulating dGTP availability in the mitochondria, an important ingredient for mtDNA repair. This possibly creates a link between oxidative metabolism to DNA maintenance. My role in this project focused on optimizing protein purification protocols for NDUFA10 targeting and evaluating protein stability using biochemical assays to establish a foundation for subsequent molecular biology investigations. Given this functional role, pharmacologic activation or stabilization of NDUFA10 may represent a novel mitochondrial-stimulatory strategy. In contrast to current approaches that predominantly inhibit mitochondrial oxidative phosphorylation, targeting NDUFA10 could provide a new therapeutic avenue for research into disorders characterized by mitochondrial dysfunction.

From Static Binders to Dynamic Sensors: A General Approach for Computational Design of Ligand-Sensing Proteins

Student: Irene Chaey
Mentor(s): Jerry Yao
Faculty Advisor(s): Nicholas Polizzi
University of California, Berkeley | Molecular & Cellular Biology | 2027

Many biological processes depend on proteins that undergo conformational changes. Although advances in *de novo* protein design have enabled the creation of stable protein scaffolds, designing binders with programmable ligand-dependent conformational changes remains a challenge. We previously designed a four-helical bundle binder, the exatecan-protein interaction complex (EPIC), with a single structural state that binds exatecan with nanomolar affinity (K_D = 1 nM). We hypothesized that reducing the folding core of this rigid binder would increase access to alternative conformational states. Ligand binding would preferentially stabilize one state from this ensemble, thereby coupling binding to conformational change. To test this idea, we pursued two design strategies. First, we designed shortened four-helical proteins, named smEPIC, derived from the binding core of EPIC. Second, we added two flanking helices to smEPIC in different topologies to provide additional structural support. To experimentally validate these designs, we used fluorescence anisotropy to measure their binding affinities for exatecan. For designs that retained exatecan binding, we appended a fluorescent protein FRET pair to the N- and C-termini to detect exatecan-induced conformational changes via changes in FRET. We found that most shortened constructs remained capable of binding exatecan, although with binding affinities reduced by one to four orders of magnitude. We also identified one design that exhibited a notable exatecan-induced conformational change and found that the distance between the protein termini and the ligand-binding site may be a critical factor in designing ligand-induced conformational changes. Together, these studies provide a general approach for converting static binders into dynamic ligand-sensing proteins whose conformational landscapes can be modulated by ligand binding. This capability could serve as a foundation for designing binding cascades in which ligand-induced structural transitions trigger downstream protein interactions, enabling increasingly complex *de novo* protein systems.

Using SEARCH-MaP to Validate RNA Long-Distance Interactions Within the SARS-CoV-2 Genome

Student: Aminah Coleman
Mentor(s): Gabriel Romero Agosto
Faculty Advisor(s): Silvi Rouskin
Howard University | Molecular & Cellular Biology | 2027

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is a positive-sense single-stranded RNA virus responsible for the COVID-19 global pandemic. The SARS-CoV-2 genome contains a frameshift stimulatory element (FSE), which regulates -1 programmed ribosomal frameshifting (-1 PRF), allowing for translation of essential viral proteins. The FSE is composed of a slippery site sequence and an RNA pseudoknot involved in a long distance-interaction (LDI) of approximately 1kb. The LDI is hypothesized to have some function involved in -1 PRF. To characterize these interactions, we have developed Structure Ensemble Ablation by RNA Hybridization with Mutational Profiling (SEARCH-MaP). SEARCH-MaP uses antisense oligonucleotides (ASOs) to disrupt RNA structures in one region and observe whether this causes a structure change in the LDI region. RNA secondary structures in both regions are analyzed using dimethyl sulfate-mutational profiling and sequencing (DMS-MaPseq), a chemical probing technique used to analyze RNA secondary structures. While validated *in vitro*, I am further developing the method in cellular contexts to assess its efficacy in living systems. Due to the dynamic nature of RNA structure, it is necessary to develop methods in cells to observe how cellular conditions may impact the structure. In cells, the structure of the expressed RNA from plasmid constructs is determined by DMS-MaPseq, which will produce a DMS reactivity profile of bases likely to be unpaired. When comparing the ASO- and non-ASO-targeted samples, I expect to see a distinct drop in the rolling correlation coefficient of DMS reactivities at the ASO-targeted FSE region and the LDI region. This will indicate the ASOs successfully disrupted the structure of the FSE, and prevented long-range base pairing to the LDI region. Developing this method in cells will allow further understanding of long-range RNA interactions, structure, and function, which provides a foundation for targeted therapeutic development.

Mapping the Brain's Circuit for Learning From Mistakes

Student: Claire Dokko
Mentor(s):
Faculty Advisor(s): Jonathan Green
Emory University | Neuroscience | 2028

Learning is a fundamental mechanism that allows for a wide range of adaptive behaviors and capabilities in biological systems. Error-based learning requires the brain to detect a discrepancy between the expected outcome and the actual outcome, and this feedback is used to guide future behavior. A previously identified subtype of somatostatin inhibitory neurons called Sst44 neurons in the cortex has been shown to encode error signals across various regions. For example, Sst44 neurons in the posterior parietal cortex respond to repeated action prediction errors, while those in the visual cortex respond to repeated visual prediction errors. This broader shared functionality of Sst44 neurons as an error response across various cortical regions suggests the possibility of other cell types that contribute to a cortex-wide circuit for processing errors. We aim to systematically assemble a comprehensive map of the cortical error circuit by identifying specific cell types that are recruited during error experiences and characterizing their activity profiles. To achieve this, we will perform two-photon calcium imaging to record neural activity during behavior, followed by multiplexed error-robust fluorescence *in situ* hybridization (MERFISH) on the same brain tissue to assign molecular identities to the imaged neurons. Mice will be trained on a virtual reality navigation task in which sensory or action outcomes can be systematically manipulated to elicit prediction errors under controlled conditions. By establishing this framework that integrates behavior, imaging, and spatial transcriptomics, these datasets will provide insight into learning on molecular, cellular, and circuit levels.

Identifying Neurons that Survive West Nile Virus Infection

Student: Jade Griffin
Mentor(s): Sophie Spector
Faculty Advisor(s): Jérémie Le Pen
University of Michigan, Ann Arbor | Chemical & Physical Biology | 2028

West Nile virus (WNV) is the leading cause of mosquito-borne disease in the United States and can lead to severe neuroinvasive disease. Neuroinvasive WNV has a fatality rate of 10% and 50-70% of survivors have severe long-term neurological sequelae that are poorly understood. Although chronic neurological conditions have traditionally been attributed to irreversible neuron loss after WNV infection, persistent viral RNA suggests that surviving neurons may experience chronic inflammation. We hypothesize that neurological sequelae are driven by persistent immune responses in neurons instead of neuron loss alone. Unlike neuron death, chronic inflammation can be rescued through therapeutics, making research on surviving neurons critical. Current methods cannot readily identify neurons that survive infection while preserving viral biology. To address this challenge, we created a cell-based fluorescent reporter system that is activated through cleavage by the WNV protease during infection. This method can allow for the identification of infected cells through subsequent nuclear relocalization of the fluorescent protein. We are building on this system by using a *Cre* protein tethered to the endoplasmic reticulum. During infection, cleaved *Cre* translocates to the nucleus where it permanently switches the cell from expressing red to green, allowing surviving neurons to be identified even after the virus is gone. Additionally, we optimized a complementary focus-forming assay that visualizes foci of infection by staining for WNV and markers of innate immune activation. Moving forward, this method can be applied to neurons, allowing surviving neurons in the path of infection to be identified. Together, these systems will identify and spatially map surviving cells, allowing research into whether persistent innate immune responses continue after viral clearance. This research will determine whether chronic inflammation in surviving neurons contributes to long-term neurological sequelae and could identify therapeutic targets that mitigate long-term neurological disability following WNV infection.

Using Protein Nanoparticle Antigen Delivery to Activate CD4+ T Cells

Student: Luisa Parker
Mentor(s): Michelle Walsh
Faculty Advisor(s): Elliot Chaikof
Case Western Reserve University | Biomedical Engineering | 2027

Cancer vaccines have historically focused on CD8+ T cells because these cells directly kill malignant cells; however, current approaches are often limited by an inability to sustain CD8+ T-cell activation. Elastin-like polypeptides (ELPs) are proteins whose behavior changes with temperature and pH. The Chaikof lab has engineered ELPs that self-assemble into protein nanoparticles at room temperature, providing a novel platform for cancer vaccine antigen delivery. Preliminary studies of ELP nanoparticles bearing CD8+ T-cell antigens have generated anti-cancer immunity, but with limited durability. In this study, we sought to determine if ELP nanoparticles can be engineered to activate antigen-specific CD4+ T cells, which are known to support CD8+ T-cell activation. This study used OT-II as a model antigen derived from ovalbumin and encoded it into the ELP backbone. To determine if OT-II ELP nanoparticles mediate antigen presentation and activate CD4+ T cells, murine antigen-presenting cells (APCs) were treated with OT-II ELP nanoparticles and co-cultured with CD4+ T cells isolated from transgenic mice containing T-cell receptors against OT-II. APCs treated with un-encapsulated OT-II peptide served as positive controls and APCs treated with ELPs containing an irrelevant antigen served as negative controls. CD4+ T-cell activation was assessed by flow cytometry at 18 hours post co-culture. The expression of CD69, an early activation marker on CD4+ T cells, in the OT-II ELP condition was comparable to CD69 expression in the positive control. Future experiments will further characterize CD4+ T-cell activation by quantifying CD25 and CD44 activation markers at later time points, and observe proliferation and pro-inflammatory cytokine release. This work will establish proof-of-concept that ELP nanoparticles can be utilized for antigen-specific CD4+ T-cell activation. Future studies will seek to activate both CD4+ and CD8+ T cells using the ELP nanoparticle platform to develop a cancer vaccine with sustained impacts on tumor control.

Mapping Neomorphic Substrate Recognition in KBTBD4

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Molecular glue degraders are emerging as a powerful therapeutic modality that functions by inducing chemical proximity between E3 ubiquitin ligases and their substrates. However, most molecular glues have been discovered by serendipity, and there remains no general strategy for their rational design. Recent work from our lab established the mechanism of action of the molecular glue UM171, demonstrating that it induces a binding interface between the E3 ligase KBTBD4 and the chromatin-modifying enzyme HDAC3, ultimately resulting in the degradation of the corepressor CoREST. Remarkably, we also discovered that cancer-associated mutations in KBTBD4 mimic UM171 to affect degradation of CoREST. Building on this concept, we recently discovered a novel set of KBTBD4 mutations that complex with HDAC3 to degrade the corepressor NCOR1 in an analogous mechanism. Now, we are using deep mutational scanning to generate thousands of KBTBD4 variants and measure their ability to induce NCOR1 degradation in a pooled functional screen. This approach will enable the systematic identification of KBTBD4 variants that acquire the ability to degrade NCOR1, providing insight into the sequence determinants of neomorphic substrate recognition. Understanding how mutations reprogram KBTBD4 substrate specificity is a key step toward the rational discovery and design of molecular glue degraders.

Ribonucleoside Synthesis through Stereospecific *N*-Glycosylation with Anhydrofuranoses

Student: Leah Wiebe
Mentor(s): Antonio LaPorte
Faculty Advisor(s): Eric Jacobsen
Hobart and William Smith Colleges | Chemistry | 2027

Ribonucleoside analogues compose a class of versatile anticancer and antiviral agents and are also used as chemical probes, due to their structural similarities to naturally-occurring nucleotides. Ribonucleosides are composed of ribose and a nitrogen heterocycle. These serve as donor and acceptor, respectively, in the synthesis of ribonucleosides via *N*-glycosylation. This approach allows ribonucleosides to be synthesized modularly, improving access to analogues with distinct properties. However, coupling of the ribose donor and *N*-heterocycle acceptor introduces the formidable challenge of controlling absolute configuration at the anomeric carbon (stereoselectivity) and *N*-site selectivity (regioselectivity) during glycosylation. The most common synthetic methods for the production of ribonucleosides rely on harsh Lewis acidic conditions and often result in a mixture of regio- or stereoisomers, necessitating anchimeric assistance and/or complex leaving groups and specialized catalysts to promote stereospecific, regioselective pathways. To streamline modular syntheses of nucleoside analogues, we developed an elegant method towards highly stereospecific and *N*-site selective glycosylation using 1,2-anhydroribose donors. We demonstrated the efficacy of these methods via the preparation of various natural and unnatural nucleosides, including the FDA-approved anti-CMV drug Maribavir (79% yield, pending deprotection). An investigation of the applicability of these methods to pyranose systems is underway, with preliminary results suggesting a successful coupling of a 1,2-anhydrogalactose with uracil (84% yield, pending deprotection). These promising syntheses suggest that *N*-glycosylation methodology may obviate the need for strong Lewis acids and/or highly tailored substrates and catalysts which currently present obstacles in the modular, stereospecific synthesis of therapeutically- and biologically-relevant nucleoside analogues.

Defining Interactions of Regulatory T Cells in Human Melanoma

Student: Cole Woody
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Faculty Advisor(s): Catherine Wu
University of Houston | Molecular & Cellular Biology | 2027

Regulatory T cells (Tregs) are specialized CD4+ immune cells that are essential for maintaining immune system homeostasis by suppressing overactive immune responses following recognition of an antigen on a target cell. Each T cell carries a T cell receptor (TCR), a unique surface protein that determines which antigens the cell can recognize. However, many cancers, particularly melanoma, have evolved mechanisms to hijack Tregs and suppress the immune response against cancer cells, allowing tumors to evade detection. This project seeks to investigate the extent to which a Treg's TCR sequence influences its phenotype and ability to detect cancer cells in the context of human melanoma. This project analyzed paired single-cell gene expression and TCR sequencing data from tumor and lymph node biopsies across nine melanoma patients. *In vitro* TCR specificity screens identified 20 antigens (viral, tumor-associated, and neoantigens) that clonally expanded TCRs specific to Tregs. The Seurat package in R was used to process the data and group Tregs by phenotype. This analysis identified seven distinct Treg phenotypes within the tumor microenvironment, including two effector-like populations that were especially active in suppressing inflammation. 19 of the 20 antigens screened in vitro primarily led to clonal expansion of effector Treg populations. Current work is examining whether specific features of the TCR sequence help predict which phenotype a Treg will ultimately adopt. Future directions include expanding this analysis across more patients and utilizing spatial single-cell sequencing to investigate how Tregs interact with other cells in the tumor microenvironment. Because Tregs can either suppress or support anti-tumor immunity, understanding what drives these different roles could help guide the design of immunotherapies that favor pro-inflammatory over immunosuppressive Treg responses.

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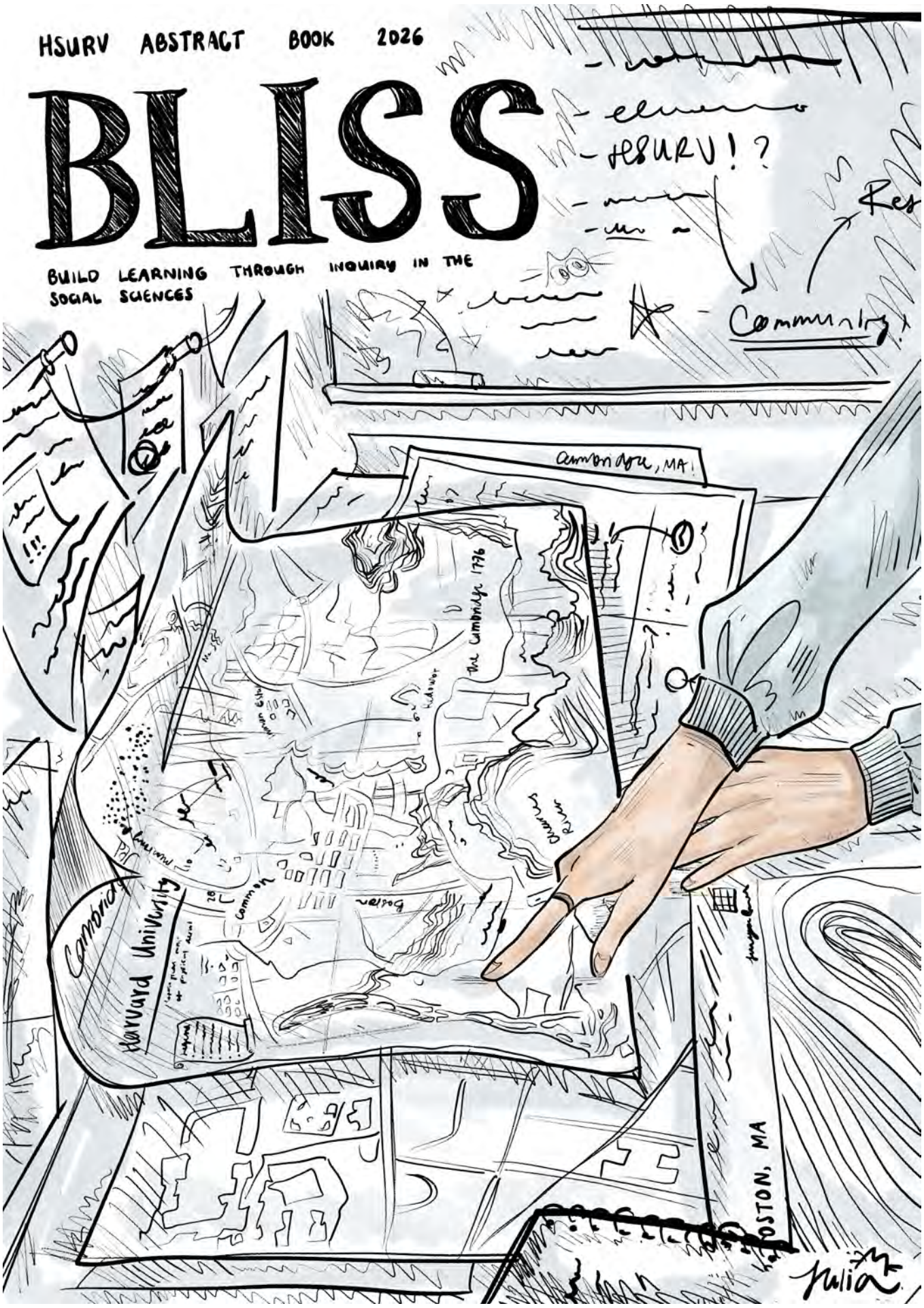
BUILD LEARNING THROUGH INQUIRY IN THE SOCIAL SCIENCES



Colonialism on Undeveloped Lands: How Harvard's Acquisition and Sale of Isaac Royall Jr.'s Properties Contributed to Colonial Expansion and Native Displacement

Student: Daniel Bittner
Mentor(s): Jordan Clark & Kabl Wilkerson
Faculty Advisor(s): Phil Deloria & Alan Niles
Harvard College | Leverett House | History | 2027

In 1781, Isaac Royall Jr., a prominent businessman and colonial elite, bequeathed 1,267 acres of largely undeveloped forest throughout Massachusetts to Harvard College for the establishment of the Royall Professorship of Law. These lands, consisting of properties in Royalston and Granby, as well as a strip of land between Leominster and Westminster known as the Gore, were later sold by Harvard between 1796 and 1809 for a combined 6,837.90. Despite the fact that these lands likely contained no active Native settlements at the time of their donation, this project argues that Harvard's brief possession of them nevertheless played a critical role in the broader phenomenon of colonization and Native displacement within Massachusetts. Drawing on town histories, Harvard's Records of Land and Property, military conscription rolls, legislative records, and other contemporary sources, this project examines Harvard University's role in surveying and selling these frontier properties. It argues that these activities helped validate earlier military land grants, facilitated colonial settlement, and advanced the dispossession of Native peoples in contested lands throughout the Native Northeast. In doing so, this research builds upon existing scholarship that emphasizes direct forcible removal as the primary mechanism of colonization by arguing that the possession, administration, and transfer of land could themselves serve as means of colonial expansion.

Investigating Harvard and Colonialism

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For over thirty years, Harvard held more than 12,000 acres of land in modern-day Maine, granted in 1719 and between 1762 and 1774 across 25 townships. Even though Harvard claimed roughly 1,000 acres in the townships of Fryeburg, Brownfield, and Lovell, little is known about Harvard's connection to these lands or its role in the dense processes of colonial speculation and violence. Drawing on the Harvard University Archives, the Massachusetts State Archives, and other repositories, the Investigating Harvard and Colonialism project aims to provide a fuller context for Harvard's entanglement with European colonization in North America by examining townships in Maine. In doing so, it shows that towns like Lovell, Fryeburg, and Brownfield are part of a precedent in which Massachusetts commoditized Native land and gave portions to Harvard as indemnity for the loss of its library in a fire. Harvard then profited from the sale of such lands, some for over one shilling per acre, in the early nineteenth century. By examining Harvard's historical enrichment through the English colonial system, this project seeks to make a broader point about the inadequacy of master narratives of the United States' founding. Ultimately, it illuminates how places like colonial Maine offer a crucial historical window into emergent systems of settler colonialism.

Tracking Of Objects Split Into Halves By Preschoolers

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Harvard College | Cabot House | Neuroscience | 2029

Prior studies suggest that children under seven may have difficulty tracking the number of objects in working memory when objects are split or cut in half. They also label the split parts in non-adult-like ways, e.g., calling a cup cut in half "two cups" rather than "two halves of one cup." So, how are children representing objects that undergo splitting in working memory? The present study hypothesizes that children exposed to object splitting during the experiment will track objects more successfully than those not exposed. To test this, participants aged 42–60 months will be randomly assigned to two conditions. In the functionality condition, children will observe water being poured into a whole cup and spilling from a pre-cut cup before trials. During trials, two whole cups will be placed in a box and each cut in half. Children will then be asked to infer whether the box still contains pieces upon seeing the retrieval of a subset of one to three cut pieces, choosing what remains in the box from three options: a half cup, a whole cup, or a whole cup and a half. Comparing this with a baseline condition will determine whether providing functional information improves children's working memory. We predict that observing the cups' functionality will help children individuate intact and cut cups, allowing them to encode the transformation effectively. If children in the functionality condition outperform those in the baseline condition, it would suggest that providing functional cues improves how children represent transformed objects in working memory. If no difference occurs, it would indicate that children's difficulties reflect a more fundamental conceptual representation of object identity that is not easily altered by brief experience. This study will advance understanding of cognitive development and working memory by providing a framework for how children represent objects that transform.

Designing Better Public Services - How Cities Learn From Residents

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Harvard College | Dunster House | Economics | 2028

Residents face fragmentation when seeking city services, predominantly due to a lack of knowledge on eligibility, arduous and confusing application procedures, and lengthy bureaucratic processes across several siloed departments. This study aims to scale federal initiatives to improve the customer experience at the city level, by assisting cities with the identification of frictional points along a customer service journey and navigating improvements to maximize impact and accessibility across different demographics. In particular, this project seeks to explore ways in which artificial intelligence can be applied to both internal operations and external resident-facing services by the city government. This project has a two-pronged task outline. First, our team is designing workbooks for cities to improve their service delivery. This includes defining a service, segmenting their customer base, mapping a service journey, identifying frictional points that impede a service's usability, pinpointing KPIs, and planning out iterative improvement processes to maximize resident impact and accessibility. Second, an AI environmental scan is being conducted to analyze how cities are already pioneering AI solutions to expedite their services across four key areas: 311 assistance, procurement, housing infrastructure, and benefit delivery. As AI rapidly evolves globally in increasingly complex environments, human-centered service delivery remains a central goal for cities worldwide. Faced with slow operating systems, cities must explore diverse ways that AI can shape public services to better serve their residents.

Do children have third-party expectations about intimate sharing in intergroup relationships?

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Faculty Advisor(s): Ashley J. Thomas
Harvard College | Cabot House | Sociology | 2029

Adults have long expressed concern about intergroup intimacy. For example, in many places, close relationships between races, ethnicities, and castes have been legally and socially regulated. What are the developmental origins of these biases? Do young children already hold expectations about who should be socially close that align with these regulations? Research suggests that young humans can recognize and reason about social groups. Infants attend to ingroup members more, looking longer at faces within familiar social categories. Children also prefer ingroup peers, choose them as friends, share more resources with them, and selectively trust them. They further expect ingroup members to favor one another. However, it remains unknown whether children specifically expect ingroup intimacy, which is theorized to be distinct from broader categories of prosociality. Humans do reason about intimacy from infancy. Infants and children have distinguished intimate-sharing acts (sharing the same bite of food) from prosocial acts that do not involve intimate sharing (sharing a toy). Children also expected family members to engage in intimate sharing more than non-family members, suggesting they view intimacy as appropriate within some relationships but not others. It remains unclear whether children's expectations about intimacy are shaped by expectations of ingroup relationships or their understanding of real-world categories such as race. Our investigation examines whether children expect intimacy to occur more often between members of the same social group. We test this question using both novel groups, shared shirt color, and real-world groups, shared skin tone, and ask children to infer who will share resources that either require physical intimacy (e.g., licking the same lollipop) or do not (e.g., blueberries). Together, these studies aim to advance our understanding of how children use shared group membership to reason about closeness and intimacy, and may illuminate developmental roots of adult concerns about ingroup intimacy.

Profs and Politics in Latin America: "To Govern is to Educate"

Student: Pablo Martinez Palop
Mentor(s):
Faculty Advisor(s): Doris Sommer
Harvard College | Eliot House | Social Studies | 2029

This project examines how education has shaped political leadership in Latin America, focusing on Mexico as a case study. The larger research asks how the figure of the "prof" or "profe," a familiar Latin American term of affection and respect for a teacher or professor, can offer an alternative to the caudillo, patrón, jefe, or mano dura ruler. Rather than understanding government only as command, force, or administration, this project studies moments when political leadership becomes pedagogical, shaping citizens through schools, public art, textbooks, rural teachers, and cultural institutions. My research uses historical and bibliographical methods to study Mexican figures who connected politics and pedagogy. I focus especially on José Vasconcelos, who used the Secretaría de Educación Pública to rebuild Mexico through schools, libraries, publishing, and public art; Moisés Sáenz, who connected rural and Indigenous education to national policy; and Othón Salazar, whose teacher activism challenged both the state and official union power. These cases suggest that Mexico reveals both the promise and danger of government as education. Educational leadership could expand citizenship and public participation, but it could also become ideological control, assimilation, union corporatism, or reform imposed from above. This research matters today because education remains a political battlefield in Mexico. Current conflicts over teacher unions, pensions, evaluation, and state reform show that the question of who gets to educate the nation is still unresolved. Future work will organize the Mexico section person by person, adding endnotes with reliable scholarly references for each claim.

The Enlightened Elite? Socioeconomic Advantage and Attitudes Toward Democracy and Race

Student: Arav Mehta
Mentor(s): Jennifer Perry
Faculty Advisor(s): Meenakshi Verma-Agrawal
Harvard College | Winthrop House | Government | 2029

Research on U.S. race relations, democracy, and polarization has often emphasized the white working class as an indicator for national sentiment. This project instead contextualizes a smaller but disproportionately influential segment: socioeconomically advantaged Americans who are college-educated, higher-income, white, and older, against the broader population. We draw on two surveys combining closed and open-ended questions to measure attitudes toward democratic strength, racial equality, political tolerance, intergroup sentiment. The primary survey samples the aforementioned high-income respondents, offering unusual depth on this advantaged segment. A companion survey, drawn from a racially balanced pool of respondents, allows these attitudes to be contextualized against a more racially diverse population. The quantitative analysis examines how these attitudes vary across race, class, and political ideology—including whether socioeconomic advantage predicts distinct patterns of political identity and attitudes toward minority groups. This analysis seeks to understand whether the perception that education and wealth correlate with a stronger commitment to equality, liberty, and the broader American system is grounded in evidence. We anticipate that greater socioeconomic advantage will be associated with distinct ideological alignments, and that expressed support for neutral principles may coexist with less favorable attitudes toward specific minority and activist groups. A second, qualitative analysis applies a structured coding method to open-ended responses on the state of race relations, mapping how respondents assign blame and how they frame the trajectory of race relations across political ideology. We anticipate that more advantaged respondents will locate the sources of democratic and racial strife in ideology, political actors, and specific groups, rather than in structural or economic institutions, where respondents of color or of a lower income may identify fault. By clarifying how socioeconomic advantage shapes perceptions of democracy and race, this work aims to inform efforts to address the divides that contribute to democratic backsliding and inequality.

Complexity, uncertainty, and pedagogy of moral norms

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Mentor(s): Ariel Levy
Faculty Advisor(s): Fiery Cushman
Harvard College | Currier House | Psychology | 2027

People teach moral norms in two distinct modes: as rules and examples. Bayesian models of concept learning suggest that teachers prefer to use examples when they are uncertain about a concept's boundaries. Existing work in this area has focused on numerical concepts. This paper aims to extend these findings to moral concepts in two online studies. To control for prior moral beliefs, both studies use novel norms belonging to a fictional fishing society. In Study One, 100 participants on Prolific learn each community's norm through trial and error, with uncertainty manipulated by varying the number of learning opportunities; they then teach the norm using either a rule (a numeric range) or examples (specific acceptable values). Study Two manipulates norm complexity (two versus five relevant dimensions) and tests whether uncertainty mediates the effect of complexity on teaching mode. It is hypothesized that greater uncertainty and greater complexity will each increase preference for teaching with examples, and that complexity operates by increasing uncertainty. By identifying different ways uncertainty can be induced and how it influences when and why moral norms are transmitted as rules versus examples, this work may deepen the current understanding of computational models of Bayesian concept learning.

Infant Representation of Symmetric and Asymmetric Interactions

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Mentor(s): Pablo Rodriguez Osztreicher
Faculty Advisor(s): Ashley Thomas
Harvard College | Quincy House | Psychology | 2027

When viewing interactions between people, it is unclear what exactly babies are tracking. Previous research has focused on whether infants can represent individual roles, specifically, whether they distinguish between active and passive roles. For example, research shows that after infants become habituated to scenarios in which a giver repeatedly passes an object to a receiver, they dishabituate to a similar event in which the roles are reversed, with the former receiver handing the object back to the former giver. These results have been taken as evidence that infants represent interactions by parsing the individuals involved and their roles. However, it may be that infants are also tracking the specific relationship between the characters. For example, if presented with events in which one person always acts on another, infants may infer an asymmetric relationship, in which one person is more dominant, and be surprised when actions do not conform to such a hierarchy. The current study aims to test the possibility that infants track relationships in addition to roles in an interaction. We will familiarize 10- to 12-month-old infants with a video of symmetric interactions between two people, such as two people hugging each other. During testing, participants will be presented with videos of a different symmetric and asymmetric interaction; for example, two people holding hands versus one person grabbing another person's hand. We predict that infants will display longer looking times for the interaction type they were not familiarized with, i.e., the asymmetric action. Because the test events involve new actions rather than a role reversal, this would suggest that infants represent interactions by attending to the relationship between two people rather than just their individual roles. Findings on how babies understand social relationships can help future researchers design interventions to enhance infants' relationships with the people around them.

Sizing the Specialty Cocoa Market

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Mentor(s):
Faculty Advisor(s): Carla D. Martin
Harvard College | Leverett House | Statistics | 2028

How big is the specialty cacao market? Despite continued interest from buyers, researchers, and investors, the sector still lacks reliable volume figures. This uncertainty deters investment and frustrates researchers and firms trying to operate under it. The market's opacity stems from two challenges. The data itself often exists only informally between farmers, traders, surveys, and relationships, but is not structured in verified research-ready form. Compounding this, there is conceptual invisibility with no single shared definition of specialty. As a result, although the International Cocoa Organization (ICCO), the sector's intergovernmental authority, publishes a country-level "fine/flavour" designation based on sensory qualities and aromatic and flavour notes, this struggles to fully capture the specialty cacao market. To address this, we have devised a research verification/intake pipeline that fits into the current survey and relationship-based means of knowledge-sharing within the sector to build a structured database. By compiling data from expert interviews with organizations across the specialty cacao ecosystem including farmers, exporters, cooperatives, traders, and chocolate makers, we standardized inconsistently structured information into consistent fields. To reduce the burden on those sharing their knowledge, we deployed Claude to capitalize on existing revenue and gather import data available online, cross-checked by a layer of human verification. The existence of this data allowed for various applications, including a geospatial arcGIS map to display linkages between players in the market; a bottom-up market sizing to generate a credible market floor in number of metric tons of cacao, building on Dr. Martin's previous top-down approach to devise a market ceiling based on number of specialty chocolate buyers; and a web-app that allows for farmers to easily look-up potential buyers. Having a reproducible data infrastructure for a fragmented market will revolutionize an already thriving specialty cacao market, enabling its growth, attracting investment, and informing policymakers.

Infants' Understanding of Non-Solid Objects

Student: Audrey Sun
Mentor(s): Sanghee Song
Faculty Advisor(s): Elizabeth Spelke
Harvard College | Kirkland House | English & Physics | 2028

Previous work has suggested that infants readily infer behaviors of solid objects early in development. However, much less is known about whether they form expectations about non-solid substances, despite everyday exposure to materials such as water, sand, and food. This study will investigate whether infants also hold expectations for non-solid, cohesive objects, and whether this understanding follows a different developmental trajectory. Two age groups (4–6 and 13–15 months) will undergo four familiarization trials showing computer-simulated videos of a jelly-like cube being shaken or poured onto solid surfaces (a glass, a floor, and stairs). It jiggles, rolls, and flattens, but does not split. In the test events, the cube will be poured onto a wedge, where it either splits or remains intact. Because infants look longer at unexpected behaviors, their looking times for the two outcomes will be the metric for identifying their expectations. Based on past studies showing that 3-month-old infants can detect solidity and non-solidity as invariant properties of objects, we hypothesize that infants will look longer at the cube-splitting outcomes. Older babies may show more contrasted looking patterns than younger babies, indicating clearer expectations of non-solid objects. This might suggest that expectations for deformable objects become more robust over time. Our findings may indicate that infant knowledge of cohesion extends beyond solid objects, and that the developmental trajectory depends on the degree of cohesiveness. Future studies should test non-solid objects that behave differently (e.g., slime or sticky sand), further investigating infants' understandings of a wider range of materials.

Unionization, Strikes, and Activist Career Outcomes in the Academe

Student: Luca Tovazzi
Mentor(s):
Faculty Advisor(s): Richard Freeman
Harvard College | Adams House | Applied Math | 2027

While union membership in the United States has declined for decades, higher-ed labor has moved in the opposite direction. Graduate students and other academic workers have organized at a pace that raises two related questions. First, why have unionization and strike activity spread so quickly across universities in a context where bargaining rights have come under scrutiny? Second, what does participation in union activism do to the later career trajectories of the graduate students who engage in it? These questions are especially relevant as federal and state governments place new political and economic pressure on universities. To answer them, we assembled a dataset of graduate student unions, strikes, and union leaders using news articles, the 2024 Directory of Bargaining Agents and Contracts in Higher Education (Herbert et al., 2024), official union websites, and university announcements. We then linked these data to a panel of university characteristics (demographic, geographic, and financial) from the Integrated Postsecondary Education Data System and to individual career-outcome data from Revelio, ORCID, and related sources. In our analysis, we test two main hypotheses. First, unionization and strikes may spread across institutions in patterns similar to social contagion, as graduate workers learn from nearby or peer institutions during regional waves of graduate student organization. Second, union activism may affect graduate student career outcomes in opposite directions: it could primarily reduce research time and slow career progress, or it could also build helpful skills and social networks. By connecting higher-ed mobilization to both institutional and individual outcomes, our research helps explain the continued push among graduate students to organize inside universities against a rapidly changing political and economic landscape and investigates how the financial condition of universities contributes to strikes. Our ultimate goal is to use the results of our analysis to build artificial agent models of the relevant actors (students, university administrators, and policymakers) to simulate unionization and its outcomes.

Unionization of the "Best and Brightest": A Mixed-Methods Analysis of Graduate Student Strike and Unionization Activity

Student: Ella Witalec
Mentor(s):
Faculty Advisor(s): Richard Freeman
Harvard College | Quincy House | Economics | 2029

In the past decade, the United States has seen rapid growth in the number of graduate students represented by a labor union, despite declining unionization in other sectors of the economy. Even more recently, two graduate student unions have staged strikes in just the first half of 2026. However, despite the growing importance of graduate student unions, there remains a lack of research comprehensively cataloguing and analyzing strike and unionization activity in this unique sector of the economy. To fill this gap, we aim to understand what factors influence graduate student union formation, drive strike decisions, and impact strike success. We began by using large language model-assisted search to comb online records and historical newspaper articles, compiling a novel database of union formation, strikes, and strike authorization votes by graduate student unions in the US dating back to 1969. We then combined this original dataset with the Integrated Postsecondary Education Data System records on university characteristics to investigate potential factors associated with union and strike activity, such as university financial status, composition, size, and union support level. We will also take advantage of changes in state and federal labor laws to investigate whether the legal environment impacts unionization and strike success. To add depth and qualitative insight to our analysis, we will employ a mixed-methods approach by interviewing graduate student union leaders at Harvard University in order to develop a case study focused on the Harvard Graduate Student Union's recent strike. At a time of heightened attention on higher education and growing graduate student unionization, this research will provide a systematic catalogue of graduate student union and strike activity and insights for universities and union leaders alike into what factors make graduate student unionization and strike campaigns more likely to succeed.

Unionization of the "Best and Brightest": Graduate Student Strikes, Bargaining Outcomes, and Career Consequences

Student: Iris Xue
Mentor(s):
Faculty Advisor(s): Richard Freeman
Harvard College | Leverett House | Economics | 2028

Over the past decade, graduate students, postdoctoral researchers, and faculty members across American higher education have organized unions and engaged in strikes at unprecedented rates, even as recent shifts in federal and state policy under the Trump administration threaten to reshape the academic and financial landscape in which these unions operate. Despite this rapid growth, existing scholarship on academic labor organizing remains fragmented, often limited to case studies of individual institutions rather than a systematic analysis of the factors that shape strike outcomes. This project investigates two questions. First, what institutional, legal, and economic factors determine whether a graduate student strike succeeds in winning union recognition or a collective bargaining agreement? Second, does participation in strike leadership affect union leaders' academic and professional trajectories? To address these questions, we compiled an original database of graduate student and faculty strikes across U.S. higher education institutions, recording each strike's duration, bargaining demands, mandatory bargaining laws, and federal political environment, including presidential administration and National Labor Relations Board composition. We merged the strike database with institutional data from the National Center for Education Statistics to identify predictors of bargaining success. We anticipate that presidential administration, institutional funding structure, and national union affiliation are meaningful predictors of local strike outcomes. To add qualitative insights to our analysis, we will survey and interview recent graduate student organizers to assess whether union involvement delayed degree completion, research productivity, or career progression. Future work will collect data on the content of collective bargaining agreements secured after successful strikes to assess which contract terms are most commonly won and how they vary across institutions. We also hope to model the spread of unionization across institutions as a form of social contagion and use artificial agent models to simulate how universities and student workers respond to shifting political and financial conditions.


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DBSP
DU BOIS SCHOLAR PROGRAM
frontal lobe
parietal lobe
pons
W. E. B.
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Julia

Who Gets Their Way?: Children's Use of Relative Group Size and Ingroup Leadership to Infer Social Power

Student: Taylor Allen
Mentor(s): Christina Steele
Faculty Advisor(s): Ashley Thomas
Howard University | Psychology | 2028

White U.S. Americans have long expressed concern about the growing size of minority groups. Prior work suggests that information about demographic change, especially projections that White Americans will no longer be the numerical majority, can increase racial bias and support for conservative policies. Where do concerns about shifting group size and power originate? Developmental research suggests that humans reason about social groups early in life. Infants attend preferentially to same-race faces and are more likely to accept objects from people who speak the same language as their caregivers, suggesting early ingroup biases. Children also favor ingroup members over outgroup members, allocating more resources to ingroup members and expecting ingroup members to show loyalty to their own groups, even when groups are novel or fictional. Children also reason about numerical group size and dominance. Infants and children expect members of larger groups to prevail, and older children use relative group size to infer power: they see smaller groups as leaders, whereas larger groups are able to obtain resources. These findings suggest that children may integrate ingroup membership and relative group size when reasoning about which groups are likely to "get their way." The current work will examine whether children have intuitions about how relative ingroup-outgroup size shapes social power. First, we test whether children expect ingroup members to favor ingroup leaders. Second, we test whether children expect group members to get their way more often when they have an ingroup leader (2a) and when they are in the majority (2b). Finally, we examine whether children combine these cues, expecting groups to be most powerful when they are both relatively larger and represented by an ingroup leader. Together, these studies aim to advance knowledge on how children reason about group identity, hierarchy, and power, and may illuminate developmental origins of adult concerns about demographic change and the consolidation of power.

How Has Race Been Theorized in Organizational Research Since 1964?: A Review of Workplace Scholarship

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Post–Civil Rights era workplaces have become increasingly diverse. In response to this demographic shift, scholars have devoted significant attention to understanding the role of race in organizational and workplace contexts. Consequently, a rich body of research has developed, illuminating the dynamics, experiences, processes, and outcomes associated with race in organizations and the workplace. We reviewed 28 business-related research articles examining race in workplace settings. Using a coding framework, we analyzed how race was conceptualized and studied across these articles, capturing each study's organizational context, industry setting, research design, and theoretical treatment of race. Through this analysis, we identified the primary outcomes of the studies and evaluated whether each article could be categorized as presenting evidence of sanctioning and, if so, whether such sanctioning occurred through authorization (organizational processes that grant individuals/groups access, legitimacy, or opportunity), discipline (processes that constrain, exclude, or regulate), or a combination of both. In a preliminary analysis, we find that much of the literature demonstrates that across a range of organizational contexts, formal and informal organizational practices are associated with how employees understand, express, and navigate their racial identities and relationships with majority and minority groups. We also find within the literature that race is not simply a static demographic characteristic but has been conceptualized and redefined in a multitude of ways which have influenced the varied relational dynamics and outcomes across different organizational levels. Future research will expand the scope of analysis by incorporating a larger sample of studies and additional analytical parameters, enabling a more comprehensive examination of patterns and trends across organizational contexts and management research.

A Resting Place: Mapping the Daily Lives of Enslaved Individuals in Colonial Cambridge

Student: Avery Bennekin
Mentor(s):
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Howard University | African & African American Studies | 2028

In the northwestern corner of Cambridge's Old Burial Ground, separated from the community they inhabited, two headstones mark the graves of enslaved people: Cicely, 13, and Jane, 22. Though signified in death, little is known about how they lived, worked, and moved through space. This project centers the experience of the enslaved, separate from their enslavers, by uncovering where and how they lived in colonial Cambridge during the 17th and 18th centuries. Using archival research, paleography, and critical fabulation, this project examines extensive primary sources like municipal and judicial records, estate documents, deeds, receipts, and personal writings to compile mentions of enslaved people across various institutions in a single database. By organizing the primary sources in a central archival catalog, our project creates a more comprehensive look at daily enslaved life in colonial Cambridge beyond prominent narratives. Additionally, by detailing the lives of two enslaved Cantabrigians, our project highlights the complex relationships between the enslaved and their enslavers, often falsely remembered as benevolent and dismissive of slavery's inherent violence. Our project centralizes primary sources detailing both geographical and personal information about what it meant to be enslaved in colonial Cambridge. In contrast to earlier scholarship, this project emphasizes the humanity of the enslaved, often flattened to one dimensional characterizations in documentary records. Though Cicely and Jane are the only enslaved people memorialized in the Old Burial Ground, our project stands as a living monument to the public memory of Cambridge's enslaved.

Cooling Solutions for High-Risk Urban Adults Experiencing Heat Waves

Student: Derrick J. Bradley II
Mentor(s):
Faculty Advisor(s): Gary Adamkiewicz
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As extreme heat events become more frequent and severe, older adults face heightened risks because of age, chronic health conditions, and environmental exposures. The Beat the Heat study investigates indoor heat exposure and the cooling strategies older adults use during extreme heat events, including air conditioning use and access to cooling resources. Building on this work, the present study examines how outdoor neighborhood environments influence indoor heat experiences and heat adaptation behaviors through an environmental justice and green infrastructure lens. Specifically, it investigates whether disparities in tree canopy, shaded public spaces, park access, and neighborhood investment contribute to differences in heat exposure and cooling strategies among older adults. Using surveys and interviews alongside geographic analyses of green infrastructure, the study will explore perceptions of neighborhood green space, barriers to cooling, air conditioning use, and the relationship between outdoor environmental conditions and indoor heat management. Findings will provide insight into how green infrastructure shapes cooling strategies and heat exposure, the health implications of inequitable neighborhood environments for older adults, and policy interventions that support equitable landscape planning, public health, and climate resilience in heat-vulnerable communities.

Community-based Scholarship and Service

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Community-centered healthcare depends on meaningful partnerships and effective evaluation to improve health outcomes and advance health equity. However, community-based programs often face challenges in measuring their impact and sustaining meaningful engagement with the populations they serve. This project examined strategies to strengthen community-based health initiatives through quality improvement, program evaluation, and community engagement. This project involved two complementary initiatives. First, existing pre and post-service surveys used by the JRI Health Law Institute to evaluate legal services for clients living with HIV were reviewed to identify opportunities to improve question clarity, strengthen the relevance of survey content, and address barriers to survey completion. Recommendations were developed to improve survey design and increase post-service response rates, enabling a more comprehensive assessment of client experiences, program outcomes, and service effectiveness. Second, community engagement efforts were supported through the planning and facilitation of Mission Main Tenant Task Force's annual Family Fun Day, a community event serving residents of the Mission Main public housing development. The event fostered connections between residents and partnering organizations while promoting access to health-related resources and community services. Preliminary findings suggest that strengthening evaluation methods while cultivating authentic community partnerships enhances the effectiveness of interdisciplinary programs addressing the social determinants of health. Ongoing work will focus on implementing and evaluating the proposed survey revisions while exploring how community-centered evaluation practices can improve equitable, person-centered care and inform future community health initiatives.

A Resting Place: Mapping the Daily Lives of Enslaved Individuals in Colonial Cambridge

Student: India Crowe
Mentor(s):
Faculty Advisor(s): Jason Ur
Howard University | African & African American Studies | 2028

In the northwestern corner of Cambridge's Old Burial Ground, separated from the community they inhabited, two headstones mark the graves of enslaved people: Cicely, 13, and Jane, 22. Though signified in death, little is known about how they lived, worked, and moved through space. This project centers the experience of the enslaved, separate from their enslavers, by uncovering where and how they lived in colonial Cambridge during the 17th and 18th centuries. Using geospatial visualization, 3D modeling, and spatial analysis, this project reconstructs the living environments of enslaved individuals and provides insight on how they moved through space. Additionally, by detailing the lives of two enslaved Cantabrigians, our project highlights the complex relationships between the enslaved and their enslavers, often falsely remembered as benevolent and dismissive of slavery's inherent violence. Our project centralizes primary sources detailing both geographical and personal information about what it meant to be enslaved in colonial Cambridge. Through vectorization of historical maps and reconstructions alike and cataloging geographical locations from textual evidence, the project's database examines the lives of the enslaved through time and space. In contrast to earlier scholarship, this project emphasizes the humanity of the enslaved, often flattened to one dimensional characterizations in documentary records. Though Cicely and Jane are the only enslaved people memorialized in the Old Burial Ground, our project stands as a living monument to the public memory of Cambridge's enslaved.

Examining Patient and Citizen Engagement in U.S. Health Technology Assessments

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Spelman College | Economics | 2027

Health technology assessment (HTA) organizations play an essential role in evaluating the value and affordability of new medical treatments. As healthcare decision-making increasingly highlights incorporating patient perspectives along with clinical and economic evidence, it is important to understand how patients and other stakeholders– including manufacturers, patient advocacy organizations, researchers, payers, and citizens participate–in the HTA process. This study examines the factors associated with patient and stakeholder engagement in reports published by the Institute for Clinical and Economic Review (ICER). We developed an analytic dataset of publicly available ICER assessments published between 2017 and 2026 that included the following variables: disease prevalence, patient engagement measures, stakeholder participation, patient representation within reports, and overall report lengths. The dataset was used to report descriptive statistics, correlation analyses, and regression analyses to examine their association with engagement. Every HTA included in our analysis (n=46) included patient input in a dedicated section of the report, 8 of which (27%) included a patient quote on their experience with the disease or treatment being considered. Most (29, 97%) included a comment from the manufacturer of the technology, and 20 (67%) included input from a patient advocacy group. Preliminary analyses of ICER assessments suggest that disease prevalence does not predict the degree of patient engagement, but could predict other elements of HTAs such as the total length of the report. Correlation analyses showed no meaningful relationship between disease prevalence and patient engagement ($r = -0.12$), while disease prevalence was moderately associated with total report length ($r = 0.57$). Regression analyses also found no statistically significant association between patient engagement and either rare disease status ($p = 0.43$) or disease category ($p = 0.67$). Future analyses will expand on the dataset to further examine whether rare diseases and disease burden are associated with increased patient and stakeholder engagement.

Perceptions of Public Servants: Analyzing Trends in Terminology Use

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Spelman College | Government | 2028

The language used to describe how Americans view government workers has continuously evolved due to political and social discourse. The goal of our project is to understand when and how different terms such as “bureaucrats”, “public servants”, “civil servants”, have been used over time to describe government employees, including by whom, in what contexts, and with what differences in tone/sentiment/framing. Our study examines trends in the frequency, sentiment, and framing of these terms across political institutions, mass media, and social media. We are collecting text data across three domains of discourse: political institutions, mass media, and social media. We will then apply a text analysis framework using ChatGPT to filter relevant passages and classify them according to sentiment, perceived warmth, competence, integrity, innovativeness, and thematic framing. We will incorporate human validation throughout the process including human classification of sentiments and framings on subsets of the corpus. Our project is currently in the data acquisition and corpus construction phase, with priority datasets being collected and processed for relevance filtering. Potential data sources include academic databases of user posts from Twitter and Reddit, as well as transcripts of congressional floor speeches and presidential speeches. This initial stage will determine the scope of our corpus and determine what trends in terminology use we will be able to capture from the data. One way we are examining shifts is in comparing positive and negative sentiments associated with different terms and assessing whether political changes predict changes in the frequency of those terms over time. Our future work will include classifying the filtered corpus using GPT and then begin with human validation of filtering and scoring steps.

Thin Accretion Disk Luminosity of Rotating Black Holes in Perfect Fluid Dark Matter

Student: Nia Freeman
Mentor(s):
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Howard University | Astrophysics | 2028

Motivated by the observational evidence that dark energy and dark matter comprise more than 60% of our universe's matter, we considered a Kerr black hole surrounded by perfect dark matter (PFDM) to study the accretion processes of its thin disk. Using the Novikov-Thorne model for accretion disks, we analyzed how the PFDM parameter influences the properties of the circular geodesics. First, we derived the spacetime metric using the Einstein-Hilbert action and the metric's spacetime properties. Then we found the radius of the innermost stable circular orbit (ISCO), the specific angular momentum and velocity, the energy flux, and luminosity of the thin disk. The results indicated that for a given PFDM parameter, the ISCO radius decreases. In contrast, the spin parameter increases, and at a fixed spin parameter, the ISCO radius decreases to a critical value. Our findings show that, in the presence of PFDM, thin accretion disks are hotter and more luminous than those around Kerr black holes without dark matter. Therefore, our findings of dark matter incorporated Novikov-Thorne thin disk flux, temperature and spectral-luminosity calculations will provide a direct comparison to archival Chandra X-ray spectra of accreting black hole candidates. Additionally, our code can be reusable for adapting other alternative gravity spacetimes to test against current observations.

Classifying SPHEREx Sources Using Machine Learning

Student: Abdul-Majeed Hamidu
Mentor(s):
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Hampton University | Astrophysics | 2028

We apply machine learning techniques to classify infrared (IR) spectral sources for NASA's SPHEREx mission, with a particular focus on identifying Young Stellar Objects (YSOs) and distinguishing them from other astrophysical sources. Accurate classification of YSOs is critical for studying the early stages of stellar evolution; however, traditional approaches based on infrared color-color and color-magnitude diagrams often suffer from overlapping source populations and provide limited confidence in the resulting classifications. In this paper, we leverage the low-resolution near-infrared spectral data of SPHEREx to carry out the automated spectral classification based on the supervised learning techniques. A set of labeled templates with 5,412 objects was applied to train and test various machine learning models by dividing them into thirteen different astrophysical categories, e.g., Class I, II, and III YSOs, carbon-rich and oxygen-rich Asymptotic Giant Branch (AGB) stars, Active Galactic Nuclei (AGN), and main-sequence (MS) stars with effective temperatures between 3500 K and 6500 K. The template comprises 316 Class I YSOs, 500 Class II YSOs, 385 Class III YSOs, 524 carbon-rich AGB stars, 258 MS 3500 K stars, as well as about 500 samples for each other stellar class. Several supervised learning algorithms were evaluated using cross-validation to identify the model with the strongest classification performance. We found that among the models tested, the highest overall cross-validation accuracy (73.3%) was achieved using a Convolutional Neural Network (CNN classifier. The classifier performance was high for several source types, e.g. Class II YSOs (97%), carbon-rich AGB stars (95%), MS 3500 K stars (88%), MS 6500 K stars (87%), and AGN (84%). Lower accuracies were obtained for intermediate-temperature main-sequence stars due to their spectral similarities which cause confusion between the adjacent temperature classes. The best-performing CNN model was subsequently applied to 21,524 previously unlabeled SPHEREx sources to predict their astrophysical classifications, providing an efficient and scalable framework for identifying unknown objects from their infrared spectra.

Resolving Long Period Planet Ambiguities in TESS Data

Student: LaMyla Hill
Mentor(s):
Faculty Advisor(s): Jason Eastman
Howard University | Astrophysics | 2028

Understanding the periods of exoplanets, which are any planets that exist outside of our solar system, is vital to understanding basic properties of the entire planetary system. NASA launched TESS (the Transiting Exoplanet Survey Satellite) in 2018 to discover transiting planets. Transiting planets pass in front of the star and block a percentage of the star's light as seen from Earth. TESS has 106 distinct sectors that are independently observed for 27 days, roughly every two years. For long period planets (>20 days), the data gaps often result in ambiguous orbital periods, as many transits are often missed when unobserved. We analyzed two planets, which TESS reported as long-period: TOI-5626 with a period of 716.22 days, and TOI-1861, with a period of 742.51 days. Using the EXOFASTv2 modeling software, we fit the transits, their orbits, and the host star with a variety of possible periods to determine a viable period and the system's parameters. Along with the data from TESS, we used follow-up observations from the Exoplanet Follow-Up Observing Program (ExoFOP) to assess if the combination of data could resolve ambiguous periods. By including detections and non-detections alike, we determined that TOI-5626 has a period of 23.10 days, a semi-major axis of 0.1550 AU, and an eccentricity of 0.353. Additionally, TOI-1861 has a period of 185.63 days, a semi-major axis of 0.643 AU, and an eccentricity of 0.29. From the period, we got a temperature of 354 K, meaning TOI-1861 is in the habitable zone. The habitable zone is the distance away from a host star at which a planet can sustain liquid water. Despite there being 6,316 confirmed exoplanets, only a handful have periods comparable to TOI-1861, and it is among the easiest to study, making it a valuable testbed for understanding habitable planets more broadly.

Creating Justice Together: An Undergraduate Adaptation of Harvard Kennedy School's Client-Centered Policy Course

Student: Nola James
Mentor(s):
Faculty Advisor(s): Cornell William Brooks
Spelman College | Educational Studies | 2027

Although experiential policy education equips learners with the knowledge and practical skills necessary to address complex justice-related problems, opportunities to participate in client-centered policy advocacy remain largely limited to graduate education. Client-centered policy advocacy engages students in developing campaign strategies for real-world clients, allowing them to translate policy knowledge into advocacy on behalf of community organizations and public institutions. To expand this model of learning, this project adapts the Harvard Kennedy School's William Monroe Trotter Collaborative for Social Justice Clinic (WMTC) class, "Creating Justice in Real Time: Visions, Strategies, and Campaigns" (CJRT), taught by Professor Cornell William Brooks, JD., M.Div., into a condensed, week-long J-Term course for undergraduate students from Historically Black Colleges and Universities (HBCUs). The adapted course equips undergraduates with the advocacy skills necessary to develop and contribute to campaign plans addressing contemporary voting rights challenges. To adapt CJRT for an undergraduate audience, this project examines the existing graduate-level syllabus, course materials, pedagogical literature on experiential learning, and diverse scholarship on voting rights. These materials were analyzed to identify the course's instructional strategies and learning objectives. Readings and instructional exercises were selected to introduce students to the foundational principles of effective advocacy, including policy research, coalition-building, strategic communication, negotiation, and campaign planning. Interactive components, including case studies, simulations, policy design activities, guest speakers, and multimedia resources will prepare undergraduate students to work alongside graduate students in designing campaigns that advance voting rights. The proposed J-Term establishes a reciprocal partnership between the William Monroe Trotter Collaborative for Social Justice and selected HBCU students. Undergraduate participants will contribute community-informed perspectives shaped by their proximity to the clients, who are located in HBCU communities. In turn, the J-Term will provide practical advocacy skills, preparing HBCU undergraduates to become the next generation of policy advocates.

Strategy and Performance in Private Equity: The Market for CFOs in Private Equity

Student: Kawika Keys
Mentor(s): Henry Woo
Faculty Advisor(s): Paul Gompers
Howard University | Economics | 2028

Most research conducted on the labor market for CFOs has revolved around publicly traded companies with very little research addressing the market for CFOs in Private Equity, specifically in companies acquired through Public-to-Private (P2P) deals. This project explores both the nature of and the dynamics of the hiring of CFOs within both the public and private CFO labor markets, focusing on external versus internal appointments and their implications for firm-specific human capital. In line with the work of Gompers, et al. regarding the CEO labor market, we utilize Pitchbook company and deal-level data to accurately assess the labor market for CFOs in companies acquired by private equity. Specifically, we analyze the rate of internal hiring of the acquired company's CFO as opposed to external hiring of a new CFO after acquisition, industry-related experience of the new CFOs relative to their new company/industry placement, buyout and equity incentives used to attract new CFOs, and size of firm relative to turnover rates for CFOs. We additionally seek to gain a greater understanding of the background of PE-backed CFOs prior background, how they were recruited to the companies, and what their action plan for the firm is. We then compare these findings to their counterparts in publicly traded companies, allowing us to gain deeper insights into the labor market for CFOs in both publicly traded and privately held companies.

How Children Use Parent-teacher Value Alignment to Establish Who They Can Trust

Student: Kathya Lavado-Arrington
Mentor(s): Maya Hernandez
Faculty Advisor(s): Ashley Thomas
Spelman College | Sociology | 2028

Previous research suggests that children evaluate whom to believe. Long before they can articulate why, they're tracking who has been right before, who knows what is correct, and to whom other people listen. However, we do not know if children notice whether a potential teacher shares the values they have learned at home. While a child's foundational understanding of the world and moral rules is heavily shaped by their parents at home, entering school requires them to extend that trust to unfamiliar adults in a different setting. This study explores how parent-teacher value alignment impacts a child's willingness to trust new information and to complete difficult tasks. We hypothesize that children will be more likely to trust and learn from potential teachers whose values align with their parents' values, but less likely to do so from potential teachers whose values align with those of an unfamiliar adult. This hypothesis is informed by research suggesting that children trust their parents' moral testimony and draw inferences about social relationships. We present 6- to 7-year-old children, over Zoom, with novel action words (e.g., turbing), two animal avatars, and either their parent in the parent condition or a stranger in the yoked control condition. One character agrees with their parents that 'turbing is ok' and another character disagrees with their parent. Then both characters give an impossible task, and we measure how long children spend on the tasks. Finally, we ask children questions about interpersonal and epistemic trust toward the two characters. The premise is that when children encounter potential teachers they believe are socially connected to their parents, they may be more receptive to learning from them. By examining how children develop trust in new potential teachers, this study highlights the importance of consistency between home and school life.

Youth Behavioral Health Equity and Justice Involvement Mapping Pathways to Care in Boston

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Mentor(s):
Faculty Advisor(s): Kevin Simon
Howard University | Global Health & Health Policy | 2027

Clinical care accounts for only a fraction of health outcomes. Housing, safety, education, and community support shape much of the rest. Boston youth with co-occurring mental health and substance use needs, particularly those involved in the legal system, often move among public health, child welfare, education, juvenile justice, and public safety systems with limited coordination. Traditional diversion models assume a linear path from crisis to care. In practice, Boston's youth behavioral health and juvenile justice ecosystem is recursive. Youth cycle through services and legal-system involvement simultaneously, often for years. The central challenge is not the first referral but sustained engagement across systems. Guided by the Sequential Intercept Model, this project maps the pathways Boston youth travel between behavioral health services and legal-system contact. The research team is conducting a landscape scan of the city's youth-serving infrastructure, synthesizing literature on legal-system return, auditing summer operations with cross-sector partners, and conducting qualitative interviews with community experts. This work examines how youth are referred to and connected with mental health care and pro-social supports, where those pathways weaken, and why breakdowns are often most pronounced immediately following return to the community from justice settings. Through this ongoing analysis, the team is identifying gaps in early recognition, psychiatric care coordination, and continuity of care. Youth with less visible mental health needs or limited prior behavioral health contact may be overlooked during law enforcement and detention encounters. Upon reentry, fragmented clinical handoffs, disrupted medication access, weak cross-agency communication, and limited structured supports can rapidly erode engagement. Families are often left to navigate systems that rarely communicate. The team is developing an engagement fit framework that integrates system involvement, clinical presentation, and family context alongside recommendations for a community-based model combining psychiatric care and pro-social programming to strengthen continuity after reentry.

Understanding the Cause of Broad Emission Lines of Lyα in the Broad Line Region using Monte Carlo Simulations

Student: Xavier Maple
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Morgan State University | Physics | 2027

The broad line region (BLR) is an enormous region bordering the accretion disk of a black hole full of rapidly moving ionized gas clouds. These gas clouds are known to broaden emission lines, but they present two major issues. It is not well known what gas clouds parameters cause the broadening of the emission lines. Additionally, in order for these ionized gas clouds to remain intact there must be a medium that provides enough outside pressure for their existence to be observed. This presents the idea of a Hot Intercloud Medium (HIM), which is a hot cloud of freely moving electrons theorized to have two main purposes, to provide pressure support to clouds in the BLR and to scatter highly energized photons from the accretion disk. Using Monte Carlo Simulations we analyze the emission lines of Lyα photons after passing through the hot intercloud medium in the broad line region. We analyze the temperature, gas density, and ionization states, and we find higher temperatures correlate to broader emission lines.

Perceived Unfair School Discipline and Dual Harm Among U.S. Adolescents: Evidence From the 2023 National Youth Risk Behavior Survey

Student: Imani Marc
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Youth who experience both suicidal behaviors and physical fighting, referred to here as dual harm, are at an increased risk for long-term morbidity and mortality. Schools can significantly affect the mental health of adolescents. Researchers are just starting to explore how schools influence adolescent mental health. One under-studied aspect is whether or not perceived unfair school disciplinary practices contribute to dual harm. To test this association, we used data from the 2023 National Youth Risk Behavior Survey (YRBS), which contains a representative sample of all high school students in the United States. Using survey-weighted multinomial regression models, we examined if there were significant associations between perceived unfair school discipline and being part of one of four categories: no harm, having engaged in suicidal behavior only, having engaged in fighting only, and having experienced both. After controlling for demographic factors and adverse childhood experiences (ACEs), we found that the perceived unfairness of school discipline was positively correlated with each category, and specifically, that adolescents who perceived that they received unfair school discipline had significantly higher odds of experiencing dual harm when compared to youth without any form of harm (adjusted OR = 3.62, 95% CI: 2.81–4.67, $p < .0001$). In addition to the significantly positive correlation between perceived unfair school discipline and dual harm, we also observed statistically significant correlations between perceived unfair school discipline and engaging in either fighting only (adjusted OR = 2.31, 95% CI: 1.92–2.79) or suicidal behavior only (adjusted OR = 1.53, 95% CI: 1.25–1.88). Thus, our findings suggest that perceived unfair school discipline may represent a point where a vulnerable subgroup of adolescents experience overlap in their internalizing and externalizing risk factors due to structural vulnerabilities present within their educational environments, even before these same adolescents experience ACEs. As such, school-based encounters with discipline procedures may provide opportunities for behavioral health screenings and identifying suicidal risk prior to the onset of identifiable symptoms.

FDA Front-of-Package Nutrition Labeling: Balancing Public Health, Regulation, and Commercial Speech

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2028 | Law | North Carolina Agricultural & technical State University

Front-of-package nutrition labeling raises important questions about how federal agencies communicate nutrition information while balancing public health objectives, statutory authority, constitutional limitations, and practical implementation concerns. As the U.S. Food and Drug Administration considers a proposed rule requiring front-of-package nutrition labeling, this project examines how public comments submitted during the federal rulemaking process illuminate broader debates surrounding consumer protection, regulatory authority, scientific evidence, industry burden, and the First Amendment's protection of commercial speech. This project employs legal and policy research methods, including reviewing Federal Register materials, examining the federal rulemaking process, and conducting a thematic analysis of preliminary findings from public comments submitted in response to the proposed rule. The research identifies recurring stakeholder perspectives and evaluates how those perspectives relate to the FDA's statutory authority under existing food labeling laws, the evidentiary support for the proposed rule, implementation and compliance challenges, and the constitutional framework governing compelled commercial disclosures. Preliminary findings suggest that while many stakeholders support improving consumers' access to clear and accessible nutrition information, significant disagreement remains regarding whether the proposed front-of-package labeling system is the most effective, evidence-based, and legally defensible approach. Public comments raise questions concerning the FDA's authority, the adequacy of the scientific record, potential economic and operational burdens on manufacturers, the scope of required disclosures, and whether the proposed labeling requirements satisfy constitutional protections afforded to commercial speech. This research contributes to a broader understanding of the legal and policy considerations that will shape the development and implementation of the FDA's final rule.

Uncovering the Roles of Host Cell Proteins Incorporated into Coronavirus Virions

Student: Barak Meachem
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Host-cell proteins incorporated into enveloped viruses during viral assembly have been shown to influence viral attachment, entry, and infectivity of viruses such as HIV. However, the role of host-derived surface proteins in coronavirus infectivity remains poorly understood despite the significant global health burden posed by coronaviruses. Our laboratory identified the host proteins CD49e (integrin α5) and CD29 (integrin β1) on the surface of human coronavirus (HCoV)-OC43. Because these proteins function in cell adhesion and receptor-mediated interactions, we hypothesized that their incorporation into HCoV-OC43 virions contribute to viral attachment, entry, and infectivity. To test this hypothesis, we first used flow virometry to antigenically validate individual HCoV-OC43 virions and confirmed the presence of CD49e and CD29 on viral envelopes. We then infected susceptible HEK-derived target cells with HCoV-OC43 and quantified infectivity using a luminescence-based assay. To determine the functional contribution of these host proteins, we performed antibody-mediated depletion to remove CD49e- and CD29-positive virions and antibody-mediated neutralization to block their function before infection. Infectivity following each treatment was compared with HIgG isotype controls and an anti-spike (H501-008) positive control to determine the contribution of CD49e and CD29 to OC43 infectivity.

Measurement on the Color Line: A Historical Analysis of Scientific Instruments Created to Measure Skin Tone

Student: Abiba Moncriffe
Mentor(s):
Faculty Advisor(s): Evelynn Hammonds
Howard University | History & Science | 2028

This research project examines three objects from Dr. Evelynn Hammonds' upcoming exhibit on the history of the scientific idea of race in the Harvard University Collection of Historical Scientific Instruments. This project conducts a historical analysis of the backgrounds of three different tools of measurement of skin color. These tools are the Bradley Color top, a tool used in the early 20th Century (1928) by physical anthropologists of the time. Another tool is the von Luschan Scale, designed in 1905 by Austro-Hungarian Anthropologist, Dr. Felix von Luschan. The third object is the Monk Skin Tone Scale created by Dr. Ellis Monk, a professor of Sociology at Harvard University in 2022. Measurement on the Color Line: A Historical Analysis of Scientific Instruments Created to Measure Skin Tone, provides examples and historical backgrounds of three different tools used to quantify skin color and reveals the limitations of each method. In doing this, the project works to establish a lineage of tools scientists have used to understand skin color difference. The project asks how different disciplines and scientists asked this question, pursued their answers, and what were their results? Most importantly, this project asks how do these different tools produce answers to the same questions and how they still affect our ideas of skin color difference today? This research was conducted from reading primary and secondary sources on the function of the objects, their flaws, and their implications. This project shows examples of various measurements of skin color difference in scientific contexts over the course of a century (early 20th century to the 21st century). This research shows the relationship between scientific thought, discovery, and experimentation along with biological and sociological ideas of race.

The First American Music: William Levi Dawson, Institutional Resistance, and the Legacy of the Negro Folk Song

Student: Chioma Okoro
Mentor(s):
Faculty Advisor(s): Andrew Clark
Tuskegee University | Economics | 2027

This research argues that Negro folk songs constitute among the first genuinely American musical traditions, emerging from enslavement and collective memory rather than from any single composer. W.E.B. Du Bois described them as ”the most beautiful expression of human experience born this side the seas,” a claim this project takes seriously as a starting point rather than a rhetorical flourish. The project traces how these songs moved from suppression and minstrel caricature toward institutional legitimacy through the arranging work of Harry T. Burleigh, R. Nathaniel Dett, and William Levi Dawson, whose twenty-six years directing the Tuskegee University ”Golden Voices” Concert Choir produced some of the most widely performed works in the American collegiate choral canon. Drawing on archival research and comparative analysis, the project examines Tuskegee’s choral tradition alongside Harvard’s, where influential music department figures John Knowles Paine and Archibald T. Davison disputed the authenticity of Negro folk songs as American music for nearly a century combined. This comparison illuminates how institutional gatekeeping shaped which musical traditions were canonized and which were marginalized, with consequences that extended through Jim Crow and persist today. Preliminary findings point to a significant gap between the ubiquity of Dawson’s arrangements in collegiate choirs today and singers’ awareness of their origins and significance. Building on this research, the project proposes a freshman seminar course syllabus on the history of collegiate choral singing, intended to close that gap by giving student performers the historical and cultural context behind the music they sing.

Antimalarial Treated Bed Nets Block *Plasmodium falciparum* Infection in Mosquitoes

Student: Oluwafunke Oladokun
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Faculty Advisor(s): Flaminia Catteruccia
Fisk University | Molecular & Cellular Biology | 2027

Malaria is a severe, life-threatening infectious disease caused by *Plasmodium* parasites transmitted through the bite of infected female *Anopheles* mosquitoes. The widespread insecticide resistance of *Anopheles* vectors has compromised the effectiveness of long-lasting insecticide-treated bed nets, necessitating the development of novel vector control strategies. Recent studies from our lab have demonstrated that the transmission of *Plasmodium falciparum* parasites can be efficiently blocked when exposing female *Anopheles gambiae* mosquitoes to antimalarials incorporated in bed-net like polyethylene films in 6-minute tarsal contact assays. These films contained Endochine-like quinolone (ELQ) inhibitors of the *P. falciparum* cytochrome bc1 complex and utilized two lead compounds - ELQ-453 and ELQ-613. Here, we demonstrate that a prototype polyester net formulation coated with either ELQ-453 alone or a combination of ELQ-453 and -613 completely blocks the establishment of *P. falciparum* oocysts when exposed to mosquitoes shortly before infection. Building upon this, our current work focuses on scaling this strategy by testing a broader library of antimalarial compounds to identify additional candidates suitable for this use. To this end, we tested new iterations of ELQs incorporated in LDPE films, with two compounds showing complete blocking activity against the establishment of a *P. falciparum* infection. We also test novel transmission-blocking compounds selected in an *in vitro* screen against *P. falciparum* ookinetes for their *in vivo* blocking activity in Standard Membrane Feeding Assays (SMFAs). These results show promise for continued development of antimalarial-treated bed nets and highlight new compounds with potential to enhance malaria transmission-blocking interventions.

Pubertal Timing, Loneliness, and Externalizing Behaviors: Examining Social Disconnection in Adolescence

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Howard University | Psychology | 2028

Adolescence is a development period marked by rapid social and biological change, as well as increased risk for psychopathology. Early pubertal timing, which is defined as physical maturation that outpaces same-age peers, has been identified as a risk factor for psychopathology, particularly internalizing symptoms (e.g., depression and anxiety), and externalizing behaviors (e.g. aggression and rule-breaking). Although pubertal timing is often studied in relation to emotional distress, it may also alter adolescents' social experiences by reshaping friendship contexts and increasing exposure to more deviant peer socialization. A previous cross-sectional analysis using the Human Connectome Project in Development (HCP-D; n = 652, 325F, ages 9-17) reported that loneliness mediated the relationship between early pubertal timing and internalizing symptoms; however, it is unknown if the mediating effect of loneliness generalizes to other forms of psychopathology. Using the same HCP-D sample, stratified by sex, we will run a mediation model linking externalizing behaviors with early pubertal timing and loneliness while also exploring its relationship with other social factors (e.g., friendship, emotional support). Pubertal timing will be operationalized as a composite of self-reported pubertal status (i.e., Tanner Stages), controlling for age to represent relative timing compared to same-age peers. Externalizing symptoms are assessed using two validated questionnaires: the Child Behavior Checklist (parent-report for ages 6-18) and the Youth Self-Report (ages 11-18). Percentage scores will be used to standardize across surveys. Loneliness is measured using the NIH Toolbox Loneliness Survey. Preliminary findings show that males report significantly higher overall externalizing behaviors while females show higher internalizing symptoms. Within externalizing behavior subscales, males scored significantly higher on rule-breaking but not for aggression. Overall, these findings may help clarify if early-maturing youth are vulnerable to not only emotional symptoms, but also behavioral difficulties shaped by friendships, peers, and relational contexts.

Lewis Community: How a Free Black Family Influenced 19th Century Massachusetts

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Mentor(s):
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North Carolina Agricultural & Technical State University | African & African American Studies | 2028

After the publication of the *Report of the Presidential Committee on Harvard & the Legacy of Slavery*, there has been an enhanced understanding of the role enslaved Black and Indigenous persons played in supporting Harvard University and Massachusetts. However, seldom has been explored about the influence of free Black residents in 1800s Massachusetts and their connection to Harvard University. To address this knowledge gap, this study explored free Black residents, specifically members of the Lewis family of Cambridge, and their influence on 19th century Massachusetts. Archival research was conducted by referencing the Massachusetts Archives, census records, newspapers, special collections from the Cambridge Historical Society, and Harvard special collections. As predicted, the study identified the Lewis family had a significant political impact through their involvement in the Liberian Emigrant Association and signing of civil rights petitions. Also as hypothesized, the Lewis family made notable contributions to the financial system of Massachusetts by serving as business owners and Harvard University employees. These significant results indicate the Lewis family played an integral role in shaping the Black Massachusetts community of the 19th century, contributing to the economy and advocating for civil rights. This study could be referenced by the Harvard Legacy of Slavery Committee in their creation of memorials and local tours that commemorate notable Black figures. Future research could explore the prospective relationship between the antebellum colonization movement in Massachusetts and 1920s Back-to-Africa Movement.

Historical and Contemporary Measures of Social Vulnerability in Relation to Metals Concentrations in Public Park Water Samples and Lead Service Line Infrastructure

Student: Caitlyn Thompson
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Howard University | Environmental Science & Public Policy | 2028

Water is a known source of toxic metals exposure, with exposures varying by communities due to social vulnerability. Past policies, such as historical redlining and contemporary measures, such as the Centers for Disease Control and Prevention's Social Vulnerability Index (SVI) are linked to a disproportionate burden of harmful environmental exposures. This study expands on limited research evaluating associations between historical redlining and SVI with metals concentrations in public drinking water samples collected from Boston parks. As a secondary analysis, we assessed the total number of lead service lines by HOLC and SVI within Boston. A total of 36 parks with functional drinking water stands were sampled in 9 racially, ethnically, and socioeconomically diverse Boston neighborhoods. Using ArcGIS, we linked the parks census tract data to HOLC grade maps and SVI ranks. Water samples collected from all parks were analyzed by the Metals Core Lab at Dartmouth College using ICP-MS. Of the metals assessed, 10 toxic metals were above the limit of detection (i.e. As, Ba, Be, Cd, Cr, Cu, Mn, Pb, Se, Tl) and included in the present analysis, where we calculated mean metal concentrations by HOLC grade and SVI ranks and used ANOVA to assess differences in mean concentrations across groups. Spatial analyses were conducted to determine associations between redlining, SVI, and metal concentrations. We found specific patterns of contamination rather than systemic elevation across all analyzed metals. Specifically, historically redlined neighborhoods had significantly higher concentrations of Barium ($p = 0.0017$), while neighborhoods with higher SVI levels exhibited significantly higher concentrations of Cadmium ($p = 0.0431$). No statistically significant differences across groups were observed for the remaining eight metals. These data provide key information about public drinking water from parks as a disparate source of metals exposure in marginalized communities that could benefit from targeted infrastructure interventions.

Differences in the Distribution of Tau and α-Synuclein Pathologies in Serotonergic Brainstem Regions and its Clinical Significance within Neurodegeneration

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Faculty Advisor(s): Veronique VanderHorst
Howard University | Neuroscience | 2028

Alzheimer's disease (AD) and Parkinson's disease (PD) are neurodegenerative disorders characterized by cognitive and motor impairment. Some of their key neuropathologies, phosphorylated tau (p-tau) in AD and phosphorylated alpha-synuclein (p-αsyn) in PD, first accumulate in the brainstem before spreading to other brain regions. Among brainstem sites, serotonergic nuclei are particularly vulnerable and play essential roles in cognitive and motor function. However, the regional distribution of p-tau and p-αsyn across the serotonergic system remains poorly understood. This study characterized the burden of p-tau and p-αsyn within serotonergic brainstem regions. We analyzed 37 postmortem brainstem tissue from the Memory and Aging Project (ages 78–101 years; 28 female, 9 male; 11 with AD and 3 with PD) using immunohistochemistry for serotonergic neurons, p-tau, and p-αsyn. Analyses focused on the dorsal raphe nucleus (DRN), median raphe nucleus (MR), raphe magnus/obscurus/pallidus complex (ROPM), and lateral paragigantocellular nucleus (LPGI). In $1mm^2$ regions of interest (ROIs), we quantified p-tau tangles, p-αsyn Lewy bodies and filled neurons manually, and pathology particle density using image analysis software. All 37 cases exhibited p-tau pathology. Tangles were detected in the DRN (37/37), MR (33/37), LPGI (24/37), and ROPM (22/37), with the DRN showing the highest tangle burden and p-tau particle density. In contrast, only 8 cases were positive for p-αsyn pathology, with pathology identified in the ROPM (7/8), DRN (7/8), LPGI (6/8), and MR (6/8). The rostral ROPM showed the greatest Lewy body burden, filled neurons, and p-αsyn particle density. These findings demonstrate distinct patterns of AD and PD pathology burden in serotonergic brainstem nuclei. P-tau predominated in rostral ROIs, particularly the DRN, and p-αsyn in caudal ROIs, especially in the ROPM. As the DRN innervates forebrain cognitive regions and the ROPM innervates spinal sensorimotor structures, future studies will correlate these regional pathological gradients with cognitive and motor impairment.

Implementation Barriers and ERIC Strategies for Supporting Doula Presence in the Operating Room

Student: Kennedy Watson
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Faculty Advisor(s): Elysia Larson
Spelman College | Chemical & Physical Biology | 2028

Cesarean birth is a common component of childbirth, but unexpected surgical delivery may require changes to a patient's planned support. Doulas are trained professionals who provide continuous emotional, informational, and physical support during childbirth, but their role in the operating room (OR) during cesarean birth is often unclear. Identifying barriers to doula inclusion and implementation strategies to support collaboration may improve efforts to promote patient-centered care during cesarean birth. A secondary qualitative analysis was conducted of previously collected in-depth, semi-structured interviews focused on doula care and cesarean birth. These interviews included 49 participants: 27 clinicians, 11 doulas, and 11 patients who either experienced a cesarean birth or were involved in cesarean delivery care. Interview transcripts were analyzed using a framework analysis approach to identify barriers to doula presence in the OR and participant-informed strategies to address those barriers. Findings were then used to create an educational tool for clinicians. Qualitative analysis identified seven clinician-perceived barriers to doula presence in the OR: limited space, clinician misunderstanding of the doula's role, low trust between clinicians and doulas, lack of standardized OR policies, liability concerns, poor teamwork, and the need for interdisciplinary education. Participant-informed strategies to address these barriers included standardized policies, interdisciplinary education, and improved communication, and were mapped to implementation science approaches to identify potential methods for supporting doula integration during cesarean birth. Implementation of these strategies, including use of the educational tool, may help clinicians better understand doulas' roles and improve team collaboration in the OR, thus supporting doula integration during cesarean birth. Future implementation should focus on developing and testing standardized OR protocols and interdisciplinary education to support doula presence during cesarean birth. Future research should evaluate the feasibility and acceptability of these strategies among clinicians, doulas, and patients in cesarean birth settings.

Genetic Engineering and Functional Characterization of AmiB2 and GlpK in Mycobacterial Growth and Carbon Metabolism

Student: MaKyra Wilson
Mentor(s): Xin Wang
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Spelman College | Molecular & Cellular Biology | 2027

Tuberculosis (TB), caused by Mycobacterium tuberculosis (Mtb), remains one of the leading infectious causes of death worldwide. During infection, Mtb disseminates multiple anatomical sites, including the lungs, lymph nodes, and other extrapulmonary tissues. Each tissue presents a distinct microenvironment characterized by differences in nutrient availability and immune pressure. These heterogeneous environments shape bacterial physiology and metabolism, ultimately influencing bacterial growth and response to antibiotic treatment. Previous studies have demonstrated that clinical Mtb isolates exhibit strain-specific preferences for different host organs and carbon sources, suggesting that genetic variation contributes to tissue tropism and metabolic adaptation during infection. However, the bacterial determinants that govern these phenotypes remain largely unknown. Two candidate genes implicated in these processes are glpK, encoding glycerol kinase, and amiB2, encoding a putative amidase. Mutations in glpK alter glycerol utilization and have been associated with changes in bacterial physiology, growth, and antibiotic tolerance, indicating that carbon metabolism can profoundly influence bacterial adaptation. In contrast, the function of amiB2 is poorly understood. Based on sequence prediction, amiB2 may participate in amide metabolism and cell envelope homeostasis, processes that could influence nutrient utilization and bacterial fitness in distinct host environments. We therefore hypothesize that both glpK and amiB2 contribute to Mtb tissue tropism by regulating metabolic adaptation to different host niches. In this study, we investigate the roles of amiB2 and glpK using Mycobacterium smegmatis as a model organism. We combine genetic manipulation, molecular biology, and phenotypic analyses to determine how these genes influence bacterial growth under different carbon sources and environmental conditions. This work aims to define the mechanisms by which metabolic genes regulate bacterial adaptation to diverse host microenvironments and to identify genetic determinants of tissue tropism in mycobacteria.

Transitional Justice, ICC Complementarity, and Responses to Human Rights Violations

Student: Madeline Wright
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Spelman College | Government | 2028

How should international law respond when societies confront crimes against humanity, genocide, and gross violations of human rights? This project examines how domestic transitional justice practices interact with criminal trials at national and international levels. Transitional justice includes measures such as truth commissions, reparations, and restorative sanctions that societies use to address legacies of mass violence. The project focuses on the International Criminal Court (ICC), a permanent court that prosecutes individuals for the gravest international crimes, and complementarity, the principle that the ICC generally acts only when national authorities are unwilling or unable genuinely to investigate or prosecute the same cases. To investigate this relationship, the project conducted a comparative review of legal scholarship, theoretical critiques, empirical public opinion studies, and case studies. The research gave particular attention to Colombia and Cambodia while drawing comparative materials from South Africa, Ukraine, Iraq, Bosnia and Herzegovina, and Gaza. Across these contexts, the analysis compared truth-seeking, reparative, restorative, and criminal mechanisms and assessed how they pursue accountability, involve survivors, preserve evidence and collective memory, and distribute authority between domestic and international institutions. The findings suggest that responses to human rights violations should not be judged only by how closely they resemble adversarial prosecution. Colombia illustrates how restorative sanctions may combine criminal accountability with acknowledgment, repair, and victim participation, while Cambodia demonstrates both the importance and limitations of relying on trials to achieve truth, education, memory, reparations, and reconciliation. Across the broader case studies, different mechanisms often work most effectively when treated as complementary rather than interchangeable. Guided by complementarity and jurisdictional redundancy, which emphasizes the value of overlapping legal authority, the next phase will develop criteria for determining when domestic transitional justice practices should supplement, reshape, or receive recognition from the ICC and the United Nations without replacing genuine accountability.

HSURV ABSTRACT BOOK 2026

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Modeling Parkinson's Disease: *pdr-1* Knockout and Habituation Behavior in *Caenorhabditis elegans*

Student: Anika Chakravarthy
Mentor(s): Nicole Fisher & Kathleen Quast
Faculty Advisor(s): Dan Kahne
Harvard College | Leverett House | Molecular & Cellular Biology | 2029

Parkinson disease (PD), the second most commonly diagnosed neurodegenerative disorder, is characterized by progressive dopaminergic neuron loss in the substantia nigra and α-synuclein aggregation. While PD is typically studied in aging populations, PD-related neuronal changes may begin well before clinical symptoms appear, raising the question of whether early behavioral markers can be identified during development. This project uses young *Caenorhabditis elegans* (Day 1-Day 3) to investigate whether RNAi-mediated knockdown of *pdr-1*, the ortholog of human *PRKN*, alters habituation to repeated mechanosensory stimuli, and whether these changes correlate with dopaminergic neurodegeneration. Establishing this link would provide a behavioral proxy for early neurodegenerative change, potentially enabling detection of PD-like symptoms before overt neuronal loss. If there is a cognitive decline expressed we suspect it will mirror what is assumed in humans. The transgenic strain BY250 (*Pdat-1*::GFP), expressing GFP in dopaminergic neurons, is fed *pdr-1* RNAi and for our controls an empty-vector control bacteria. Worms are assessed across developmental stages (Day 1-3 adults) using a habituation assay measuring response decrement to repeated touch to extract qualitative measures of neurodegeneration from habituation behavior. It is hypothesized that *pdr-1* knockdown will slow habituation and reduce the physical intensity of the worm's response relative to controls, with deficits worsening at later stages as degeneration progresses. Future directions include using fluorescence imaging to quantify intact sensory neurons and degeneration signs. Combining behavioral and imaging data from the same time course aims to extract quantitative measures of neurodegeneration from habituation behavior. Additionally by comparing *pdr-1* to other PD models (*pink-1, bcat-1*) we can assess whether early habituation deficits generalize across PD-associated genes as those strains can be used as positive to controls.

Effects of Acute and Generational Starvation on Habituation in Adult *C. elegans*

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Harvard College | Quincy House | Neuroscience | 2029

Learning is a key topic in neuroscience, and *C. elegans* is commonly used as a model for learning through habituation. It is well established that L1 arrest, a developmental pause triggered by the lack of food after eggs hatch, alters long-term physiology. However, it remains unclear how these changes induced by early-life starvation impact learning behavior in adults. This study examines how acute and generational L1 arrest affect habituation rates in adult *C. elegans*. We compare three experimental N2 groups: a control of normally fed worms, a group subjected to a single 96-hour period of L1 arrest, and a group subjected to 3 generations of L1 arrest before a final generation was fed normally. All groups were age-synchronized via bleach synchronization to ensure testing at comparable developmental stages. Each tested day-1 adult hermaphrodite receives 30 anterior touches with an eyelash pick, spaced 10 seconds apart, following a 5-minute acclimation period. Experimenters were blind to the treatment conditions while scoring the worms' responses as a reversal, no reversal, or ambiguous. The reversal probability is calculated at each touch number for each group to analyze differences in habituation rates. Data collection is currently ongoing. Progress has been focused on establishing the experimental groups and initiating the habituation assays. Once complete, we will generate habituation curves for each group, followed by statistical analysis. Faster habituation could suggest an adaptive shift to ignore repetitive stimuli in favor of conserving energy, while slower habituation could suggest impaired learning due to disrupted neural development. A difference in habituation rates between the control and generationally starved group would support how epigenetic memory of stress persists across generations. Beyond *C. elegans*, these findings could offer insight into how early-life stressors impact cognitive development in humans, given the homology between the two species.

Investigating the Neuroprotective Effects of Turmeric on Learning and Memory in a *C. elegans* Model of Alzheimer's Disease

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Alzheimer disease is a devastating neurodegenerative disorder with no known cure. Current FDA-approved treatments only slow symptom progression, and their underlying mechanisms remain poorly understood. Natural compounds such as curcumin, the primary active component of turmeric, have demonstrated neuroprotective properties in preclinical models, but their effects on learning and memory are not fully characterized. We hypothesize that treatment with a water-soluble turmeric extract (standardized to 20% curcuminoids) will improve learning and memory in a *Caenorhabditis elegans* (*C. elegans*) model of Alzheimer's disease. Using the CL2355 strain, which expresses human amyloid-beta pan-neuronally at 25°C, we will measure habituation to repeated mechanosensory stimulation as a readout of learning and memory. Worms will be divided into four groups: untreated CL2355 (negative control), untreated N2 (positive control), CL2355 treated with turmeric (experimental), and N2 treated with turmeric (turmeric control). We have initiated a pilot experiment with healthy N2 worms to confirm that turmeric does not affect baseline habituation rates, establishing safety before testing in the Alzheimer model. We predict that turmeric-treated CL2355 worms will habituate faster than untreated CL2355 worms, approaching the habituation rate of healthy N2 controls. This research may identify a natural compound with therapeutic potential and clarify mechanisms underlying neuroprotection in Alzheimer disease.

Synthesis of Asparagine-based Cyclimide Warheads Coupled with a Valine Group for Targeted Protein Degradation

Student: Chris Garrabrant
Mentor(s): Cait Moffatt & Dilek Dogutan-Kiper
Faculty Advisor(s): Dan Kahne
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Targeted protein degradation (TPD) is increasingly important in many biomedical fields such as oncology, inflammatory diseases, and neurodegenerative disorders. TPD removes harmful proteins by bringing these proteins into proximity with E3 ubiquitin ligases that promote polyubiquitination and further disposal by the proteasome. Immunomodulatory drugs (IMiDs) result in the successful ubiquitination of specific substrates play an important role in this process. However, current challenges in the field are mechanism-based toxicities caused by off-target protein degradation. To fix this selectivity problem, this project focuses on a more selective CRBN-recruiting source: cyclimids. Cyclimids enable greater modularity to fine-tune the molecule to specific targets, while reducing off-target degradation. This project aims syntheses including: 1) preparation of tert-butyloxycarbonyl (Boc)-protected cyclic (**c**) Asparagine (**N**) (**Boc-cN**), 2) Deprotection of Boc-group with 4N HCl in dioxane affording cN•HCl, 3) coupling cN•HCl with three different Boc-protected amino acids Boc**Tryptophan**-OH (Boc-**W**-OH), Boc-**Valine**-OH (Boc-**V**-OH), and Boc-**Isoleucine**-OH (Boc-**I**-OH), 4) isolating **Boc-W-Boc-cN, Boc-V-cN, Boc-I-cN**, 5) Deprotection of **Boc-W-Boc-cN, BocV-cN, Boc-I-cN** with 4N HCl affording **WcNHCl, VcNHCl, and I-cNHCl,** 6) coupling **WcNHCl, VcNHCl, and IcNHCl** with biologically compatible acids. We have shown for the first time that steps 1-6 can be executed without column chromatography having significantly improved the isolated yields. Our next steps include coupling **W-cNHCl, V-cNHCl, and I-NHCl** with biologically compatible acids to complete the six-step warhead syntheses. Our purification techniques include liquid-liquid extraction, trituration, sonication, and crystallization. The improved methodology shortens the synthesis and purification time affording higher yields. Additionally, eliminating halogenated solvents highlights the environmentally friendly component of our revised procedure.

Investigating the Role of H19F in the Bacterial Deacetylase LpxC

Student: Chris Irankunda
Mentor(s): Cait Moffatt
Faculty Advisor(s): Sien Verschave & Dan Kahne
Harvard College | Lowell House | Chemical & Physical Biology | 2029

Lipopolysaccharide (LPS) is a large glycolipid found on the outer membrane of Gram-negative bacteria (such as *E.coli*). LPS maintains the permeability barrier of the outer membrane. Lipid A acts as an anchor for LPS, giving the cells protection from otherwise potent antibiotics. LpxC is an essential deacetylase and zinc-dependent metalloenzyme in Gram-negative bacteria that catalyzes the first committed step in lipid A synthesis. Therefore, the inhibition of LpxC would prevent LPS formation,and make Gram-negative cells more vulnerable to antibiotics. For our study, we are investigating the effects of mutating histidine-19 to phenylalanine in LpxC for *E. coli*. We introduced this H19F mutation using site-directed PCR mutagenesis, and our experimental results are still pending. However, we hypothesize that the H19F mutation removes a polar, hydrogen-bonding side chain and introduces a larger hydrophobic aromatic side chain that may alter the local packing interactions or the flexibility near the LpxC N-terminus region. These structural changes may influence the stability or function of LpxC. By evaluating the effects of the H19F mutation on outer membrane formation, we aim to better understand how this residue contributes to LpxC-substrate interactions. These findings may help guide the development of novel antibiotics targeting LpxC in gram-negative bacteria.

Examining the Effect of a T191V Mutation on the LpxC Enzyme in *Escherichia coli* Outer Membrane Synthesis

Student: Ifra Iyoob
Mentor(s): Cait Moffatt
Faculty Advisor(s): Sien Verschave & Dan Kahne
Harvard College | Eliot House | Human Developmental & Regenerative Biology & History of Science | 2029

Lipopolysaccharide (LPS) is an important component of the Gram-negative bacterial outer membrane, and is known to confer antibiotic resistance. While the outer membrane acts as a physical barrier, charged sugars within the LPS layer prevent hydrophobic antibiotics from entering the cell. Lipid A anchors LPS to the outer membrane. The irreversible deacetylation step of Lipid A biosynthesis is catalyzed by the essential and highly conserved enzyme LpxC. Given LpxC's potential as a successful antibiotic drug target, existing literature has proposed several mechanisms for *Escherichia coli* (*E. coli*) LpxC enzymatic activity. Notably, mass spectrometry analysis has identified a bound phosphate in the active site, which is stabilized by several key residues that collectively mimic the tetrahedral oxyanion of the reaction's transition state. Previous studies have mutated several of these residues. We introduced the novel threonine 191 (Thr191) to a valine mutation in *E. coli* LpxC to examine the effect on outer membrane formation. The O-H group on Thr-191's sidechain forms a hydrogen bond with the phosphate mimic, and therefore is thought to stabilize the transition state's oxyanion. In mutating to a valine with a hydrophobic sidechain, we remove the residue's ability to form this hydrogen bond. We predict that this alteration will significantly decrease Lipid A production, subsequently hindering LPS anchoring to the outer membrane. In understanding the impact of our T191V LpxC mutant, we aim to better understand interactions between the enzyme and its substrate, which will allow us to comprehensively inform future drug design techniques against Gram-negative bacterial infections.

Investigating LpxC Alterations in *E. coli*

Student: Joy Jiang
Mentor(s): Cait Moffatt
Faculty Advisor(s): Sien Verschave & Dan Kahne
Harvard College | Eliot House | Molecular & Cellular Biology | 2029

Gram-negative bacteria contain an outer membrane of which the outer leaflet is predominantly composed of lipopolysaccharides (LPS). The presence of LPS contributes to the impermeability of the outer membrane, making Gram-negative bacteria intrinsically antibiotic-resistant. LPS synthesis is dependent on the production of lipid A, which anchors LPS to the outer membrane. The essential LpxC enzyme catalyzes the first committed step in the biosynthesis pathway of lipid A, therefore making LpxC a promising target for developing antibiotics that can effectively target Gram-negative bacteria. Here, we investigate LpxC in *Escherichia coli* (*E. coli*) by using site-directed mutagenesis to substitute aspartic acid at position 246, a conserved residue across LpxC enzymes, with lysine. This mutation introduces a negative to positive charge swap in residue 246, which we believe will interfere with LpxC binding to lipid A. We will study how this mutation affects the ability of *E. coli* to form a sufficiently impermeable membrane by visualizing the outer membrane of our mutants using electron microscopy. The successful completion of our proposed project will ideally disrupt the binding of LpxC and lipid A, facilitating antibiotic entry due to the absence of LPS in the outer leaflet. Nonetheless, we hope that our studies will improve our understanding of residue 246's role in LPS synthesis, and determine whether it is an important residue for inhibitor design.

pdr-1 Knockdown in Habituation Impairment and Dopaminergic Neuron Degeneration in *Caenorhabditis elegans*

Student: Xin Lin
Mentor(s): Nicole Fisher & Kathleen Quast
Faculty Advisor(s): Dan Kahne
Harvard College | Lowell House | Human Developmental & Regenerative Biology | 2029

Parkinson disease (PD) is a progressive neurodegenerative disorder affecting more than 10 million people worldwide. Although research has characterized dopaminergic neuron degeneration in adult models of PD, less is known about how disruption of PD-associated genes affects behavior, learning patterns, and neuronal integrity during development. We are using *Caenorhabditis elegans* as a model organism to examine the effects of *pdr-1* knockdown, the ortholog of human *PRKN*, on habituation and dopaminergic neuron degeneration across developmental stages. RNA interference will be used to knock down *pdr-1* in the transgenic strain BY250 (*pPdat-1*::GFP), with empty vector-fed worms serving as controls. Habituation will be assessed using a mechanosensation assay, in which worms receive repeated gentle touch stimuli. Response amplitude, number of stimuli before habituation, and recovery after rest will be measured at the young adult and day 3 adult stages. GFP imaging will then be performed on the same populations to quantify intact dopaminergic neurons and identify signs of degeneration, such as missing neurons or broken dendrites. We hypothesize *pdr-1* knockdown worms will show slower habituation, more variable responses, and reduced response amplitude with degeneration and behavioral deficits becoming more pronounced at later developmental stages. Minimal degeneration is expected in early stages, with more substantial neuron loss by the L4 and adult stages. We hope to clarify how loss of *PRKN* function contributes to early manifestations of PD for earlier intervention work, and inform future work examining the implications of the human homolog.

Targeted Mutation in *LpxC* to Affect Binding and LPS Protein Production

Student: Matthew Mihalik
Mentor(s): Cait Moffatt
Faculty Advisor(s): Sien Verschave & Dan Kahne
Harvard College | Winthrop House | Integrative Biology | 2029

Lipopolysaccharide (LPS) is a glycolipid essential for Gram negative bacteria. Its synthesis is catalyzed by the enzyme LpxC, making LpxC a strong target for antibiotic development. In *Escherichia coli*, LpxC has a histidine at residue 19 (H19) that stabilizes the protein and recognizes its substrate at the mouth of the active site. H19 contributes to a hydrogen bond network which stabilizes the transition state of LpxC's reaction as both a donor and acceptor. We mutated H19 to phenylalanine (H19F) in *E. coli* LpxC and plan to express this His-tagged mutant(H19F) alongside wildtype LpxC to observe what effects that this mutation has on protein stability or function. Protein stability and function will be observed by overexpressing the LpxC gene and observing the amounts of protein as compared to the wild type under the same conditions. The shape of histidine and phenylalanine are very similar, allowing the identification of functions of the positive polar charge of H19 at the mouth of the active site without strong effects from shape discrepancies. If the mutation H19F changes the production LpxC enzyme and decreases the production of LPS, it would prove to be a step toward developing more effective antibacterial drugs.

Optimizing the Synthesis of Monopeptide-Based Cyclimid Warheads for Targeted Protein Degradation

Student: Natalie Mosakowski
Mentor(s): Dilek Dogutan Kiper
Faculty Advisor(s): Sien Verschave & Dan Kahne
Harvard College | Leverett House | Chemistry | 2029

Targeted protein degradation (TPD) is a therapeutic strategy that utilizes endogenous E3 ubiquitin ligase enzymes to tag harmful proteins with ubiquitin, a regulatory protein signaling for degradation by a proteasome. By degrading proteins instead of merely inhibiting them, TPD provides more effective treatment for undruggable cancers and neurodegenerative diseases. Mechanistically, a substrate receptor in the E3 ubiquitin ligase complex called cereblon (CRBN) binds to small molecules called immunomodulatory drugs (IMiDs), and the bound CRBN-IMiD complex targets and ubiquitinates specific proteins for degradation. However, IMiDs have proven to be highly hazardous as they unintentionally degrade essential proteins in addition to their targets, which can cause adverse effects including birth defects, blood disorders, and nerve damage. Our research is centered on increasing CRBN binding specificity by replacing the high-risk IMiD with a cyclimid, a structurally similar alternative that preserves the cyclic imide binding site for CRBN but removes the hazardous phthalimide region of the IMiD altogether. In order to achieve this, we are focused on optimizing the synthesis and purification process of monopeptide-based, amino acid-coupled cyclimid warheads with increased binding specificity. The six steps synthesis includes: 1) preparation of tert-butoxycarbonyl (**Boc**)-protected cyclic Asparagine (**cN**) (**Boc-cN**), 2) deprotection of Boc-group with 4N HCl in dioxane, affording **cN•HCl**. 3) coupling **cN•HCl** with three non-polar Boc-protected amino acids: Boc-Tryptophan-OH (Boc-**W**-OH). Boc-Valine-OH (Boc-**V**-OH), and Boc-Isoleucine-OH (Boc-**Ile**-OH), 4) isolating **Boc-W-Boc-cN**, **Boc-V-cN**, **Boc-Ile-cN** via diethyl ether trituration, 5) deprotection of **Boc-W-Boc-cN**, **Boc-V-cN**, **Boc-IIe-cN** with 4N HCl affording **WcNHCl**, **VcNHCl**, and **IIe-cNHCl**, 6) coupling **WcNHCl**, **VcNHCl**, and **IIe-cNHCl** with biologically compatible acids. We have shown that these steps can be executed without column chromatography or halogenated solvents. This improved procedure not only shortens the synthesis and purification time but also affords a two-fold increase in isolated yield, enabling a more efficient, environmentally-friendly preparation of cyclimid warheads for TPD.

Early-Life Starvation and Habituation Learning in *Caenorhabditis elegans*

Student: Antonio Plaza
Mentor(s): Nicole Fisher & Kathleen Quast
Faculty Advisor(s): Dan Kahne
Harvard College | Quincy House | Neuroscience | 2029

Habituation is one of the simplest forms of learning and serves as a powerful model for investigating neural plasticity. Although early-life nutritional stress is known to influence nervous system development, its effects on simple forms of learning remain incompletely understood. This project investigates whether starvation during the L1 larval stage alters habituation to repeated gentle touch in *Caenorhabditis elegans*. Because *C. elegans* possesses a well-characterized nervous system and reproducible behavioral responses, it provides an effective model for examining how developmental experiences shape neural function. Age-synchronized populations were generated through bleach synchronization. Experimental worms underwent L1 arrest by hatching on agar plates without food for 4 days before being transferred to bacterial food and allowed to develop to adulthood. Control worms developed continuously with access to food. Adult worms were then tested using a standardized gentle-touch assay consisting of 30 anterior mechanical stimuli delivered at ten-second intervals with an eyelash pick. Behavioral responses were scored to quantify habituation across repeated stimulation. Behavioral testing is currently underway. Thus far, this work has focused on establishing a standardized assay that minimizes experimental variability and allows reproducible measurement of habituation. Ongoing experiments will determine whether early-life starvation alters learning and behavior. If differences are observed, future studies can investigate whether repeated generations of nutritional stress produce cumulative effects on habituation, providing further insight into how developmental stress may influence neural plasticity.

Development of Cyclic Asparagine-Based Building Blocks for Targeted Protein Degradation

Student: Jennifer Santos
Mentor(s): Dilek Dogutan Kiper
Faculty Advisor(s): Sien Verschave & Dan Kahne
Harvard College | Dudley Community | Chemistry | 2029

Targeted protein degradation is an emerging therapeutic strategy that selectively removes disease-related proteins rather than simply inhibiting their function. Developing efficient and sustainable synthetic methods for cyclimid derivatives used in targeted protein degradation is essential for advancing future therapeutic research. This project focused on improving the synthesis and purification of novel cyclimid derivatives while increasing overall efficiency and reducing environmental impact. Novel cyclimid derivatives were synthesized through a six-step synthetic sequence consisting of: (1) synthesis of tert-butyloxycarbonyl (Boc)-protected cyclic Asparagine (Boc-cN), (2) Boc deprotection with 4 N HCl in dioxane to produce cNHCl, (3) peptide coupling with Boc-protected tryptophan, valine, and isoleucine, (4) isolation of the resulting intermediates, (5) a second Boc deprotection to generate the corresponding amino acid-cNHCl derivatives, and (6) coupling with biologically compatible acids. Reaction progress and product identity were monitored using thin-layer chromatography (TLC), proton nuclear magnetic resonance (^{1}H NMR) spectroscopy. Purification was accomplished using liquid-liquid extraction, trituration with sonication, and crystallization, allowing all six synthetic steps to be completed without column chromatography while eliminating the use of halogenated solvents such as dichloromethane.The revised synthetic workflow streamlines synthesis and purification, improves isolated yields, and reduces hazardous solvent use, providing a more efficient and environmentally sustainable approach for preparing cyclimid derivatives. These improvements establish a practical method for future targeted protein degradation research. Future work will focus on coupling the synthesized intermediates with biologically compatible acids to complete warhead synthesis while maintaining a column chromatography-free purification strategy

Sleep's Impact on *C. elegans* Learning Through Touch Habituation

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Harvard College | Pforzheimer House | Neuroscience | 2029

Learning is a fundamental process in neuroscience. Learning is modeled in *Caenorhabditis elegans* (*C. elegans*). Through mechanosensory habituation, in which repeated gentle touch leads to a progressive decrease in behavioral response. Circadian rhythm genes are known to modulate sleep -like states in *C. elegans*, yet its role in habituation remains unclear. To investigate this relationship, *flp-11* mutant worms, deficient in a neuropeptide associated with sleep regulation, are being used to test how disruptions in the circadian rhythm alter habituation. Baseline habituation curves have been established in wild-type worms. Preliminary progress indicates that habituation assays reliably lessen responses in wild-type worms. Upcoming experiments will compare these wild-type responses to *flp-11* mutants under stress□induced sleep conditions. Heat shock is expected to trigger sleep in wild□type worms, producing habituation patterns similar to unstressed controls. In contrast, *flp-11* mutants are predicted not to enter stress□induced sleep, and we hypothesize this will lead to reduced habituation rates. The ongoing analysis will determine whether circadian disruption changes the rate or extent of habituation, suggesting that learning may depend on internal physiological states rather than just sensory adaptation. If *flp-11* gene knockouts modify habituation, this would imply that circadian systems regulate learning. Future work can examine *flp-11* mutants across developmental stages and explore impacts on habituation and learning. These findings could broaden understanding of how circadian rhythms impact learning in *C. elegans.*

Behavioral Effects of Curcumin in a *C. elegans* Alzheimer's Model

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Faculty Advisor(s): Sien Verschave & Dan Kahne
Harvard College | Winthrop House | Neuroscience | 2029

Alzheimer's disease (AD) is a progressive neurodegenerative disorder that is characterized by the accumulation of amyloid-β (Aβ) peptides that are produced through the proteolytic cleavage of amyloid precursor protein. The accumulation of Aβ disrupts neuronal communication which in turn impairs learning and memory, contributing to neuronal degeneration. CL2355, a genetically engineered *Caenorhabditis elegans* strain, expresses human Aβ pan-neuronally that is induced by a temperature upshift from 15°C to 25°C, which results in behavioral deficits that help model essential aspects of AD pathology. This study will investigate if water-soluble turmeric extract, which contains 20% curcuminoids, can reduce learning deficits associated with Aβ in the CL2355 strain. The N2 wild-type strain will serve as a control and undergo the same temperature shift to account for possible effects of elevated temperature on behavior. A total of four experimental groups will be evaluated, consisting of untreated CL2355, turmeric-treated CL2355, untreated N2, and turmeric-treated N2. The L4 larvae will be transferred to treatment plates which either contain distilled water or turmeric solution, set at a final concentration of 20 μM in the plate, and will be incubated at 25°C for two days to induce Aβ expression in the CL2355 strain. Learning will be measured using a habituation assay, where individual worms will receive 30 repealed gentle anterior touch stimuli at 10-second interstimulus intervals. The number of responses before habitation will be compared among the treatment groups to determine whether turmeric treatment improves learning in the AD model without negatively affecting healthy worms. Through exploring the neuroprotective potential of turmeric-derived curcumin in a genetically modified model organism, this study aims to further investigate plant-derived compounds as potential therapeutic agents for mitigating cognitive impairment associated with Alzheimer's disease.

Investigating the Effect of FLP-11 Loss-of-Function on Habituation to Mechanosensory Stimuli in *Caenorhabditis elegans*

Student: Emily Zhou
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Faculty Advisor(s): Sien Verschave & Dan Kahne
Harvard College | Adams House | Neuroscience | 2029

In *C. elegans*, the neuropeptide FLP-11 is the primary sleep-inducing signal for Stress-Induced Sleep (SIS), a state of behavioral quiescence following heat stress or cellular damage. Despite its established role in homeostatic recovery, no known studies have examined how the absence of SIS affects learning and habituation. This study investigates how the loss of FLP-11 impairs non-associative learning after environmental stressors in *C. elegans*. N2 wild-type *C. elegans* were compared with *flp-11* mutants. 80 day-one adult worms of each strain underwent a 30-minute heat shock at 37°C and were subjected to one of four resting conditions (20 worms per condition): 2 minutes on ice, 1 hour at 25°C, 3 hours at 25°C, or 2 minutes on ice followed by 3 hours at 25°C. The worms then received 30 gentle touches with eyelash picks at 10-second intervals between the pharynx and mid-body to elicit a reversal response. The mean response rate and percent response over time were measured to assess habituation. Response rate and percent response were compared between groups to characterize differences in habituation dynamics.*flp-11* mutants, which fail to release FLP-11 and induce SIS quiescence following heat stress, were hypothesized to habituate more slowly than N2 worms. We predicted a decreased response rate over successive touches and a higher mean percent response across trials in *flp-11* mutants relative to N2 wild-type, indicating a less-adapted response to repeated mechanosensory stimulation. Since *C. elegans* is a well-established model for studying conserved mechanisms of learning and memory, our findings may help clarify how sleep disruption affects non-associative learning, with potential implications for understanding the relationship between sleep disruption and learning more broadly.

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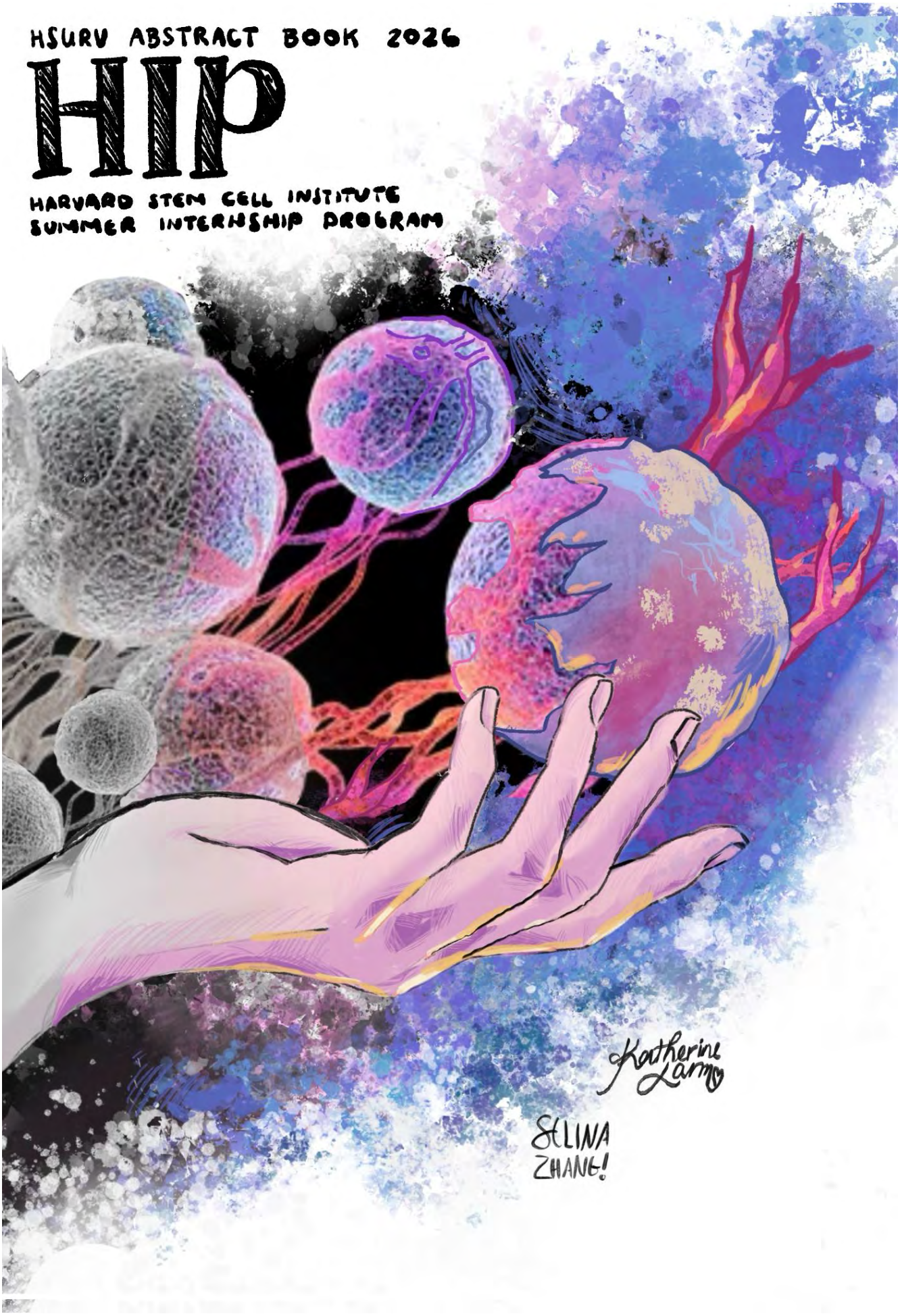

Molecular Targets Regulating BMP2 Signaling in Skeletal Stem and Progenitor Cells

Student: Ilhan Ali
Mentor(s):
Faculty Advisor(s): Vicki Rosen
Amherst College | Biochemistry & Biophysics | 2028

Bone formation, growth, maintenance, and repair depend on the differentiation of skeletal stem and progenitor cells (SSPCs) into osteoblasts. The periosteum supplies SSPCs during appositional growth, bone remodeling, and fracture healing, yet the molecular mechanisms that direct the differentiation toward osteogenic or chondrogenic lineages remain unknown. Bone morphogenetic protein 2 (BMP2) is a potent inducer of skeletal differentiation that activates intracellular signaling cascades, transcriptional changes, and chromatin remodeling to establish lineage specification, but the precise molecular mechanism and functional role of many early BMP2-responsive genes remains to be clarified. To identify regulators of early cellular response to BMP2, we analyzed RNA-sequencing transcriptomic data from multipotent periosteum-derived cells and embryonic mouse limb bud cells following short-term BMP2 treatment. We identified *Sox9*, a master regulator of chondrogenic differentiation with a pioneer transcription factor role, as an early BMP2-responsive gene. Using knockdown experiments, we are testing whether reduced *Sox9* expression shifts cell fate in BMP2-treated SSPCs away from chondrogenic and toward osteogenic differentiation across these developmentally distinct cell lines. Subsequent studies will investigate the epigenetic function of *Sox9* in SSPCs and its interactions with other transcriptional regulators. Because bone formation can occur through endochondral ossification, which proceeds through a cartilage template, these experiments may also clarify how Sox9 regulates the temporal progression of skeletal lineages. We also identified the netrin receptors *Unc5B* and *Neogenin* as early BMP2-responsive genes. These receptors have been proposed to regulate the protein tyrosine phosphatase SHP2, and we are investigating their role in BMP signaling in SSPCs. Together, these studies aim to expand our understanding of the molecular mechanisms that drive osteogenic vs. chondrogenic cellular programs in response to BMP signaling and to identify novel potential targets for enhancing bone maintenance and regeneration.

Scalable Generation of hiPSC-Derived Vascular Organoids via Fully Suspension-Based Differentiation

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University of Florida | Biomedical Engineering | 2028

Vascular organoids (VOs) are three-dimensional tissue constructs that replicate the structure and function of human blood vessels using endothelial cells (ECs) and perivascular mural cells (MCs). Recent approaches to generating VOs utilize engineered hiPSC lines carrying doxycycline (*Dox*)-inducible *ETV2* or *NKX3.1* cassettes, which efficiently differentiate hiPSCs into induced endothelial cells (iECs) and mural cells (iMCs), respectively. In this workflow, hiPSCs first undergo CHIR-mediated mesodermal induction in 2D. The resulting mesodermal progenitors are then transferred into 3D suspension culture with *Dox*, where inducible *ETV2* and *NKX3.1* expression drives iEC and iMC differentiation and the cells self-assemble into aggregates that form VOs. Given their significant potential as cellular therapies, there is a need to produce VOs at scale for large animal preclinical testing and human therapeutics. However, current techniques are constrained by the limited number of cells that can be cultured in 2D. Our project addresses this limitation by initiating mesodermal differentiation directly in 3D culture. We hypothesize that iPSCs will differentiate efficiently under these conditions and exhibit gene expression and cell-surface markers comparable to those of traditionally generated VOs. We will optimize parameters such as cell density and reagent concentration, confirming mesodermal differentiation via qPCR analysis of *TBXT* and *MIXL1* expression, genes upregulated in mesodermal cells, and by measuring iPSC aggregate diameter to verify that differentiation consistently occurs throughout the spheroid. To confirm subsequent differentiation into iECs and iMCs, we will perform qPCR for *PECAM1* and *CDH5*, which are upregulated in ECs, as well as *ACTA2* and *MYH11*, which are upregulated in MCs. Flow cytometry will be used to detect the cell-surface markers CD31 and CD144, confirming iEC presence within our VOs. Establishing an efficient method for generating VOs in 3D culture will enable scaled-up studies and advance treatment options in the growing field of cellular therapies.

Differentiation and Characterization of Human Induced Pluripotent Stem Cells into Corneal Endothelial Cells

Student: Aditi Desai
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Faculty Advisor(s): Sunil Chauhan
University of Maryland, College Park | Neurobiology & Physiology | 2029

Corneal endothelial dysfunction, which is one of the leading causes of corneal blindness, is largely irreversible due to limited regenerative capability of corneal endothelial cells (CEnCs) *in vivo*. Although corneal transplantation is the current standard treatment, the global shortage of donor tissue, risk of graft rejection, and use of long-term immunosuppression highlight the need for alternative therapies. Human induced pluripotent stem cells (iPSCs) represent a promising renewable source of CEnCs, due to their self-renewal and differentiation properties. This study aims to optimize the direct differentiation of human iPSCs into CEnCs. Prior to differentiation, the iPSC line was characterized by qRT-PCR, flow cytometry, and immunofluorescence to confirm stemness. Expression of the stemness markers *OCT4*, *NANOG*, and *SSEA4* was assessed. iPSC pluripotency was then verified by differentiation into the three germ layers of ectoderm, mesoderm, and endoderm for 3 days. Trilineage-specific markers *OTX2*, *SOX17*, and *Brachyury* were characterized by immunofluorescence and qRT-PCR, respectively. After confirming stemness and pluripotency, human iPSCs were then cultured under feeder-free conditions on Matrigel-coated plates in mTeSR1 medium. Differentiation was designed to mimic embryonic development by first generating neural crest cells (NCCs) through dual SMAD inhibition and Wnt activation, followed by directed differentiation into CEnCs using defined culture conditions. Our results showed that the iPSCs had elevated expression of *OCT4* and *NANOG*, and demonstrated the ability to differentiate into the three germ layers of the ectoderm, endoderm, and mesoderm by expressing *OTX2*, *SOX17*, and *Brachyury*, respectively. These findings demonstrated that the iPSC line maintained pluripotency and was suitable for differentiation. Currently, we are inducing further differentiation of iPSCs into CEnCs and evaluating their characteristics *in vitro*.

Optimization of a Serum-Free Human iPSC- Based Model of Endochondral Ossification

Student: Grace Edney
Mentor(s): Tim Hammerson
Faculty Advisor(s): April Craft
Florida Agricultural Mechanical University | Chemistry | 2028

Endochondral ossification is the process through which cartilage is replaced with bone during skeletal growth and development. It depends on the transition of chondrocytes to hypertrophic chondrocytes, followed by mineralization of the surrounding extracellular matrix (ECM). During hypertrophy, hypertrophic chondrocytes secrete COL10A1, an ECM protein that provides the template for matrix mineralization, as well as alkaline phosphatase, encoded by the gene *ALPL*, which initiates mineralization by converting organic phosphate into calcium minerals. These coordinated events have been modeled *in vitro* using human cells to study skeletal diseases. However, these models depend on fetal bovine serum (FBS), an ill-defined substance that may cover disease-specific processes. Previous work in our lab has developed a FBS independent human endochondral ossification model. However, mineralization was restricted to the tissue's surface. The objective of my research is to enhance mineralization to deeper layers of the tissue. We hypothesized that supplementing human induced pluripotent stem cell (hiPSC)-derived cartilage *in vitro* with thyroxine (T4) or purmorphamine will promote hypertrophy, thus preparing the ECM for efficient mineralization. Additionally, we hypothesized that activating the WNT pathway using the small molecule CHIR will further stimulate matrix mineralization. To test these hypotheses, iPSCs were differentiated into cartilage progenitors and supplemented with BMP4 to produce hypertrophic cartilage. The effects of T4 and purmorphamine on hypertrophic differentiation were assessed by qPCR for *COL10A1* and *ALPL* expression as well as histological analysis of chondrocyte morphology. Matrix mineralization in response to CHIR treatment was assessed by histology and micro-computed tomography (micro-CT). Overall, this study seeks to enhance hypertrophic differentiation to promote a more thorough hypertrophic differentiation to enhance the extra cellular matrix for mineralization, optimizing a serum-free human model for disease and skeletal development.

Human Airway Microfold Cell Differentiation and Function

Student: John Vo Huynh
Mentor(s): Manalee Vishnu Surve
Faculty Advisor(s): Jayaraj Rajagopal
Princeton University | Molecular & Cellular Biology | 2029

The airway epithelium is a frontline barrier that coordinates immune surveillance and protects the host from inhaled environmental particles and respiratory pathogens. Recently, microfold (M) cells were identified as specialized antigen-sampling epithelial cells in the murine airway that promote mucosal immune responses during respiratory infection. Unlike intestinal M cells, which are abundant at steady state, airway M cells are rare and are induced during inflammation and viral infection. Although RANKL–RANK signaling is known to regulate airway M cell differentiation in mice, it remains unknown whether human airway epithelial cells can differentiate into functional M cells and whether these developmental pathways are conserved. This project aimed to establish a robust *in vitro* model of human airway M cell differentiation and evaluate their antigen uptake capacity. We hypothesized that RANKL signaling is sufficient to induce functional M cell differentiation in primary human airway epithelial cultures. Primary human basal stem cells isolated from donor lungs were differentiated at an air–liquid interface (ALI) and stimulated with recombinant RANKL. Functional antigen uptake was assessed using fluorescent nanoparticles (20, 100, and 500 nm). Our findings demonstrate, for the first time, that RANKL induces the differentiation of functional human airway M cells in primary ALI cultures. These cells exhibited efficient uptake of 20 nm nanoparticles across all the donor lung tissue derived cultures, supporting a conserved role for M cells in antigen sampling. This human ALI platform provides a valuable model for investigating the molecular regulation and immune functions of airway M cells. Future studies will leverage this system to identify inflammatory signals that promote M cell differentiation, define mechanisms of antigen transcytosis, and examine interactions with clinically relevant respiratory pathogens. These studies may ultimately guide the development of novel mucosal vaccines and targeted therapies for inflammatory and infectious lung diseases.

Identification of Novel Bone-Derived Exerkines Mediating Mechanical Regulation of Bone and Systemic Metabolism

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Faculty Advisor(s): Yingzi Yang
University of California, Los Angeles | Biochemistry | 2028

Exercise induces systemic anti-aging effects, including reduced inflammation, cognitive enhancement, and the preservation of muscle mass. These physiological benefits are largely mediated by signaling molecules secreted in response to physical activity, termed ”exerkines”. Bone, acting as a mechanosensory organ heavily stimulated during exercise, upregulates the expression of numerous exerkines. Given the extensiveness of the skeletal system and its established endocrine functions, these bone-derived molecules are important candidates for initiating systemic responses downstream of exercise-induced mechanical loading. Preliminary data comparing bones from exercised and sedentary mice identified a set of differentially expressed genes (DEGs) encoding secreted proteins. Intersecting this dataset with DEGs from mice with intermittently activated *YAP* in bone yielded eight candidate genes implicated as downstream targets of Piezo1 mechanostransduction. A pilot study co-culturing candidate gene-expressing Huh-7 cells with Ocy454 osteocytes in 3D collagen media demonstrated that *PROK2* and *FST* promote osteocyte dendrite formation, critical cellular processes mediating bone mechanotransduction. To further elucidate the systemic effects of these identified factors on fat metabolism, ongoing experiments will treat 3T3L1 adipocytes with conditioned media from the transfected Huh-7 cells to evaluate changes in adipogenic differentiation. Ultimately, characterizing these bone-derived exerkines would unveil novel therapeutic targets to mimic the systemic benefit of exercise for mobility-impaired patients.

Unraveling Effects of *TET2* Mutations on Differentiation in CD34+ Hematopoietic Stem and Progenitor Cells

Student: Vivian Liu
Mentor(s): Deborah Wells
Faculty Advisor(s): Annalisa Di Ruscio
University of Massachusetts, Amherst | Biology | 2029

Myelodysplastic Syndromes (MDS) are clonal disorders of hematopoietic stem cells (HSCs) characterized by ineffective hematopoiesis. Patients present with fatigue, shortness of breath, and infection. Each year, an estimated 10,000 to 15,000 new cases are diagnosed in the United States, and in 30% of cases, the disease progresses to acute myeloid leukemia, an aggressive blood cancer. Stepwise acquisition of somatic mutations drives MDS, resulting in aberrant DNA methylation and impaired hematopoietic differentiation. Ten-Eleven-Translocation 2 (*TET2*), which initiates active DNA demethylation, is mutated in 22-35% of patients with MDS. Patients with *TET2*-mutant MDS often receive hypomethylating agents (HMAs), such as azacitidine and decitabine. These drugs attempt to reverse hypermethylation by inhibiting DNA methyltransferases (DNMTs), the enzymes that catalyze DNA methylation, but they do so indiscriminately and carry high toxicity. While patients harboring *TET2* mutations respond better to HMAs, most relapse due to resistance, posing challenges in clinical management. Our laboratory has developed a targeted RNA-based approach to selectively inhibit DNMT1 (aptaDiR_Ce-49 sh_v1), which could potentially counterbalance *TET2* mutation-driven epigenetic rewiring. Our preliminary data demonstrate that aptaDiR_Ce-49 sh_v1 induces robust myeloid differentiation in an established *TET2*-deficient murine model. We hypothesize that the ineffective hematopoiesis caused by *TET2* loss can be overcome by selective inhibition of DNMT1. In this project, we plan to abrogate *TET2* function in primary human CD34+ cells using CRISPR-Cas9 ribonucleoprotein (RNP) delivery, utilizing non-targeting RNPs as experimental controls. Editing efficiency will be confirmed by Sanger sequencing, and loss-of-function will be confirmed by *TET2* immunoblot. Regular flow cytometry analyses will be used to assess cell population composition during differentiation, and cytospin will be performed to examine morphological differences. This model will define how *TET2* loss-of-function mutations affect differentiation and test whether selective DNMT1 inhibition offers a targeted alternative to HMAs.

Development of an AAV-CRISPR Screen to Identify Novel Regulators of Skeletal Muscle Stem Cell Differentiation

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Mentor(s): Parker Lin
Faculty Advisor(s): Amy Wagers
Duke University | Biomedical Engineering | 2029

Skeletal muscle stem cells (MuSCs) decline in number and regenerative capacity with age, yet genetic regulators governing the proliferation-to-differentiation switch that underlies exhaustion remain incompletely characterized. This study develops and validates an adeno-associated virus (AAV)-mediated CRISPR screen system to identify novel regulators of MuSC differentiation. Two modifications were made to a previous AAV vector system. First, we adopted a modified Sleeping Beauty transposition system that confers durable editing in dividing muscle cells, in which AAV episomes would otherwise be diluted across cell divisions. Via a cut-and-paste mechanism, the transposase integrates a cassette comprising two gRNAs and an mScarlet fluorescent reporter, flanked by Inverted Repeat/Direct Repeat elements, into genomic DNA. Second, we introduced paired lox recombination sites that make the cassette activatable by *Cre* recombinase, rendering PCR readout specific to *Cre*-positive cells and allowing the system to be applied to a mouse line expressing *Cre* in MuSCs. PCR confirmed *Cre*-dependent reporter switching, and next-generation sequencing revealed comparable indel rates between standard and *Cre*-dependent constructs (11.58% vs. 11.52%), indicating the modification did not alter editing rates. Prior single-cell RNA sequencing and trajectory analysis identified 50 candidate genes enriched in differentiating cells; five (*Dgkz*, *Cdkn1c*, *Ccr5*, *Mymk*, *Myog*) were selected to validate guide designs *in vitro* via plasmid transfection in *Cas9*-expressing 3T3 cells. AAV vector genome copy number was quantified by droplet digital PCR, and on-target editing was assessed by amplicon sequencing across guide-targeted loci. Building on this validated platform enabling durable, traceable perturbation in muscle-lineage cells without sacrificing editing performance, additional vectors are now being generated by Gibson cloning and packaged in HEK293 cells for *in vivo* delivery of guide RNAs via intraperitoneal injection in neonatal mice. This will enable a pooled screen for developmental regulators of satellite cell differentiation and, in future work, genes whose expression declines with age.

Construction of *Cre*-Restricted AAV Vectors for Cell-Type-Specific Neuronal cAMP Imaging and Optogenetic Manipulation

Student: Jada Villaroel
Mentor(s): Peter Hogg
Faculty Advisor(s): Adam Cohen
Syracuse University | Neuroscience | 2028

Cyclic adenosine monophosphate (cAMP) is a vital intracellular second messenger that transduces extracellular signals, received by cell surface receptors, into intracellular responses that regulate internal states and neuronal function. Understanding and monitoring the dynamics of cAMP within defined neuronal populations allows for insight into how intracellular signaling influences neural circuit function. Our research aims to develop molecular tools by constructing two *Cre*-restricted adeno-associated virus (AAV) transfer plasmids, which will enable cell-type-specific monitoring and optogenetic control of neuronal cAMP signaling. The first construct, pAAV-hSyn-DIO-G-Flamp1, will express the genetically encoded fluorescent cAMP sensor G-Flamp1, allowing real-time visualization of intracellular cAMP levels through increased fluorescence as cAMP levels rise. The second construct, pAAV-hSyn-DIO-mVenus-PACmn, will express the membrane-anchored photoactivatable adenylyl cyclase mVenus-PACmn, enabling blue light-induced cAMP production with low dark activity. Both transgenes will be inserted into a double-floxed inverted orientation (DIO/FLEX), in which pairs of incompatible lox sites, *loxP* and *lox2272*, will undergo recombination to invert the transgene into the sense orientation, restricting expression to *Cre*-expressing neurons. The engineered constructs will be generated using Gibson assembly by combining PCR-amplified backbone fragments with their respective transgene inserts through overlapping homologous sequences. Following Gibson assembly, recombinant plasmids will be transformed into *Escherichia coli*, screened by colony PCR to identify correctly assembled clones, purified by plasmid miniprep, and validated through Sanger sequencing for downstream virus production. Successful completion of this project will produce two sequence-verified AAV transfer plasmids, suitable for downstream viral packaging and a multitude of neuroscience applications. In addition to generating valuable molecular tools for investigating neuronal cAMP signaling, this project will provide a framework for developing additional genetically encoded research tools to investigate intracellular signaling and neural circuit function.

Identifying the Self-Antigen Target of a VAT Treg TCR

Student: Andy Yu
Mentor(s): David Owen
Faculty Advisor(s): Diane Mathis
Pennsylvania State University | Pre-medical Medicine (BS/MD) | 2029

Regulatory T cells (Tregs) are a specialized subset of CD4+ T cells that regulate immune responses in the body. These cells exist in both lymphoid and non-lymphoid tissues; one such non-lymphoid Treg being the visceral adipose tissue (VAT) Treg. Beyond general Treg function, VAT Tregs also manage metabolic homeostasis in the VAT, preventing physiological issues like diabetes and obesity. Despite their importance, VAT Tregs remain poorly understood due to their rarity and complexity. Previously, a T-Cell Receptor (TCR) enriched in VAT Tregs was used to generate a transgenic mouse; its Tregs accumulated in the VAT, suggesting the TCR recognizes a VAT-specific antigen. While screening identified synthetic antigens capable of activating this TCR, the endogenous self-antigen is unknown. Notably, some mice expressing this VAT Treg TCR developed vitiligo, an autoimmune depigmentation disorder. This suggests the TCR may recognize a skin-associated antigen related to its unidentified VAT target. To investigate this, we will extract lymphocytes from trunk skin of vitiligo-affected and vitiligo-unaffected VAT TCR transgenic mice. If the TCR is enriched in the skin and expanded during vitiligo, it would indicate that this TCR is likely responding to melanocyte antigens. Building on this, we will develop a pipeline to identify candidate antigens that the VAT Treg TCR might be responding to. Candidate peptides will be filtered for having preferred amino acids (tyrosine, phenylalanine, etc…) at MHC anchor positions, for being expressed in the VAT and skin, and for — given that synthetic antigens were previously identified — having similar TCR-facing residues as them. Due to time constraints, the proposed antigens will not be manufactured, but future studies can test the stimulation of these candidate peptides. Identifying the antigen target of this VAT Treg TCR would be a significant advance in understanding VAT Tregs. More broadly, this finding could help illuminate relevant antigenic target(s) in autoimmunity and obesity.

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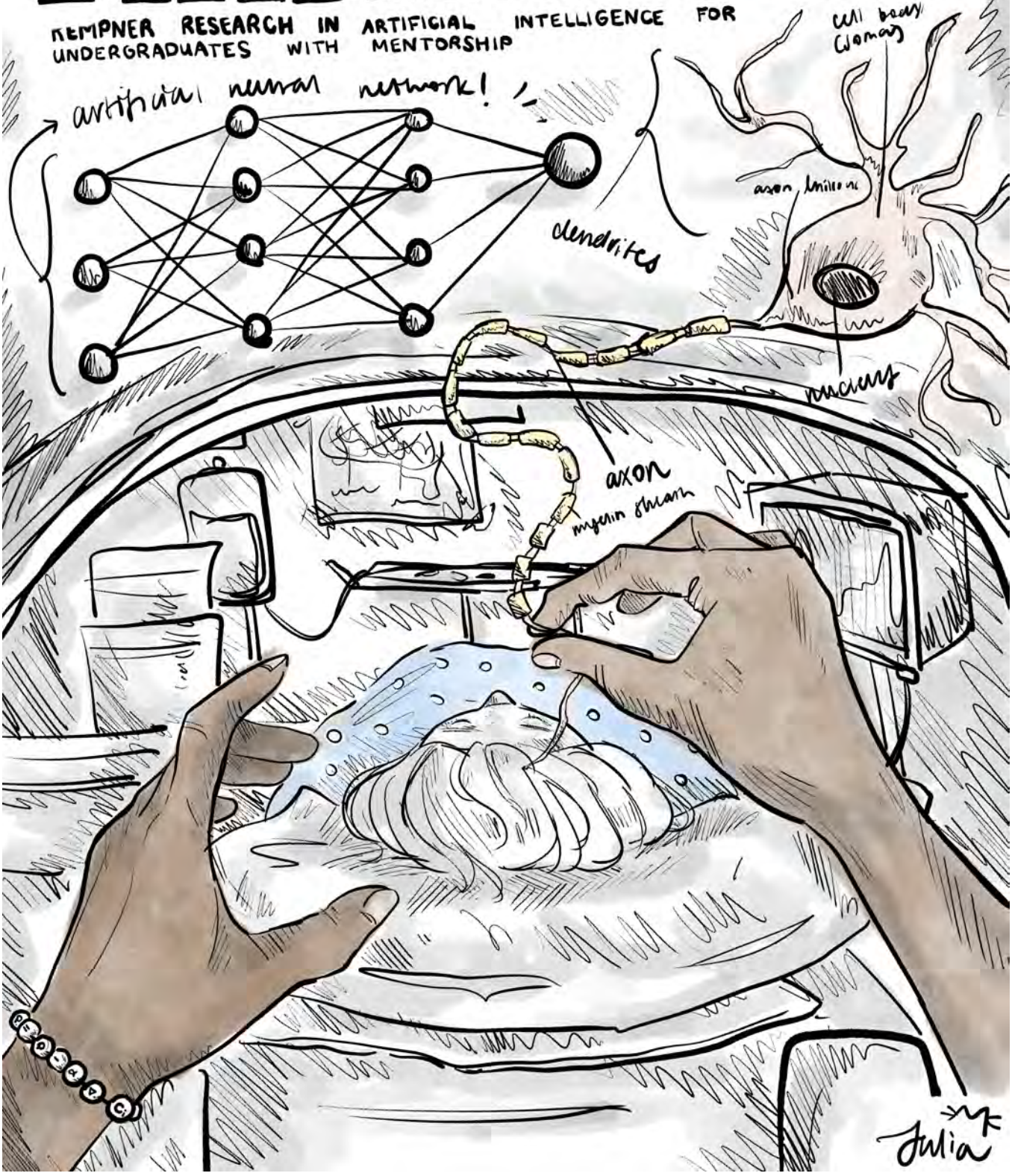
KRANIUM

KEMPNER RESEARCH IN ARTIFICIAL INTELLIGENCE FOR UNDERGRADUATES WITH MENTORSHIP



Classification Capacity of Correlated Concept Manifolds

Student: Joel Bentley
Mentor(s): Lorenzo Tiberi
Faculty Advisor(s): Haim Sompolinsky
Harvard University | Cabot House | Mathematics & Philosophy | 2027

How artificial neural networks arrange and classify concepts in their representation space remains a black box to the theoretical deep learning community. Recent work on neural representational geometry has shed much light on the issue, showing that concepts can be mathematically described as high-dimensional manifolds in the representation space of a neural network. The dynamics of how these manifolds relate to each other, however, remains unexplored. In this project, we propose a new theoretical model, derived from the classification capacity of a perceptron, for how concept manifolds arrange themselves as correlated semantic trees with observable inheritance parameters and branching patterns. We verify our theoretical model through two empirical modalities: a vision based deep convolutional neural network and a language based transformer. We use the hierarchically arranged schema tieredImageNet on ImageNet-1k images which are fed to a ResNet-50 classifier, and we use captions for those same images on a Meta-Llama-3.1-8B transformer. By verifying that the layer-wise capacity improvement in both modalities matches the theoretical generative model, we show that the classification capacity of representations in a network can be measured as hierarchically arranged, correlated manifolds. Our results provide a mathematically tractable model for future research on how different neural network architectures hierarchically arrange concepts through different modalities.

The Einstein Project

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Intuitive physics forms a major part of commonsensical reasoning. A current line of research suggests that a person's physical intuition is based in part on running an approximate mental simulation wherein the mind reconstructs a scene internally and simulates its future states step-by-step. Understanding the hindrances of mental simulations provides unique insight on the limits of cognition. Any virtual scene consists of two components: the content, which includes objects and their movement, and the reference frame, such as the playback speed or field of vision. In this study, we ask whether the temporal reference frame of these simulations can be represented and manipulated independently from their content. Four experiments were run, including animated and realistic scenes of a ball rolling off a cliff and a pendulum swinging. Participants saw stimuli at 0.5x, 0.75x, 1x, 1.5x, and 2x speed pause and were asked to imagine the object's continued motion and indicate when and where the ball will fall, or the pendulum will reach the highest point in its arc. Since a ball's falling time and pendulum's period are not affected by velocity, the time can be recorded to represent simulated playback speed independently of the click position, which indicates the participant's simulated velocity (i.e. content). Pilot data for experiments with ball stimuli show that participants appear to be able to slightly, though often inaccurately, adjust their temporal reference frame and the content of their simulation together. Preliminary results from the pendulum experiments also indicate reference-frame manipulation, but more refined data are required to understand its relationship to the content. The limitations of reference-frame manipulation have broader implications into the flexibility of imagination and provide helpful context as to how humans make informed, intelligent observations about the world, and where that reasoning might fail.

Dynamic Timestep Prediction for Text-Guided Image Editing

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Despite recent advances in text-guided image editing, AI image editing models remain unable to consistently make edits at the correct scale; they often over-edit when asked to make small changes and under-edit when prompted to make larger ones. In diffusion- and flow-based editing, the edit size is primarily controlled by the editing timestep, which determines how much information about the original image is retained before regenerating the image with the target prompt. Because different edits may require different levels of source-image preservation, this project tested whether different edit types have distinct optimal timesteps. Experiments used a modified form of ChordEdit, a text-guided image editing method, to test timestep values across edits. The results showed that optimal timesteps varied by edit, motivating the need for a dynamic timestep predictor. The project evaluated two approaches to this prediction task on the 700-image PIE-Bench dataset: vision-language models using in-context learning and a task-specific trained classifier. Preliminary results suggest that vision-language models struggle to accurately predict the optimal timestep, possibly because timestep values do not fully align with human perception of semantic edit size. The trained classifier appears more promising, although it requires further refinement. If successful, dynamic timestep prediction could make image editing systems more reliable by reducing both over-editing and under-editing.

Multi-Armed Bandit Using Empirical Bayes

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Clinical trials often involve low numbers of participants and are conducted in high-uncertainty environments. Mobile health interventions, such as apps that notify patients to exercise or take medication, must decide in real time what action to take for each person. When data are sparse, identifying the optimal treatment becomes difficult. Classical reinforcement learning treats participants independently, whereas complete pooling combines all participants' data into a single shared model and ignores heterogeneity. Although pooling is often favored for its bias-variance trade-off, it assumes that participants are homogeneous up to baseline features and context. Empirical Bayes (EB) is a partial-pooling strategy that assumes participants' parameters are drawn from a shared hyperdistribution: the learning algorithm is run independently on each participant, while action selection borrows information across the population. This may permit individualized learning while stabilizing action selection. This project evaluates EB against unpooled and pooled Thompson sampling in a contextual bandit environment with two participant-specific variables that influence reward: a time-varying state, such as whether a person currently feels well, and a time-invariant context, such as a fixed demographic trait. Because the context does not vary within a participant, its effect can only be learned by aggregating participants' data, raising an identifiability challenge that the weights associated with the state, learned within each participant, does not share. We conjecture that unpooled Thompson sampling performs best at large horizons, pooled at small horizons, and EB at intermediate horizons, with these thresholds shifting as the treatment effect, the interaction effects, and the between-participant heterogeneity decrease relative to the noise. Our simulations across differing settings produce regret curves that support this ordering. By clarifying when partial pooling is worthwhile, this work offers practical guidance for choosing between pooling strategies in mobile health and other online reinforcement learning algorithms that must optimize in data-scarce settings.

Artificial Intelligence for Developing an Educational Platform for Dermatological Data

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Artificial Intelligence's pattern recognition abilities have been increasingly applied in medical fields necessitating strong visual analysis. In dermatology, however, diverse skin tones and visual presentations of conditions can make it difficult to learn accurate identification. Using the DermLIP Contrastive Language-Image Pretraining (CLIP) Model, AI Agents, and medical literature, this project builds an interactive platform of tools to educate medical students and professionals on dermatology. To test the accuracy of the tools' information retrieval, I utilized the Lab of Medical Imaging and Computation's Proof Layer. Furthermore, to calculate DermLIP's accuracy at identifying conditions on darker skin, I used multivariable logistic regression on the ground truth diagnosis and the Fitzpatrick skin type group of an image. The preliminary results (Likelihood Ratio of $\chi^2 = 116.13$, $p < 0.001$ (Diagnosis) vs. $\chi^2 = 6.6$ $p = 0.036$ (Fitzpatrick skin type)) show that the type of condition, rather than the patient's skin tone, is a greater predictor of the model's accuracy, and differences in performance across diagnoses were largely consistent across Fitzpatrick skin-type groups. This suggests that increased accuracy for DermLIP on predictions of dermatological conditions may warrant further training on specific conditions with wide-ranging appearances, instead of on a wide range of conditions on specific skin tones.

Learning Conditional Energy Landscapes for Protein Pocket-Conditioned Ligand Generation

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The discovery of small molecules that selectively bind protein targets remains a central challenge in structure-based drug discovery. Recent advances in deep generative models have enabled the design of candidate ligands conditioned on protein binding pockets, providing an alternative to traditional virtual screening and fragment-based design. However, many conditional generative approaches emphasize direct sample generation, while offering limited flexibility for inference-time refinement, steering, or integration of additional molecular constraints. Energy-based generative models provide a complementary framework because they learn an explicit energy landscape that can support conditional refinement and composable constraints during generation. In this project, we study whether a conditional energy landscape over ligand topology can represent pocket-dependent molecular design preferences for protein-ligand binding. Building on ideas from Graph Energy Matching, we investigate protein pocket-conditioned ligand generation over two-dimensional molecular graphs, where ligand topology serves as an initial proposal space for candidate molecules. This topology-focused formulation is intended to capture pocket-dependent molecular connectivity and functional group organization before downstream three-dimensional refinement through docking or related structure-based evaluation methods. The model uses graph transformer-based representations of protein pockets and ligands to learn relationships between binding pocket features and ligand molecular topology. We will train the model on experimentally resolved protein-ligand complexes and evaluate generated molecules using standard molecular generation metrics, including validity, uniqueness, diversity, and drug-likeness, together with docking-based assessments of binding compatibility. This work explores conditional energy-based graph generation as a flexible framework for structure-guided molecular design and investigates its potential to support the identification of candidate molecules for downstream drug discovery.

Complementarity-Aware Retrieval for Linking Distant Evidence in Multi-Hop Question Answering

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Retrieval-augmented language models answer a question by first retrieving the passages most relevant to it. This succeeds when the answer lies in a single passage, but many questions can only be answered by combining facts stated in separate passages. Standard retrievers score each passage independently, so they favor passages that look relevant on their own and overlook those that become relevant only in combination, leaving the model to answer from incomplete evidence. We introduce a complementarity-aware retriever that scores passages jointly, by how well each one completes a partial set of evidence rather than by its relevance alone, together with a diagnostic that separates failures to link evidence from failures to find it. On two multi-hop benchmarks in which every supporting passage is guaranteed to be present, HotpotQA and MuSiQue, we train the retriever using supervision already contained in the datasets, requiring no additional annotation. On MuSiQue, the harder benchmark, standard retrieval assembled the full set of supporting passages for only 8% of two-fact questions and almost none of the four-fact questions, though that evidence was always available; our method raised these to 69% and 51%, with comparable gains on HotpotQA. A controlled comparison confirmed that the improvement came from scoring passages jointly rather than from model capacity, and it widened with each additional fact. The method also surpassed strong dense and reranking retrievers, and supplying its evidence to a language model raised exact-match answer accuracy from 11% to 35%. These results show that the principal barrier to multi-hop question answering is not locating evidence but recognizing which passages belong together, a capability that can be learned at negligible cost. Future work will scale the approach to open retrieval over full corpora and to longer, more specialized documents such as scientific and clinical literature.

Scaling Laws of Code-Switching in LLMs

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Multilingual large language models (MLLMs) stand out for their ability to understand and generate text in many human languages, yet little is known about how they acquire the ability to codeswitch, defined as alternating between different languages within one context. Our work characterizes the ability of MLLMs to codeswitch as a function of their size and the composition of the data they are trained on. In particular, we pretrain an array of GPT-2 models while varying size, German-English data asymmetry in pretraining, and codeswitched text seen. We score these models with both a new perplexity-based metric at switch-points ("switch-span-BPB") and on a benchmark that asks whether a model prefers a human-acceptable codeswitched sentence to a minimally altered version of said sentence (Sterner et al. 2025). Using our scored models, we first aim to establish a classical scaling law explaining how codeswitching ability scales with model size. We then aim to fit a scaling law explaining whether the model's ability to codeswitch is an emergent property of bilingual language exposure, or alternatively to what degree codeswitched data in training is necessary.

Tracing the Emergence of Linguistic Structure in Audio Language Models

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One of the fundamental questions in neuroscience is how learning reshapes the brain's internal representational spaces. In the domain of language, how do our brains transform a continuous stream of sound into structured representations of phonemes, words, and syntax? This question is challenging to study in humans as we cannot directly access neural representation during language learning. However, artificial neural network models have emerged as a promising candidate system to study these processes. In standard audio models, training requires large amounts of transcribed training data. In the current work, we study language learning in a new model system: AuriStream. AuriStream is a biologically plausible audio language model built upon the foundations of human auditory processing. The model predicts the upcoming sounds in the audio input in a fully self-supervised setting, meaning it does not rely on labelled data input. We aim to answer the question: When do representations of phonemes, words, and syntactic structure become detectable during training? Preliminary results indicate that clustering-based methods can recover broad phoneme categories in AuriStream throughout training. Phoneme accuracy starts at ~30% for the untrained model and reaches 83% at the fully trained model. The intermediate-late layers of the model also show correlation with linguistic properties such as word frequency and concreteness, but not with syllable duration or arousal. These findings suggest that the representational space in the model becomes increasingly organized by semantic information rather than low-level acoustic information. These results are further supported by the model's performance on lexical and syntactic tasks, reaching 65% accuracy in a challenging lexical discrimination task for a fully-trained model compared to only 50.2% for the untrained model. Human-like models such as AuriStream can serve to study how structured representations may emerge from raw auditory signals, offering a useful window into aspects of human language learning.

JEPA-Based World Models for Autonomous Drone Navigation

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Autonomous systems such as unmanned aerial vehicles (UAVs) must make long sequences of actions in which small prediction errors can compound and destabilize control. This project studies whether world models built on the joint-embedding predictive architecture (JEPA) can make this long-horizon control more reliable and efficient. Reinforcement learning (RL), the standard approach, maps observations directly to actions, so mistakes accumulate across a decision sequence. World models instead learn an internal simulator that predicts how the environment will evolve, letting an agent plan by imagining future states before acting, just like humans do. Most world models predict in raw pixel space, which is computationally costly, while a JEPA-style model instead predicts in a compact latent space, keeping only relevant features and discarding noise. Recent work shows that world models improve when trained to predict the next embedding rather than reconstruct observations, a strategy we plan to adapt for UAV navigation. We have implemented a JEPA-style world model and are evaluating it on the Atari 100k benchmark, a data-limited standard suite, with traditional RL agents and non-JEPA world models as baselines, before adapting the model to UAV navigation. Atari 100K is a benchmark with 26 famous Atari games, such as pong and breakout, and in the benchmark each agent gets only 100,000 episodes to master the game, which is far less than standard benchmarks. To get statistically accurate results, we run each agent on Atari100k with 4 random seeds and average the total result, all done on a single Nvidia H100 GPU. We hypothesize that JEPA-based prediction accumulates less error over long horizons and generalizes better than pixel-based world models, offering a more reliable and efficient foundation for autonomous control.

Unsupervised Inference of Behavioral Latents and States through Video Analysis

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Understanding how neural activity gives rise to motor behavior requires relating neural recordings to animal behavior. Video captures rich, high-dimensional behavioral data, but how best to extract behavior from video and relate it to neural activity remains an open question. Supervised keypoint tracking (e.g., DeepLabCut) can localize body parts but requires manual labeling and often overlooks behaviorally relevant features that aren't anticipated. Unsupervised approaches such as convolutional variational autoencoders (VAEs) avoid manual labeling by encoding video into a latent space, but standard VAEs assume temporal independence between frames, yielding latent trajectories that are neither smooth nor readily segmented into interpretable behavioral states. This project develops a temporally-aware VAE that learns smooth behavioral latent representations from raw video while integrating complementary signals: keypoint trajectories from DeepLabCut and rhythmic orofacial movement latents from FaceRhythm. It then develops and applies autoregressive hidden Markov modeling (AR-HMM) over the learned latents to segment continuous movement into distinct behavioral states, or "syllables," that capture the building blocks of the animal's movement. Its temporal awareness recovers the states and the statistical structure of how they relate and transition over time. Because the appropriate granularity is not known in advance, the project characterizes the recovered states mathematically, assessing whether behavior is over- or under-split and quantifying inter-state similarity to ensure the states are neither redundant nor collapsed before relating them to co-recorded neural activity. These methods yield a temporally-aware VAE and AR-HMM pipeline whose syllables are interpretable and distinct enough to support further study. By producing fine-grained, temporally-structured descriptions of behavior grounded in both orofacial rhythms and full-body movement, this method enables tighter correlation between neural activity and action. This analysis seeks to advance understanding of how the brain generates movement and to help isolate the neural disruptions underlying motor disorders such as stroke.

HSURV ABSTRACT BOOK 2026

LAIDLAW

LAIDLAW SCHOLARS LEADERSHIP & RESEARCH PROGRAM

CX for Cities

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In 2021, President Biden declared in Executive Order 14058 Transforming Federal Customer Experience and Service Delivery To Rebuild Trust in Government that the number of paperwork burdens imposed by federal agencies on the American public was in excess of 9 billion hours. This executive order, and the others before it, highlighted a challenge that the public sector consistently grapples with: service delivery streams remain outdated, and often blatantly nonexistent, in comparison with the private sector. As the highest level of government, the federal government has nonetheless been at the forefront of incorporating the customer experience (CX) framework, the sum of the public's interactions with any government service, into programs and work streams across its agencies. However, there's little to no work being done to translate this framework into services at the city level. This project, then, draws upon the experiences of federal CX experts to develop a comprehensive guide to merging CX work and city service delivery such that care for the American public remains at the center of every program. By building a curriculum that would guide city officials through implementing service delivery, conducting literature review that digs deeper into the breadth of EO 14058, and using design sprints for cities brainstorm areas of improvements, the CX for Cities project is creating a program of technical assistance for cities across America wanting to take a step further in their relationship with residents. In doing so, the project ensures that a human-centered design drives city services while streamlining efficiency across the various governance structures at the city level.

The Synthesis and Characterization of Novel Photocages for Efficient Photorelease

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Photocages are a specific class of organic compounds developed to meet the growing need for precise molecular release. Their structure allows for the absorption of light at specific wavelengths, triggering the release of an attached substituent at highly defined times and locations. The ultimate goal of this research is to employ these photocages in the field of drug delivery as carriers of biologically active compounds. However, due to the novelty of the field and the structural specificity of such compounds, the current scope and characterization of organic scaffolds that can potentially be used as photocages are limited. To address this gap, this project aims to synthesize and characterize a novel library of fluorene-based photocage scaffolds to optimize efficient photorelease by systematically tuning their chemical properties. This project explores the structural versatility of the fluorene core via a multi-step organic synthesis starting from a fluorene precursor, leading to the formation of a stable carbocation intermediate that can be used to rapidly generate a library of photocaged substituents. Reaction progress, purity, and photorelease efficiency are evaluated using a suite of analytical techniques, including TLC chromatography, GC-MS spectrometry, NMR spectroscopy, and UV-Vis spectroscopy to calculate quantum yield. Current focus involves optimizing the reaction pathway leading to the carbocation intermediate and establishing stocks of intermediates for further stages of the work. Beyond drug delivery, these tools promise to support advancements in kinetic studies, material science, and neurobiology by providing unprecedented spatial and temporal resolution to track complex biological processes such as brain activity, ultimately offering non-invasive control over diverse molecular systems.

Detecting Squint Behavior in Mice as a Migraine Pain Proxy

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Migraines affect roughly one third of the population, yet the exact mechanisms by which they develop are not fully understood. Rodent models are often used to study neurological and pain-related conditions such as migraines. However, mice do not naturally develop migraines which poses challenges in identifying, studying, and quantifying a headache presence and pain response. The goal of this project is to develop a robust protocol to trigger a migraine-like headache in a mouse model and quantify their behavioral response to better understand migraine pathophysiology. The mice in this study first underwent a 5 day period of chronic sensory innervation of the meninges (the nerves whose activation is considered to be responsible for migraines) using an optogenetic approach to establish a baseline migraine-like condition. They were then injected with 0.1 mg, 1 mg, and 10 mg of nitroglycerin, a drug that triggers migraines in humans, over the course of 9 days. The level of squinting of the animals in the dark as well as with ambient light in response to the drug was recorded and is predicted to correlate with the level of pain and light hypersensitivity (photophobia) they experience. The predicted outcome is a reliable protocol to measure migraine-like pain within a mouse. The results from this study will inform future investigation into migraine therapeutic treatments and pathophysiology.

Misperceptions of Group Inequality andSupport for Redistribution and Sectarian Politics: Experimental Evidence from Lebanon

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Economic inequality has risen worldwide, yet in many societies this has not translated into stronger support for redistributive policies or for political coalitions organized around class or economic interest. Instead, political competition remains structured around religious, ethnic, or cultural lines, even where income and poverty are distributed similarly across those groups. This research investigates whether correcting groups' misperceptions about each other's economic conditions can weaken support for identity-based politics and increase support for redistributive, cross-group policies. Lebanon offers a compelling case: political life is organized around sectarian identity, despite poverty and inequality cutting across religious lines in nearly identical ways. Using a representative survey of 3,300 adults in Greater Beirut, respondents were randomly assigned to a treatment group that watched a seven-minute video documenting that income inequality between Lebanon's main religious groups, Sunni, Christian, and Shia, is small, while overall inequality is high. Using large language models (LLMs), we analyzed the treatment group effects on perceived inequality between religious sects, the presence of solidarity across these groups, and the salience of class identity. We also compared our survey sample to nationally representative benchmark surveys and found that both are closely aligned, supporting the relevance of the findings. So far, it has been found that the treatment can successfully correct beliefs, reduce perceived inequality between sects, and increase support for redistribution. However, no immediate change in political preferences or costly civic behaviors, such as support for civil marriage or a non-traditional political figure, was observed. Current theoretical work on whether correcting those misperceptions can shift political preferences or promote political engagement is limited. This research addresses these gaps, providing a unique contribution that tests this mechanism.

Vascular Risk Factors and Brain Perfusion: Comparing the Effects of BMI and Mean Arterial Pressure on Cerebral Blood Flow in Gray and White Matter

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Cerebral blood flow (CBF) declines with age and may be influenced by vascular risk factors, including elevated body mass index (BMI) and high blood pressure. However, it remains unclear how these factors relate to CBF across brain regions. This gap is critical because BMI and blood pressure are modifiable, with implications for cerebrovascular health. In this study, we investigated whether BMI and mean arterial pressure (MAP) are associated with CBF in gray and white matter in older adults. We analyzed cross-sectional magnetic resonance imaging (MRI) and health data from 40 adults (aged 60-80), with CBF quantified using arterial spin labeling (ASL). We hypothesized that BMI and MAP would each be associated with lower CBF, differing by brain region. To test these associations, we used multiple linear regression, adjusting for age and sex, separately for gray and white matter. We found that both BMI and MAP were significantly associated with lower gray matter CBF ($p=0.039$; standardized $\beta=-3.14$ and -3.13, respectively). Neither was associated with white matter CBF, and neither predictor remained significant when modeled together ($r=0.57$). In participants without a hypertension diagnosis, higher MAP was significantly associated with lower gray matter CBF ($r=-0.47$, $p=0.012$), suggesting chronic blood pressure may impair gray matter perfusion before formal diagnosis. Additionally, BMI was significantly associated with higher oxygen extraction fraction (OEF; $p=0.012$), suggesting a potential compensatory mechanism where reduced perfusion drives increased oxygen extraction from available blood supply. Together, these results suggest that BMI and MAP similarly predict gray matter, but not white matter, perfusion and that blood pressure-related effects on CBF may be detectable before clinical diagnosis. These findings highlight modifiable vascular risk factors as targets for early intervention, including lifestyle or medical strategies, to preserve brain health in aging.

Exploring Novel Blood-Based Diagnostic Approach for Long COVID Patients

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Currently, there is no laboratory test to diagnose long COVID. The condition, impacting an estimated 36 % of confirmed COVID-19 patients, is instead defined as a set of symptoms present for three or more months after SARS-CoV-2 infection. Furthermore, the mechanisms behind long COVID are poorly understood. To uncover these mechanisms and work toward a diagnostic test, we processed plasma samples from patients with acute COVID and long COVID. We compared these samples to plasma from patients who experienced full recovery and from healthy donors. Patient samples were processed with a microfluidic herringbone chip. This chip has previously been validated for the isolation of cells and extracellular vesicles from cancer patients. In order to isolate SARS-CoV-2 materials from patient blood, we coated the chip in an engineered ACE2 receptor that binds to viral spike proteins. Subsequently, captured materials were lysed, releasing captured RNA. These RNA samples were analyzed with droplet digital PCR to confirm and quantify captured genetic material. Preliminary data indicate the presence of SARS-CoV-2 materials in acute COVID, long COVID, and recovered patients, suggesting the virus can remain latent in patients' bloodstream more than three months after infection. We expect in our continuing analyses to observe differences in RNA concentrations among these patients. This would validate the pursuit of a blood-based diagnostic test for long COVID. Establishing a definitive diagnostic benchmark for long COVID would enable exploration and testing of treatment methods, improving patient quality of life.

State-Dependent Processing of Vocalizations in Mouse Auditory Cortex

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The superficial layers of the auditory cortex process complex communication sounds whilst integrating top-down processing into sound's interpretation. Interneurons in these layers are well positioned to encode the emotional salience of stimuli, with a subpopulation of these cells expressing Neuron-Derived Neurotrophic Factor (NDNF) and modulating the activity of both excitatory and other inhibitory cell types. By integrating extensive neuromodulatory inputs, these neurons may shape auditory processing and influence behavioral responses. However, how the internal state affects neural responses to vocalizations remains unknown. This study examines neural representations of mating and restraint vocalizations across stages of the female estrous cycle, determining whether NDNF interneurons alter the stimulus encoding based on hormonal state. In doing such, this project expands our knowledge of the neural mechanisms necessary to understand emotions conveyed through communication. To study NDNF neurons, transgenic mouse lines expressing genetically encoded calcium indicators in cortical pyramidal neurons or NDNF interneurons were implanted with cranial windows. Two-photon calcium imaging collected neural responses to vocal stimuli in awake, head-fixed mice, allowing us to monitor cell activity through fluorescent calcium transients. All female mice underwent vaginal cytology to determine their stage of estrous cycle. To confirm the imaging site, a fluorescent dye was injected into the cranial window. Each brain was then sectioned and examined using a confocal microscope. Using the Suite2P pipeline, the two-photon recordings were movement-stabilized, and neuronal signals were extracted. Identified neurons were then tracked across multiple days using the ROICat pipeline. The resulting datasets were further analyzed using a custom MATLAB pipeline to quantify single-cell activity and extract relevant measures of neuronal dynamics. After this data refinement, statistical analysis and computational simulations examine neural variability across hormonal stages. By examining neuronal responses across hormonal states in both NDNF interneurons and pyramidal neurons, this study aims to advance our understanding of the circuit mechanisms underlying state-dependent plasticity.

Fandom and Social Connection Initiative: Investigating the Power of Shared Sports Fandom for Social Connection

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Modern day America is suffering from a growing loneliness epidemic. Previous research shows that social connectedness is essential for both physical and mental health, yet in 2025 over half of US adults reported feelings of social isolation and exclusion. This makes the connection recession a current public health crisis in the United States. We sought to mitigate causes of social isolation by investigating the relationships that can be formed and facilitated through shared sports fandom. Sports fanbases offer a unique medium through which individuals can connect, bridging common divides such as partisanship, thus making these spaces powerful tools for affinity. We executed two main experiments and a descriptive analysis this summer to investigate the ability of, and extent to which, sports fandom can connect individuals. We partnered with Minor League Baseball to display a survey which asked participants to speak to those seated around them during the second inning break, examining whether social intervention would increase feelings of connectedness or enjoyment. Alongside this, we conducted a study in Harvard Summer School classrooms asking students to either take part in a social or isolated activity, this occurred over two sessions and tracked whether individuals are present-biased in socializing. In addition, we carried out statistical analysis of Fox Sports datasets with R, finding that, on average, sports fans have stronger satisfaction in their friendships, and that families of fans have a better overall experience with youth sports when compared to families of non-fans. Though these experiments are still ongoing, our research could help to uncover effective ways to utilize shared sports fandom for individual level connection.

Customer Experience (CX) for Cities

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Beginning in the Obama administration and continuing into Trump II, the Office of Management and Budget developed the Federal Customer Experience (CX) framework. The Federal CX framework employs Human-Centered Design (HCD) principles to orient government service delivery (e.g. passport renewal, farm loan applications, veterans benefits) around people and their life experiences. The General Services Administration defines HCD broadly as "an interdisciplinary methodology of putting people, including those who will use or be impacted by what one creates, at the center of any process to solve challenging problems". Notably, President Biden's Executive Order 14058 directed the federal government to organize its efforts around a Life Experience Framework, whereby different agencies collaborated to create synergistic service offerings via HCD for particular life events (e.g. a public-private partnership led by HHS to provide newborn supply kits for mothers having a child). Our lab is investigating the application of this federal initiative to the municipal level of government in order to assist mayors with improving outcomes for families. This summer, we are applying HCD to craft a "CX for Cities" technical-assistance program, an eight-month engagement for mayoral teams that will train them in Federal CX processes (e.g. service definition, customer segmentation, service mapping, pain-point analysis). Our specific city partners are forthcoming, but we anticipate that the cities who complete the inaugural offering will emerge with ready-to-deliver plans for driving measurable improvements in residents' experience with a priority service area. Future research may study the outcome differential in service-delivery between city alumni of the CX for Cities program and non-alumni cities.

An Oxidative Stress-Based Flow Cytometry Assay for *SELENON*-Congenital Myopathy Therapeutic Development

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SELENON congenital myopathy is a rare pediatric muscle condition that prevents Selenoprotein-N production, which is an endoplasmic reticulum membrane reductase that regulates cellular redox homeostasis. Patients with *SELENON* congenital myopathy present with muscle weakness, spinal rigidity, and respiratory insufficiency, with no current non-palliative treatments. While prior lab results have measured oxidative stress in *SELENON*-deficient cells using fluorescence-based redox readouts, these assays are not suited for mid-throughput drug screening. The purpose of this project is to develop a reproducible flow cytometry based assay to measure oxidative stress at the single cell level to discriminate between *SELENON*-deficient and wild-type human and mouse cells. We hypothesize that oxidative stress levels will be elevated in the *SELENON*-knockout cells compared to the wild-type, and that this change will be robust enough to test small molecules. Assay development was performed with mouse immortalized C2C12 myoblasts as well as human immortalized myoblasts using wild-type and two *SELENON*-knockout cell lines. Wild-type and *SELENON*-knockout cells were treated with fluorescent probes: CellROX reported total cellular reactive oxygen species (ROS), MitoSOX reported mitochondria expressing ROS, and SYTOX nuclear stain was used to exclude nonviable cells from analysis. Fluorescence intensity from ROS was compared between wild-type and *SELENON*-knockouts. The *SELENON*-knockout exhibited increased redox fluorescence relative to wild-type, producing two population peaks distinguishing knockout from healthy samples. This flow cytometry assay will allow candidate drugs to be screened by how fully they reduce the *SELENON*-deficient. redox fluorescence levels down towards the wild-type reference. Results from these experiments will advance early-stage therapeutic testing for *SELENON* congenital myopathy.

Trust in Healthcare and Public Health Among Sexual and Gender Minority Young Adults

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Trust in medicine and public health has declined in the United States following the COVID-19 pandemic. However, the patterning of this decline is poorly understood, particularly among minoritized populations vulnerable to adverse health outcomes, such as sexual and gender minority (SGM; e.g., lesbian, gay, bisexual, transgender, and queer) individuals who experience health disparities due to minority stress related to stigma. This study examines how SGM young adults experience trust and mistrust in healthcare and public health. Participants will include thirty-five young adults ages 18–25 years who speak English, identify as SGM, and reside in greater Boston. Each participant will complete a demographic and healthcare usage survey, an interview, and a healthcare mistrust survey. Interview transcripts will be coded and themes will be developed using a multi-step method adapted from Braun and Clarke's reflexive thematic analysis, including data familiarization, inductive and deductive coding in Dedoose, and theme development. Survey responses will be analyzed descriptively via R. Interviews conducted thus far (N=6) have revealed a lack of trust in public health agencies; lower levels of trust in medical institutions than in the individuals within said institutions; negative experiences due to lack of provider knowledge of SGM needs; the role of social networks in determining how SGM individuals access healthcare information; and the existence of mistrust pathways before a provider interaction (e.g., through intake forms). Participants desire providers who do not convey judgement or surprise at identity change or disclosure, visibly support SGM communities through affirmation and allyship (e.g., pronoun pins), and actively listen and engage in a culturally-competent manner (e.g., using gender-neutral language). These findings may inform strategies for improving both SGM healthcare experiences and fractured relationships with larger systems. Future directions may include conducting the study nationally and comparing SGM experiences to heterosexual, cisgender populations.

Wastewater Surveillance for Community-Level Monitoring of Sexually Transmitted Infections in Greater Boston

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Mentor(s):
Faculty Advisor(s): Hannah Greenwald Healy
Harvard College | Currier House | Chemistry | 2029

Wastewater surveillance is an effective method of measuring population health and tracking the spread of infectious diseases, demonstrated with SARS-CoV-2, influenza, norovirus, and other enteric and respiratory pathogens. Recent research has demonstrated proof-of-concept for wastewater surveillance of sexually transmitted infections (STIs). Unlike clinical testing, which may underestimate disease burden due to a variety of barriers such as healthcare access, asymptomatic infections, and stigma surrounding STI testing, wastewater surveillance provides comprehensive data that is independent of individual testing. This study builds on previous wastewater surveillance research by assessing the presence of genetic markers associated with *Treponema pallidum* (syphilis), *Neisseria gonorrhoeae* (gonorrhea), and *Chlamydia trachomatis* (chlamydia) in wastewater collected at the neighborhood-scale throughout the Greater Boston Area. A total of 557 wastewater samples collected across eleven different neighbourhoods were processed for molecular analysis. Nucleic acids were extracted from the samples and Digital Droplet Polymerase Chain Reaction (ddPCR) was employed to detect and quantify species-specific bacterial DNA targets for the three pathogens. In addition, samples were also tested for *Carjivirus communis*, a bacteriophage naturally found in the human gut microbiome, which served as a normalization factor to account for differences in wastewater composition and fecal content across samples. The preliminary results indicate that the extraction and ddPCR methods used are effective in detecting bacterial targets associated with syphilis, chlamydia, and gonorrhea in wastewater. The successful conclusion of this project might identify temporal and geographic patterns in detection across sewersheds. This study supports emerging evidence of the efficacy of wastewater analysis as a complimentary tool for infectious disease monitoring, and could be used alongside traditional clinical surveillance to more accurately advise public health decision-making around various bacterial and viral infections.

Human Capital as an Institutional Alternative Asset Class: Drawing on the Innovations of Infrastructure Finance

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Mentor(s):
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Harvard University | Lowell House | Economics | 2029

Human capital (people's education, skills, and productive capacity) is one of the world's largest yet most persistently underinvested forms of capital. Although income share agreements (ISAs), contracts that finance education in exchange for a share of future income, have been proposed to mobilize private investment, previous attempts have remained limited in scale and have never evolved into a mature market. By contrast, the infrastructure sector overcame similar financing challenges through institutions and financing mechanisms that allowed individual public-private partnerships (PPPs) to form the foundation of a widespread alternative asset class. Drawing on this evolution, this project investigates two related questions. Firstly, could human capital similarly be institutionalized as a scalable alternative asset class with ISAs as the contractual basis? Subsequently, if such a market is feasible, what complementary financing mechanisms could expand private investment toward underserved populations within emerging markets? To answer these questions, the project employs a three-part mixed-methods design. Using prior literature, it first examines how infrastructure evolved into an alternative asset class and applies those insights to human capital. Using education and income data, it then develops quantitative proof-of-concept models that evaluate whether human capital could exhibit the characteristics of mature alternative asset classes using two institutional pathways: specialized investment funds that pool ISAs into diversified portfolios and securities backed by ISA cash-flows that enable capital recycling and broader institutional participation. Finally, it interviews field experts to evaluate these pathways (and the regulatory constraints that would shape such a market) and examine whether blended finance, outcomes-based contracting, and cross-subsidization could derisk and incentivize private investment in emerging markets. The novel framework produced could inform mixed financing models for educational institutions, help governments improve the efficiency of public expenditure through market-based financing, and provide developing countries with new mechanisms for attracting private capital towards education and workforce development.

Case Studies of Continuity-of-Care Initiatives for Women Across the Reproductive Life Course

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Harvard College | Leverett House | Human Developmental & Regenerative Biology | 2029

Maternal health outcomes in the United States remain poorer than those of other high-income countries despite advances in prenatal and obstetric care. Increasingly, maternal health research has emphasized continuity of care across the reproductive life course, or the degree to which healthcare across multiple encounters is experienced as coherent, connected, and consistent with a patient's medical needs and personal context. Continuity of care has been associated with improved maternal outcomes and patient experiences, yet relatively few initiatives designed to strengthen continuity across the reproductive life course become routine practice. This study examines why promising continuity-of-care initiatives, including government policies, insurance programs, digital health technologies, and healthcare delivery models, struggle to move beyond the pilot stage into sustained implementation. Eight comparative case studies were selected across government, payer, technology, and healthcare provider sectors. Publicly available documents were analyzed using qualitative content analysis to identify recurring implementation barriers, supplemented by interviews with individuals involved in these initiatives. Preliminary findings suggest that sustained implementation is frequently hindered by time-limited funding, unclear responsibility for ensuring that patients remain connected to care across transitions, and reliance on individual champions rather than institutional support. By comparing implementation efforts across multiple sectors, this study shifts attention from intervention design to the organizational and system-level conditions necessary for long-term integration into routine care. These findings may help inform policymakers, healthcare organizations, and other stakeholders seeking to strengthen continuity of care and integrate maternal health innovations into routine practice.

Effect of Degradation by dTAG System of the SOX9 Protein on Tumor Growth

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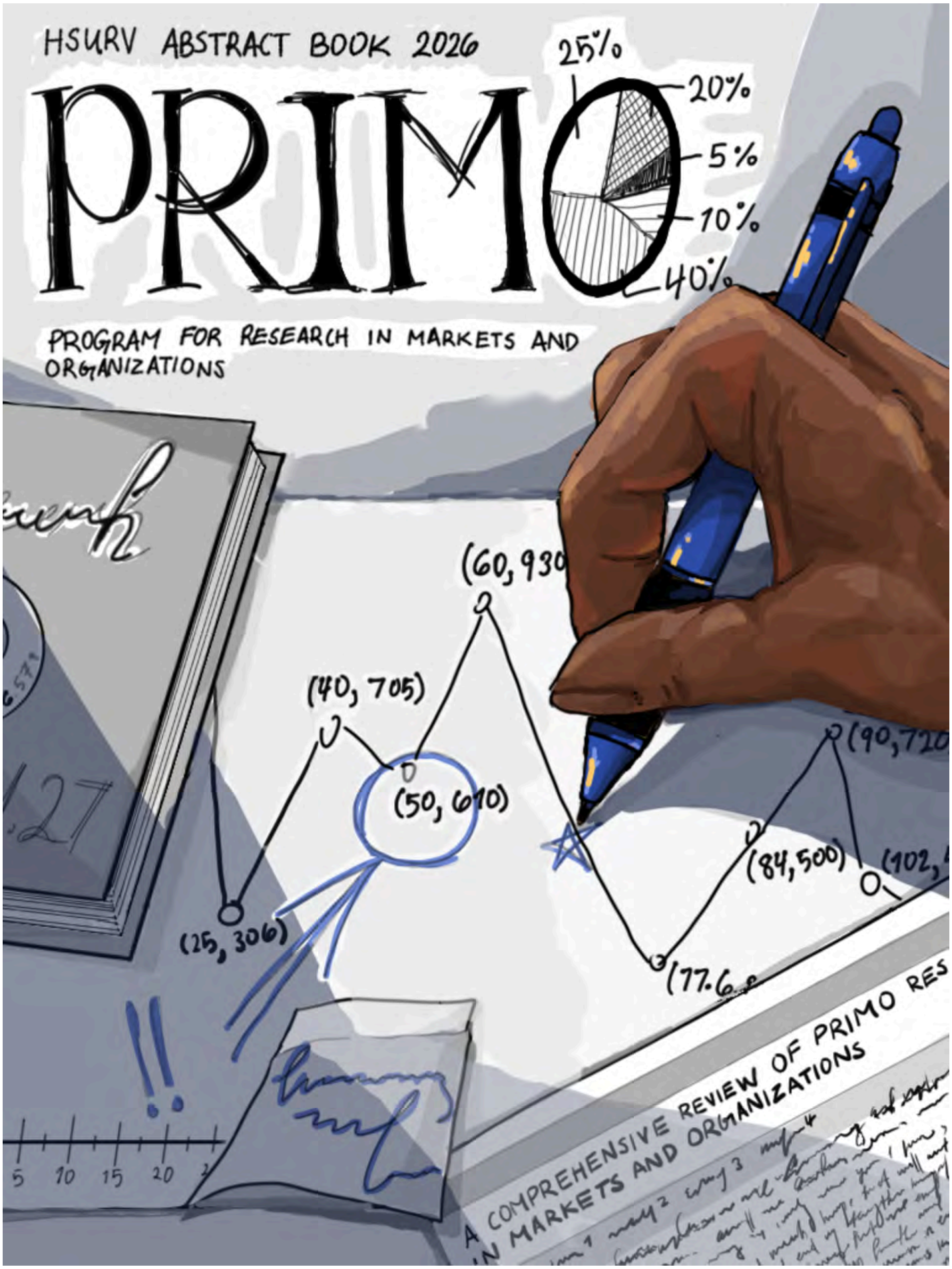
Faculty Advisor(s): Nilay Sethi
Harvard College | Currier House | Molecular & Cellular Biology | 2029

Colorectal cancer (CRC) is the second leading cause of cancer death within the United States with rates currently on the rise for young adults. The SRY-box transcription factor 9 (SOX9) is a central regulator that promotes CRC by blocking intestinal stem cell differentiation. As a key molecular mediator, observation of tumor response in its total absence is needed to further our understanding. We used the degradation tag (dTAG) system for SOX9-specific protein degradation. In the presence of a small molecule degrader, dTAG V1, SOX9 fusion protein fused with FKBP12 mutant is brought into close molecular proximity to the protein degradation machinery. Our project focuses on the viability of the general dTAG system and other mouse models for the degradation of SOX9. Organoids derived from the colon epithelium of transgenic Sox9-dTAG mice were cultured with or without treatment with dTAG V1, and their SOX9 expression levels were analyzed through Western blot and RT-qPCR. Previous evidence from transgenic mice have demonstrated that complete SOX9 knockout is difficult to achieve by *in vivo* tamoxifen injections. Preliminary immunofluorescence microscopy and flow cytometry data suggest that it is possible to transduce mouse colon organoids with knockout machinery *in vitro* followed by selection for a pure population. Whether or not the dTAG system can be more efficient or utilized for other proteins as well as if complete SOX9 knock out will not be malignant in it of itself is to be explored. The dTAG system has advantages in that it is more efficient, effective, and reversible. Using it with SOX9 opens up pathways to more definitive study of the effect of the protein's loss for CRC therapeutic targeting.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From Invention to Innovation: Strategic Sale and Licensing of Intellectual Property

Student: Patrick Arp
Mentor(s): Dafna Bearson
Faculty Advisor(s): Maria Roche
The Ohio State University | Economics | 2027

Inventors and companies that develop and seek to commercialize intellectual property (IP) face an important strategic decision. They may commercialize IP themselves, sell IP to another company, or license IP for a fixed amount of time. In this project, we examine inventors' and companies' decision to license and sell IP to other companies. Licensing and sale are critical mechanisms for IP transfer and overall business performance across industries. For example, in 2017, Bell Laboratories of AT&T sold Uber patents, which provided competitive advantage in location-based ride matching of passengers with drivers. In early 2024, videos went silent after licensing negotiations broke down between TikTok and Universal Music Group. In late 2023, several news organizations and OpenAI struck a commercial licensing deal estimated to be worth more than $10 million per year, which allows news and archives to be used in apps like ChatGPT. Our work investigates IP sale and licensing, exploiting novel data on U.S. patent sales and licensing agreements to predict decisions to sell or license IP. Our data include detailed information on hundreds of companies' most valuable IP transactions and terms of the agreements. This project is foundational to understanding patent sale and licensing as drivers of IP transfer, and the different strategic implications for these modes of technology transfer. It is important for companies whose strategies rely on developing IP that is valuable outside their boundaries and to companies whose strategies depend on using IP that they do not produce.

Managing Organizations in Extreme Uncertainty

Student: Annelise Belle
Mentor(s):
Faculty Advisor(s): Ranjay Gulati
Harvard University | Currier House | Economics | 2028

This research project investigates strategies employed by organizations to operate in the face of uncertainty. Understanding approaches used by organizations confronting uncertainty can reveal how businesses overcome setbacks. The project has two parts: (1) identify analogues between natural sciences and business to improve management techniques, and (2) leverage large language models (LLMs) to quantify courage in corporate documents. For the first part, our work consisted of extensive research into principles related to physics and biology. These fields were selected because they study micro interactions that produce enduring systems. We used case studies and management literature to draw applications to business practices. This research contributes to a deeper comprehension of organizations as systems that produce and allocate resources such as cultural energy to execute initiatives. More broadly, the project seeks to encourage the grounding of managerial strategies in the natural world to instill resilience during periods of uncertainty. The second part of the project strives to determine empirical evidence of courage from qualitative corporate communications. We define courage as "the willingness to act in the presence of risk despite the uncertainty of the outcome." Our selection of corporate communications consists of letters to shareholders, earnings calls, and annual reports because they represent leadership's perspective on their organization's actions. We evaluated methodologies utilized by scholars to measure corporate constructs to develop our scale for courage. In applying our scale, we checked the ratings from two human coders for intercoder reliability. Our next steps involve assessing LLM performance of rating courage via cross-validation, comparing LLM ratings to those of human coders, and designing strong chain-of-thought prompts. Our project aims to find a reliable way to quantify courage to inspire empirical research on the importance of corporate courage. Additional research could investigate organizational courage across time for signs of depletion and strategies for replenishment.

Estimating Bank Portfolio Choices

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Mentor(s):
Faculty Advisor(s): Mark Egan
Harvard University | Dudley Community | Economics | 2027

Large banks hold a unique position in modern financial markets. They provide liquidity across major asset markets, intermediate deposits and credit, and actively trade a broad range of securities. While banks are often studied through their traditional role in deposit-taking and lending, they also actively manage their balance sheets as investors. Building on this perspective, this project treats banks as portfolio optimizers and asks what beliefs about asset returns are implied by their observed asset holdings. We model the banks' portfolio choices in a classical mean-variance framework, in which banks choose asset weights based on tradeoffs between expected excess returns and risk. The first-order conditions of the optimization problem then allow us to recover the expected returns that rationalize each bank's observed portfolio allocation. Using detailed bank positions from FR Y-9C reports and public bank equity returns from CRSP, we classify bank holdings into ten major asset categories and construct these weights over time. Combining these weights with equity-side returns, we infer a time series of returns for the ten asset classes and estimate their covariance structure. This setup allows us to recover banks' implied expectations and examine how these beliefs vary across banks and over time. We will also examine how these patterns relate to bank characteristics such as size, leverage, and exposure to different risks.

Fitting In to Get In: Atypicality and Complexity in Accelerator Applications

Student: Hyerin Chae
Mentor(s):
Faculty Advisor(s): Jackie Lane
University of Chicago | Economics | 2028

Startup accelerators and early-stage investors evaluate thousands of founder-written applications, a process that is costly, subjective, and increasingly augmented by expert panels and large language model (LLM) scoring. This study asks how far the structural characteristics of a venture's problem and solution can be recovered directly from application text. Specifically, we explore how complexity and atypicality relate to evaluation results without the need for costly human- or model-based ratings. We analyze approximately 6,700 MassChallenge applications from 2022 to 2024 and construct embedding-based measures of textual atypicality, operationalized as the mean cosine distance of a given application's pain-point and solution text to its nearest neighbors in a semantic embedding space. We compare these measures to an established 11-dimension LLM-rated complexity rubric. The atypicality of the pain-point statement emerged as a strong, independent predictor of evaluation outcomes: applications with more unusual problem framings received systematically lower judge recommendations and subscores. The effect is nonlinear, increasing steeply at the atypical extreme, and varies by problem domain. Agricultural and marketplace ventures are most heavily penalized, while health-care and data AI ventures are unaffected. This contrasts with rubric-rated solution novelty and textual elaboration, which each independently predicted higher scores. Solution-side atypicality, however, is redundant with existing rubric dimensions once they are controlled for. We also observe that the applicant pool becomes modestly more typical over time. Our results show that atypicality, elaboration, and narrowness or broadness can be recovered from embeddings alone in a cost-efficient and valid way, while other characteristics, such as solution novelty and the narrow versus broad framing of a problem, still require expert or LLM judgment.

Generative AI and Inclusive Economic Growth

Student: Rico Chandra
Mentor(s): Hossein Alidaee
Faculty Advisor(s): Rembrand Koning & Tarun Khanna
Yale University | Economics | 2028

Grab, Southeast Asia's equivalent of Uber and DoorDash, is developing an AI assistant to help millions of small businesses in the region grow. To evaluate the impact of the AI on merchants' businesses, we conducted a randomized controlled trial across Indonesia, Singapore, Thailand, and other countries in the region. We focus the analysis on Indonesia, Grab's largest market. We find that take-up of the AI is low among all merchants sampled. Intent-to-treat effects are therefore null: simply receiving access to the AI tool does not meaningfully change average merchant behavior or business outcomes. Among merchants who engaged with the tool by messaging the assistant at least once, we first consider whether chat content is correlated with actions taken by the merchant. We find that chat discussion of a topic, such as pricing or promotions, is correlated with merchants taking the corresponding action in the same week. We also find indicative lifts in business outcomes relative to matched controls, defined as merchants who were not given access to the AI. Robustness checks suggest that these lifts may partly reflect dynamic selection: engaged merchants appear to have been on steeper growth trajectories than their matched controls even before treatment began. When we restrict the analysis to a more focused subset of heavy users, defined as merchants who sent at least ten messages to the assistant, effects scale three- to sevenfold relative to average estimates across business outcomes. Ongoing work examines the channels through which the AI does or does not help merchants improve. For example, we explore whether price convergence across cities still leaves room for effective pricing suggestions.

AI Adoption in African Firms

Student: Emefa Dake
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Faculty Advisor(s): Ebehi Iyoha
Harvard University | Lowell House | Economics | 2027

This project investigates whether exposure to concrete examples of artificial intelligence (AI) use shifts firm-level interest in adopting or investing in AI. Set within a cross-country study of AI adoption in developing economies, specifically Nigeria, Morocco, Kenya, and South Africa, the research explores how firms deploy AI across business functions, perceive its operational value, and respond to information about peer firms' AI applications. Understanding these dynamics may inform policy efforts to accelerate AI adoption in underrepresented markets. Across two project components, the fellow developed and applied a range of technical and research skills. For the survey instrument, the fellow redesigned a Qualtrics survey to reduce completion time from approximately 25 minutes to 15 minutes by refining question flow and archiving removed items in invisible blocks, a choice that preserves survey logic and documents prior iterations. The fellow also developed "Treatment 2," a dynamic information treatment that delivers tailored AI use-case paragraphs to respondents based on firm characteristics such as industry, country, and size. Building this treatment required drafting use-case content from high-quality case studies and writing JavaScript and HTML code to conditionally display the correct paragraph within Qualtrics. For a companion manuscript, *Frontier Tech in Frontier Markets*, the fellow conducted a comprehensive review in Overleaf, a collaborative LaTeX editing platform, performing copy editing, grammar checks, and citation and reference-link verification. The fellow validated that all figure descriptions correspond accurately to their figures and audited the source code generating the paper's plots to confirm accuracy and reproducibility. This work may contribute to understanding how practical AI information shapes adoption decisions across developing economies.

Managing Organizations in Extreme Uncertainty

Student: Paige Flake
Mentor(s):
Faculty Advisor(s): Ranjay Gulati
Brigham Young University | Economics | 2027

We are living through a period of exceptional uncertainty. Organizations face changes driven by geopolitical shocks, economic volatility, and rapid technological advancement. Leaders consistently need to make decisions with incomplete information, experiment in real time, and create organizational conditions that allow people to act without false certainty. In two complementary investigations, we analyzed methods that managers can apply to better lead amidst uncertainty. The first examined purpose and mission as mechanisms to mitigate common governance challenges, specifically in family-owned firms. The second synthesized process philosophy literature to evaluate how a process-oriented view of reality informs managerial practice. Both investigations involved archival research, qualitative analysis, and the synthesis of findings into research memos and literature reviews. Initial findings suggest that purpose, when integrated into daily operations and governance structures rather than treated as mere rhetoric, helps family businesses overcome governance challenges distinctive to family firms, such as succession conflicts and the blurring of family and firm interests. The process philosophy synthesis indicates that leaders who conceptualize organizations as ongoing processes rather than stable entities are better positioned to experiment, adapt, and create "decision-ready" environments. Future work will extend these insights into journal articles, case studies, lectures, and potentially a book about organizations navigating disruption and uncertainty, examining how purpose and process thinking together enable effective and bold action when outcomes remain uncertain.

Globalization and the American Business Elite

Student: Cameron Hong
Mentor(s):
Faculty Advisor(s): Rakesh Khurana
Harvard University | Mather House | Social Studies | 2028

Globalization has reshaped the American economy over the past several decades. As a result, popular backlash against the business elite tied to this transformation has intensified. This project examines the World Economic Forum (WEF) as a central hub connecting global business leaders, government officials, and cultural elites, contributing to the third installment of Professor Rakesh Khurana's book series, which traces the shift from managerial to shareholder capitalism and its extension onto the global stage. We built a qualitative dataset of approximately 9,000 WEF attendees spanning 2000 to 2013, cross-referencing outside databases to fill gaps and using large language models to assist with cleaning and verification. We analyzed the dataset for average age, primary country of residence, career trajectory, and job title, and sorted attendees into four categories (businesspeople, academics, politicians, and civil society figures) to track how these patterns shifted over time. We also examined firm-level data, categorizing firms by geographic region and industry to assess representation. Finally, we reviewed archival issues of Worldlink, the WEF's internal-circulation magazine, alongside LexisNexis media coverage to trace how WEF-affiliated elites interpreted debates over free trade, the 1999 Seattle protests against the WTO, and rising economic inequality. Preliminary findings reveal wide but uneven geographic representation. Thus far, the archival review suggests elites have framed inequality either as a temporary phenomenon or as a problem requiring further economic integration. These results suggest the WEF functions as a coordinating body that helps elites manage tensions inherent in globalized capitalism. Future work will extend the dataset's timeframe, deepening understanding of how these elite networks shape and are shaped by both globalization and its political backlash.

The Currency of Reciprocity: How Time and Money Gifts Differentially Motivate Effort in Online Labor Markets

Student: Jenny In
Mentor(s):
Faculty Advisor(s): Ashley Whillans
Rice University | Psychology | 2028

Compensation is an important predictor of worker motivation. To date, research in this area has focused on how the amount and structure of financial rewards shape worker effort. For example, prior research shows that the structure of financial rewards can have distinct motivational effects on workers. In one study, monetary rewards given in the form of an unexpected gift increased worker productivity more than an equal amount of expected incentive (Gilchrist et al., 2016). Yet, despite the growing use of non-monetary rewards in organizations (Thibault-Landry et al., 2018), most research still heavily focuses on monetary compensation. Moreover, few studies have examined time as a reward currency, which may have unique motivational effects. The present study investigates how workers perceive time-based versus monetary rewards when each is framed as either an incentive or a gift. The planned field experiment uses a 2x2 design that manipulates what is offered (money vs. time) and how it is framed (incentive vs. gift). Data will be collected from 900 online gig workers. We propose the following hypotheses. We expect gift-framed rewards and time-based rewards to produce greater effort from workers because of their relational nature, unlike incentive-framed or money-based rewards. The effect of gift-framing is expected to be stronger for money rewards than for time rewards, as adding an additional relational framing to a time reward, which is already perceived as relational, should not significantly increase effort. We further hypothesize that money rewards will only have a motivational effect comparable to incentive-framed time rewards when framed as a gift. By examining the psychological mechanisms associated with different forms and framings of reward, this study will contribute to the understanding of how monetary and non-monetary compensation shape worker motivation. The results will also offer practical guidance for designing effective compensation strategies for gig workers.

Public Perceptions of Disability Representation in Fortune 500 Companies: A Reproducible Framework for Open-Ended Survey Classification

Student: Sean Kim
Mentor(s):
Faculty Advisor(s): Alex Chan
Harvard University | Dunster House | Economics | 2028

Disability constitutes one of the largest demographic groups in the United States. More than one in four Americans report possessing a disability in mobility, cognition, hearing, vision, or numerous other functions. However, disabilities often receive less attention than race and gender in discussions of workplace diversity and inclusion. This project investigates public perceptions of how Fortune 500 companies recruit, value, and publicly report on disability relative to other demographic groups while developing a scalable methodology for analyzing open-ended survey data. Approximately 1,800 respondents answered three free-response questions regarding which demographic groups Fortune 500 companies actively seek to recruit, should seek to recruit, and appeared to consider in their diversity reporting. Three methods were invented to transform qualitative responses into reproducible data. First, a complete manual coding process established a ground-truth dataset comprising 36 binary indicator variables per respondent. Secondly, comprehensive keyword dictionaries were implemented in Stata for primary classifications and supplemented with large language model (LLM) workflows formed through iterative prompt engineering. Lastly, full automated data classification was achieved through LLM-tailored prompting. From initial comparison, we find LLM-based methods closely reproduce human coding while outperforming keyword-based approaches, with near identical performance across varying language models. Initial analyses further suggest that respondents underestimate the extent to which Fortune 500 companies acknowledge disability in public reporting relative to race and gender, despite recognizing that disability receives comparatively less emphasis. This work demonstrates an effective and scalable methodology for studying public perceptions of corporate diversity while enabling large-scale analysis otherwise requiring extensive manual coding. Further analysis will evaluate the robustness and generalizability of these findings across additional datasets.

The Role of AI in Feedback

Student: Catherine Li
Mentor(s): Louise Serre & Elizabeth Sullivan
Faculty Advisor(s): Ting Zhang & Allie Feldberg
Wellesley College | Economics | 2028

Many organizations use feedback based on inputs from multiple sources with the aim of providing a more informed view to the recipient and informing compensation and promotion decisions. However, previous research highlights that feedback aggregation is frequently unsystematic, often generating unequal developmental insights across different groups. Our project aims to better understand how feedback is aggregated, focusing specifically on working professionals within the medical field. In particular, this study aims to better understand how artificial intelligence (AI) aggregates feedback. We will generate AI feedback summaries and use natural language processing (NLP) to compare them against human-aggregated summaries. Through NLP, we aim to evaluate differences in thematic consistency, sentiment valence, and general bias. In particular, we are interested in learning more about how humans and AI aggregate conflicting feedback. This research aims to provide better recommendations on the circumstances in which AI can be a strength as well as a limitation in the feedback aggregation process.

From Invention to Innovation: Strategic Sale and Licensing of Intellectual Property

Student: Katie Murphy
Mentor(s): Dafna Bearson
Faculty Advisor(s): Maria Roche
Harvard University | Adams House | Statistics | 2028

Inventors and companies that develop and seek to commercialize intellectual property (IP) face an important strategic decision. They may commercialize IP themselves, sell IP to another company, or license IP for a fixed amount of time. This project examines the decision to sell or license IP, as patent sales and licensing agreements are critical mechanisms for technology transfer across industries. Our project uses novel data on U.S. patent sales and licensing agreements, including detailed information on hundreds of firms' high-value IP transactions. The analysis focuses on predicting whether a transaction takes the form of a sale or a license and identifying patterns in the characteristics of firms, technologies, and agreements that are associated with each mode of transfer. Current analyses show that firm location can shape deal terms and that the lexical complexity of public patent descriptions can influence licensing decisions. These findings suggest that both geographic context and the way firms publicly describe technologies may affect how IP moves through markets. Future work may refine a predictive framework, examine which transaction features best distinguish sales from licenses, and explore how these transfer modes affect commercialization strategies.

Dinner Table Alphas

Student: Nhi Hoang
Mentor(s):
Faculty Advisor(s): Lauren Cohen
University of Texas, Austin | Economics | 2028

While household relationships form an important channel of information flow, their role in facilitating professional decision-making remains underexplored. This project examines how household linkages, particularly spousal relationships, influence decision-making and abnormal returns for mutual fund managers. We begin our analysis by compiling a list of fund managers from actively managed equity mutual funds. Using a novel dataset that combines household composition data and spouses' employment histories, we identify spousal linkages by matching fund managers to their household members based on residential addresses. This data is then combined with mutual funds' returns and holdings, creating panel regressions of gross and net monthly fund returns based on indicators of spouse-linked managers while controlling for fund characteristics and year-month fixed effects. Preliminary results indicate that mutual fund managers whose spouses hold executive and C-suite positions earn higher abnormal returns than managers not linked to executive spouses. In particular, stocks purchased by executive-spouse-linked managers outperform those purchased by non-linked managers by 4.30% per quarter, with profitable trades occurring only within their spouses' industries. This suggests that household employment connections provide managers with access to industry-specific information, facilitating superior trading decisions. Consistent with this interpretation, we also find that executive-spouse-linked managers are more likely to trade in their spouses' industries and allocate greater dollar amounts to such trades. We are currently extending our dataset on household composition and employment histories by exploring alternative data sources on household information to improve representativeness and enhance the robustness of our results. Overall, these findings reinforce that spousal employment ties provide meaningful industry-level information to asset managers. Moreover, our results have implications for market regulation since these trades reflect valuable industry knowledge that is difficult to detect and regulate without imposing on household relationships.

Corporate Engagement with Societal Issues in the U.S.

Student: Joshua Olatubosun
Mentor(s): Magdalena Larreboure
Faculty Advisor(s): Vincent Pons
Howard University | Economics | 2028

Our project examines how S&P 500 firms took public positions on societal issues between 2008 and 2025, including race, gender, minimum wage, abortion, LGBTQ rights, voting, gun rights, immigration, and climate change. To classify stance-taking across thousands of news articles, we train a large language model (LLM) on a sample of about 92 articles using a three-part coding system developed by our team and refined through comparison with human coders. Category one includes stances firms take by changing or committing to change their own business operations. Category two captures stances firms take by explicitly justifying their position based on their business interests. Category three classifies stances firms take as general moral or civic positions rather than business-driven ones. Because these distinctions are subtle, we test and revise the definitions so that the model's labels increasingly resemble those a trained human reader would assign. Thus far, our work has produced a working classification system and steadily improving agreement between the model and human coders as the prompt evolves. We next aim to link these stances to measures of employee political affiliation and the degree to which the stances are controversial. Clarifying how corporate political engagement shapes these outcomes can help explain why firms increasingly treat social positioning as a frontline strategic choice.

Employment Shocks and Regional Labor Market Recovery in the United States

Student: Victoria Paraoulaki
Mentor(s):
Faculty Advisor(s): Tod Lensman
Harvard University | Mather House | Economics & Applied Math | 2028

Regional labor markets exhibit substantial variation in the probability and speed of recovery following employment shocks. This project examines the characteristics associated with more resilient labor markets. We construct a county-level panel of U.S. employment data spanning 1980 to 2020 and aggregate these to commuting zones to examine how labor market characteristics relate to employment volatility and recovery following recessions. The analysis integrates data from the Quarterly Census of Employment and Wages and the Bureau of Economic Analysis with county-to-commuting-zone crosswalks to produce a longitudinal dataset. Preliminary analyses measured employment volatility, estimated recovery rates following employment declines, and evaluated the relationship between recovery outcomes and characteristics such as pre-recession employment growth. Initial regression results indicate that larger labor markets experience significantly lower employment volatility and are more likely to recover from employment shocks. Among commuting zones that recovered, however, market size showed little relationship with the number of years required to return to pre-shock employment levels. These findings suggest that larger labor markets may be more resilient to adverse shocks, although additional factors likely influence the speed of recovery once a decline occurs. Future work will expand the analysis by incorporating industry composition, cross referencing against multiple recessions, and exploring alternative model specifications to better identify the mechanisms underlying regional differences in labor markets.

Global Human Capital: Immigration and Entrepreneurial Success

Student: Justin Raimo
Mentor(s): Henry Woo
Faculty Advisor(s): Paul Gompers
Harvard University | Winthrop House | Economics | 2029

Motivated by the evidence in Amornsiripanitch et al. (2023) that immigrant founders outperform native-born founders in entrepreneurial success, both financially and scientifically, we extend the analysis beyond the United States to a global sample spanning more than seventy countries. We examine how founder mobility shapes high-growth entrepreneurial outcomes across diverse institutional environments, with a particular focus on the role of country-level institutions. We construct a global dataset of approximately 640,000 founders by linking education and employment histories from Revelio Labs with startup records from PitchBook and Crunchbase. We classify founders into three mobility types: locals, who found ventures in their home country; sea turtles, who return home to found ventures after acquiring experience abroad; and expats, who found ventures abroad. Using the relative shares of these founder types, we cluster countries into three mobility regimes: local-dominant, expat-dominant, and balanced. Additional data collection and integration are nearing completion, and empirical analyses are underway. The analysis incorporates a broad set of country-level institutional characteristics, including taxation, labor market regulation, intellectual property protection, government effectiveness, corruption, and legal and regulatory quality, to examine how national environments moderate the relationship between founder mobility and entrepreneurial success, measured by outcomes such as IPOs and M&A. By integrating founders' initial mobility pathways with these institutional characteristics, this study aims to provide a comprehensive assessment of how human capital mobility and national institutions jointly shape high-growth entrepreneurship worldwide.

Leadership in an Era of Tectonic Shifts

Student: Fiona Reenan
Mentor(s):
Faculty Advisor(s): Krishna Palepu
Harvard University | Eliot House | History & Literature | 2027

The Leadership in an Era of Tectonic Shifts (LETS) project aims to inform and prepare CEOs to navigate global structural changes including depopulation, climate change, trust erosion, and artificial intelligence. In this time of rapid change, existing leadership principles emphasizing responsiveness are not sufficient to protect companies from these emerging shocks to their culture and balance sheets. "Tectonic" leadership requires proactive interpretation, creative solutions, and the ability to lead organizations through adaptation under pressure. This project examines economic, business, and entrepreneurship research alongside case study analyses of CEOs that have taken bold or successful steps in the face of tectonic shifts, with the ultimate goal of proposing a set of management principles and practices for global business leaders to adopt. By analyzing the choices, some advantageous and some harmful, of emerging and established companies around the globe, the LETS project explores the decisions facing CEOs now to illustrate how leaders can prepare for the tectonic future. Across multiple geographies and industries, the leadership qualities that have emerged as critical in this research are: strategic adaptation to demographic change, the ability to identify driving mechanisms during periods of instability, embrace of structural flexibility, and commitment to pursuing technological infrastructure that promotes resilient systems. Though this research is geared towards business leaders, its findings have ramifications for employees, policymakers, and shareholders alike. When CEOs fail to overcome tectonic shifts, the aftereffects are felt far beyond the boardroom, showing up in the form of supply chain disruption and delayed timelines, price shocks at the grocery store, erosion of trust in the media, and diminished confidence in global markets that stalls career trajectories, stokes political division, and stifles entrepreneurship and innovation. Preparing CEOs to identify and overcome these tectonic shifts lays the groundwork for a stronger, more resilient business environment for us all.

The Currency of Reciprocity: How Time and Money Gifts Differentially Motivate Effort in Online Labor Markets

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This study examines whether the currency of workplace rewards (time versus money) and the way those rewards are delivered (as incentives or unexpected gifts) differentially shape worker motivation and reciprocity in online labor markets. Building on gift exchange theory and research on the psychology of time and money, this project proposes a preregistered natural field experiment in which approximately 800 freelancers complete real-effort transcription tasks in a 2 (Reward Currency: Time vs. Money) × 2 (Reward Structure: Incentive vs. Gift) between-subjects design. Workers receive rewards of equivalent economic value either as monetary bonuses or paid release time, framed as either contingent incentives or unexpected gifts. The primary outcome is effort intensity, work quality, and willingness to accept a future contract from the same employer. The central prediction is that gift framing will increase effort more for monetary than time-based rewards because time is inherently perceived through a more relational lens, whereas monetary rewards require intentional gift framing to elicit reciprocity. By testing these predictions in an employment setting with real workers, wages, and performance incentives, this research extends theories of gift exchange and the psychology of time and money while offering practical insights into how organizations can design effective monetary and non-monetary rewards in the growing gig economy.

If You Can't Beat Them, Ban Them: Hotel Market Power and Short-Term Rental Regulations

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Market power affects prices and quantities directly, but it may also reshape regulation in ways that soften competition. We study this indirect channel in the U.S. accommodations market, where hotels compete with short-term rentals (STRs) and STR regulation is set primarily by local governments. We compile a novel panel dataset covering STR regulations in U.S. cities and exploit plausibly exogenous local exposure to national hotel mergers, most notably the 2016 Marriott–Starwood merger. Cities exposed to larger merger-induced increases in hotel concentration are significantly more likely to adopt STR regulations, especially policies that strengthen platform-level enforcement. This effect is concentrated in cities where the city boundary contains a larger share of the relevant hotel market. We then show that STR regulation sharply reduces STR activity and reallocates demand toward hotels, raising hotel prices and revenues. Combining these estimates, we quantify the indirect effect of merger exposure on market outcomes through changes in the regulatory environment faced by competitors.

Risk and Reputation in IPO Underpricing

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Initial public offering (IPO) prices often increase on their first trading day, suggesting that they are underpriced. While existing literature attributes underpricing to a variety of causes, little work has investigated underwriter-level heterogeneity in determining underpricing. We study underwriter risk aversion and reputation as primary drivers by constructing a novel dataset of IPOs and their underwriting fees. Using the data, we examine IPO pricing and fees over time and by underwriter. We also estimate a structural model of strategic underpricing to recover underwriter preferences over risk and reputation. Initial results suggest that first-day IPO returns primarily cluster between -100% and 25%, and have slightly increased over the 2000-2025 period. Underpricing and underwriter fees show a statistically insignificant inverse relationship. Future work will further examine differences in underwriter characteristics and simulate counterfactuals and welfare changes using an improved model.

Optimal Policy with Heterogenous Parental Altruism

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Families are a key source of inequality as parents differ in their ability and willingness to devote resources to their children. As a result, children's life chances may depend heavily on a form of luck they do not control: the altruism of the parents who raise them. Society is thus faced with a dilemma between protecting family autonomy and using redistribution to promote equality. Our research applies the Vickrey-Harsanyi-Rawls "original position" framework to build a model which determines optimal levels of redistribution in an economy featuring heterogeneous levels of parental altruism. In our model, the person in the original position is unaware of their own altruism type and the altruism type of the household that their child will be raised in. With this uncertainty, the person chooses a social welfare function that aggregates their utility over each scenario. We apply two constraints: a set endowment of resources in the economy, and the requirement that more altruistic parents are not incentivized to act as less altruistic parents. We can then solve for the optimal allocation between parents of different altruism levels and their children. We examine several different social welfare functions which result in different levels of redistribution. We also show that equal weighting between children can generate ex post Pareto violations.

Race in Organizational and Management Research

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How is race studied in organizational, sociological, and psychological research? We conducted a systematic review to understand (a) what methods they use, (b) how researchers theorize and conceptualize race in organizations, and (c) whether their findings reflect patterns of sanctioning, specifically Authorization or Discipline. To answer these questions, we followed a specific coding template to review more than 100 business articles and record their analytical framing, conceptualization, and sanctioning patterns of race. In addition, as two coders, we conducted a joint review session after each article was coded independently, comparing the results on the coding template for each article. We assess inter-rater reliability as low, medium, or high based on the number of inconsistent results on the coding template. For the results, first, we found a diversity of research methods, among which surveys and experiments are the dominant quantitative methods, and interviews are the dominant qualitative methods. Second, though the articles conceptualize race in very different ways, most included the conceptualization of race as a demographic or individual attribute that influences workplace dynamics, career outcomes, and relational demography. Finally, to answer the third question, we assessed whether the literature on race directly examines or presents evidence of sanctioning. Sanctioning describes how organizations can simultaneously permit people (i.e., Authorization) and constrain people (i.e., Discipline). Specifically, sanctioning can occur through: (a) Authorization, (b) Discipline, or (c) both. The sanctioning lens is significant for identifying the dynamics broadly experienced in relation to racial identities. By conducting the systematic review, we presented how past literature makes sense of race in organizations. We encouraged future research to address the under-investigated conceptualizations of race and adopt the perspectives of sanctioning when studying identities.

Entrepreneurship over the Business Cycle

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We aim to analyze the causal relationship between labor market conditions and new firm formation. Census Bureau data on unemployment and firm births were compiled at the county level and aggregated into a yearly panel with commuting-zone units. A Bartik shift-share instrument was constructed to isolate the causal effect of nonlocal labor demand shocks. Preliminary findings suggest that firm births are procyclical and decline as unemployment increases. This relationship remains robust when a shift-share instrument is introduced and credit conditions are controlled for. One caveat of these initial findings is that firm-birth data at the county level record only employer firms, meaning countercyclical self-employment is excluded from our analysis. The volatility of firm births within each commuting zone was also studied; initial results suggest that regions with higher baseline rates of entrepreneurship tend to have more volatile firm-birth dynamics across the panel. Further study will analyze the relationship between the labor-demand Bartik instrument and regional labor market volatility.

Not All Autocratization is Alike: Regime-Change Typologies and Their Effects on Financial Markets

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In recent years, democracies worldwide have eroded into autocracy, yet most quantitative measures collapse this process into a single dimension. This obscures a crucial distinction: some regimes are captured gradually by business and economic elites, while others are seized abruptly by militaries or populist movements. Our project asks whether these pathways carry different economic consequences, testing whether elite-driven autocratization moves national stock markets differently than military or populist autocratization. To investigate this across roughly two hundred countries, the project built a reproducible data pipeline that integrated more than thirty scholarly and institutional sources into standardized, country-keyed tables, and paired each country with a corpus of primary documents and peer-reviewed scholarship. A large language model read this evidence and produced a structured, Freedom House-style classification with one-to-ten severity scores, which the project validated against existing expert codings. With validated measures in hand, the project regressed the typed autocratization scores on national stock-market returns to isolate whether the form of democratic backsliding, not merely its severity, carries independent explanatory power. This design compares the two dominant pathways directly, capture by business elites versus seizure by militaries or populist movements, while holding overall regime decline constant. By separating a dimension that existing one-dimensional indices collapse, the framework offers a sharper tool for understanding how markets price political risk and clarifies whether investors respond to the character of autocratization rather than its presence alone. Future work will finalize these estimates, extend the framework to sectoral and sub-national markets, and probe the mechanisms that plausibly drive any differential response.

Impact of AI Adoption and Innovation in African Firms

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Pitzer College | Economics & Mathematics | 2027

This project explores how AI is used across different sectors and countries in Africa, as well as how AI firms are being developed within the continent. Existing research finds that AI adoption across Africa is uneven and concentrated in a small number of countries and sectors. However, less attention has been paid to the firm-level structure of African AI startups, including who funds them, who founds them, and how connected they are to African countries. To address this gap, the project analyzes the firmology of African AI startups, focusing on their sectoral activities, geographic distribution, main investors, founders' educational and professional backgrounds, and founders' nativity to African countries. In order to answer these questions, the project employs data from PitchBook and Stears. PitchBook is a leading global data provider with broad international coverage, but it may underestimate African firms. Stears helps fill this gap by providing more focused coverage of African companies. The project combines the two sources and analyzes the resulting dataset using descriptive statistics, cross-country and cross-sector comparisons, and investor and founder network analysis. Together, these methods aim to provide a more complete picture of the African AI startup ecosystem, and its role in the continent's broader technological development.

An Evolutionary Analysis of Specialized and General-Purpose Robotics Innovation

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The transition of robotics from specialized industrial applications to general purpose technologies represents a fundamental development in the current engineering market landscape. Traditionally, innovation in the robotics space has been dominated by robots built for task-specific automation, but current market attention is focused on general-purpose humanoids. This apparent shift from specialized to general-purpose design mirrors patterns seen in other technologies, yet little empirical account exists of the specific technical capabilities driving it. Thus, this research project investigates the evolutionary path of robotics as a general purpose technology through tracking the technical capabilities embedded in patents from traditional, specialized robotics manufacturers to the emerging wave of humanoid-focused startups. We aim to map this structural shift empirically through analyzing patent data from the United States Patent and Trademark Office. By tracking the patent claims and abstracts, we aim to decompose robotic systems into foundational components such as vision, grasping, and locomotion. From there, we aim to then segment patents into humanoid, non-humanoid, and general application typologies. This granular categorization allows for a quantitative assessment of the industry's structural evolution in robotic design. We anticipate that our analysis will reveal a growing share of patents combining multiple foundational components (e.g., integrated vision-grasping systems) among both incumbent manufacturers and humanoid focused startups, indicating a convergence towards general purpose architectures. If these patterns hold, it demonstrates that robotics is evolving to be a general purpose technology through component-level convergence rather than through the emergence of a humanoid form factor. Ultimately, the overarching goal of this research is to establish an empirical framework for how general-purpose technologies evolve and understand the future trajectory of automation.

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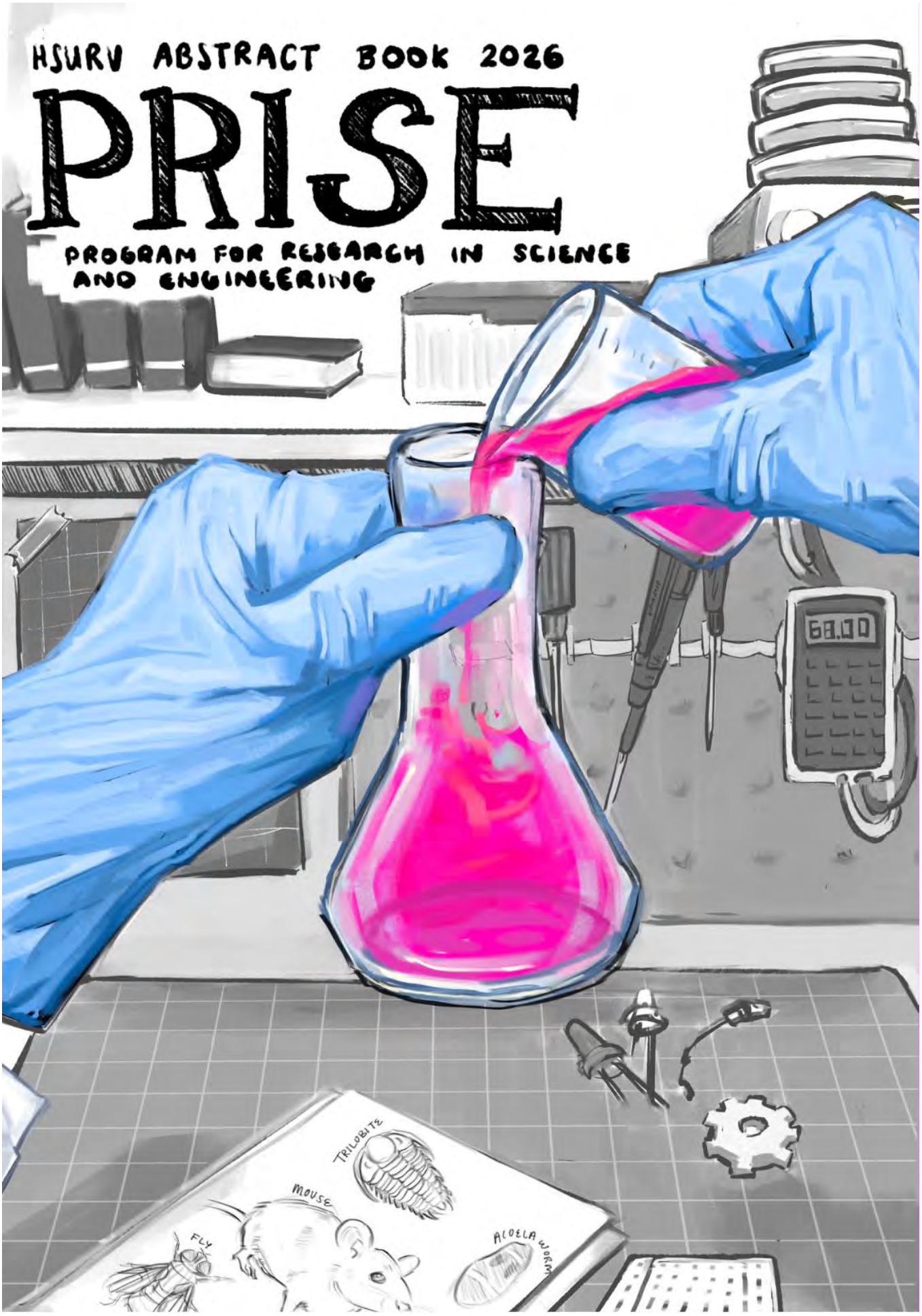

Dissecting the Toxic Species of SOD1 in Amyotrophic Lateral Sclerosis

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Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease characterized by progressive motor neuron loss for which no curative treatment exists. Misfolding of superoxide dismutase 1 (SOD1), an antioxidant enzyme that protects against oxidative stress, is a well-established cause of familial ALS, and central to disease pathology. Although aggregation has long been implicated in toxicity, the precise conformational species responsible remains unresolved. Growing evidence suggests large insoluble aggregates may serve a protective function, shifting focus toward soluble oligomeric intermediates as the primary toxic species. No study has demonstrated that a naturally forming oligomeric species is the toxic culprit, nor has the mechanism linking a specific SOD1 species to the cell death cascade been established. This project set out to determine whether cysteine-dependent metastable SOD1 oligomers, formed through oxidative misfolding of Cys6 and Cys111, activate the ASK1–p38 cascade through aberrant protein interactions, and whether disrupting those interactions rescues motor neuron toxicity. Recombinant SOD1 was expressed in *E. coli* and purified by affinity chromatography and size exclusion chromatography. Oligomers will be generated by metal stripping and oxidative incubation, then stabilized by chemical crosslinking. Oligomers will also be characterized by C4F6 immunoreactivity. A pulldown assay and mass spectrometry will be performed to assess septin–7 binding; Pathway activation and cell viability will be measured in neuronal cells treated with defined SOD1 species. Thus far, purification of recombinant SOD1 has been successfully achieved. If our hypothesis is supported and oligomers exhibit C4F6 immunoreactivity and activate ASK1–p38 through septin–7 binding, this would constitute the first demonstration that a naturally-forming SOD1 species adopts toxic conformation. The successful completion of this project might reframe SOD1 toxicity as a gain-of-function interaction, identifying the cysteine disulfide bond as the minimal structural trigger of the cell death cascade, a distinction that can represent a druggable target for ALS intervention.

Refactoring and Expanding the *penetrance* R Package for Literature-Based Prior Elicitation in Carriers of Pathogenic Germline Variants

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Penetrance, the age-specific probability that an individual carrying a pathogenic germline variant (PGV) develops a disease by a given age, is essential for assessing genetic risk. The *penetrance* R package, developed by the BayesMendel Lab, uses Bayesian methods to estimate penetrance from family-based datasets. This project aims to debug, refactor, and improve the package. In particular, bugs in its prior-specification functionality currently prevent the package from correctly incorporating informative external evidence, leaving analyses reliant on default, uninformative priors. This limitation is especially relevant when pedigree data are sparse, as informative priors can help stabilize otherwise imprecise penetrance estimates, in line with the Bayesian paradigm. The package parameterizes the penetrance curve as a modified Weibull distribution, using interpretable quantities such as the first quartile, median, and asymptote; the normalized first quartile and median in addition to the asymptote are assigned Beta distributed priors. By using information from the literature for each pathway, the expected value and the concentration of the Beta priors are determined to yield the corresponding hyperparameters. These priors sharpen posterior distributions by compensating for weaker likelihoods when pedigree data is sparse or less informative. Future versions could allow multiple evidence types to be combined within a single prior specification to further increase the precision of penetrance estimates.

Dynamics of Nuclear Speckles

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Nuclear speckles are membraneless compartments involved in splicing and transcriptional regulation. While there is elevated gene expression near speckles, we do not know what percentage of transcribed genes are transcribed in proximity to nuclear speckles, or how speckles themselves impact the transcription of these genes. The main scaffolding units of these structures are the protein SON and the long non-coding RNA metastasis-associated lung adenocarcinoma transcript 1 (MALAT1). However, the way these components dynamically rearrange to facilitate speckle function is poorly understood. This study aimed to simultaneously image SON and MALAT1 together in living cells for the first time to gain insight into the dynamic environment of nuclear speckles. In particular, we sought to observe how the scaffolding of nuclear speckles changes when transcription is perturbed to better understand how speckles affect transcriptional regulation. We first used a cell line with SON endogenously labeled with a HaloTag via CRISPR-Cas9 knock-in. Next, we plan to endogenously label MALAT1 via two approaches: CRISPR-Cas9 knock-in of MS2 repeats (RNA loops which bind fluorescent proteins) and CRISPR-dCas13 targeting with in vitro transcribed fluorescent gRNAs. Previous studies labeled SON by overexpressing GFP-SON, while MALAT1 has never been imaged live. Thus, our endogenous labeling strategies represent a large improvement over previous attempts. Using fluorescence confocal microscopy, we performed live-cell imaging of nuclear speckles. Using custom-built image analysis software, we examined the size and lifetime distributions of nuclear speckles, finding preliminarily that the average speckle volume is 2.0 μm^3 and the average speckle lifetime is 7.16 minutes. These findings advance our understanding of the organization of nuclear speckles in space and time. In the future, our results can be leveraged to understand how nuclear speckles impact gene expression and influence human disease and illness.

Neuroimmune Pathways Controlling *Borrelia Burgdorferi*-Induced Chronic Pain

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Lyme disease is a tick-borne bacterial disease caused by Borrelia spp., with an estimated 476,000 cases occurring annually in the United States. Approximately 10–20% of patients develop Post-Treatment Lyme Disease Syndrome (PTLDS) despite bacterial clearance, a condition characterized by persistent pain, fatigue, and neurological dysfunction. The mechanisms underlying these chronic symptoms remain poorly understood. Emerging evidence suggests that different *Borrelia* strains vary in their tissue tropism and pathogenicity, but whether these differences influence pain development has not been determined. In addition, the contribution of macrophages to *Borrelia*-induced pain during infection and following bacterial clearance remains unclear. Preliminary data demonstrate that infection with the *Borrelia burgdorferi* strain 297 induces long-lasting pain phenotypes in mice. Our current studies are focused on two independent objectives: (1) determining whether the *Borrelia* strains B31, 297, and *B. garinii* differ in their ability to induce persistent pain and (2) characterizing macrophage localization in the dorsal root ganglia (DRG) during active infection and following bacterial clearance. Mice infected with different]textitBorrelia strains undergo behavioral assessments, including von Frey and acetone sensitivity tests, to evaluate mechanical and cold hypersensitivity. DRGs from infected mice, infected mice treated with doxycycline following bacterial clearance, uninfected mice treated with doxycycline, and uninfected mice receiving sucrose vehicle are analyzed by immunofluorescence using IBA1 to assess macrophage localization and NeuN to identify neuronal cell bodies. Epifluorescence microscopy is used to characterize neuroimmune changes associated with infection. These studies will provide insight into strain-specific mechanisms of *Borrelia*-induced pain and the neuroimmune responses that may contribute to persistent pain in Lyme disease and PTLDS.

Synthesis and Biological Evaluation of Fluorescent Alectinib Derivatives in ALK-Positive Cancer Models

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Alectinib is a targeted drug used to treat ALK-positive non-small cell lung cancer (NSCLC) and is valued for its selectivity and effectiveness. Although alectinib has had common clinical usage, the reactivity and behaviour of its structural modifications have been left mostly unexplored. This project investigates the binding of fluorescent alectinib derivatives to better understand these changes and explore potential applications in fluorescence-based cancer research. The proposed work focuses on replacing an oxygen atom with an amine group within the alectinib system to enable attachment with a boron-dipyrromethene (BODIPY) fluorophore. The synthesis was selected from established literature and adapted to current conditions. The resultant compounds will be characterized by treatment in ALK-positive and ALK-negative cell lines, Western blotting, FLOW cytometry, and the use of phospho-ALK antibodies to analyze drug reactivity. Thus far, the required reagents and compounds have been obtained, and experimental preparation is underway. Preliminary planning suggests that substitution of the heterocyclic oxygen would alter the reactivity of alectinib during conjugation reactions and may influence the biological mechanism of action. Future work will focus on generating new derivatives and testing their activity and localization in cancer models. This study may help determine if fluorescent labeling changes uptake, localization, or selectivity.

Investigating the Role of Vasculature in Determining Eye Size in Zebrafish

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The Mexican tetra, *Astyanax mexicanus*, has cave- and river-adapted populations which diverged around 200,000 years ago and remain interfertile. Cave-adapted fish lack pigment and eyes. 'Cryptic' genetic variation, which does not impact phenotype under "normal" conditions, is thought to be buffered by the chaperone protein HSP90 under homeostatic conditions and is revealed in response to harsh cave environments. It has been proposed that this mechanism may be a key factor in the evolution of eye loss in *A. mexicanus*. To identify hidden variants that contribute to eye loss in the cavefish, we identified 19 client genes of Hsp90 in genomic regions associated with small eyes in *Astyanax* that show altered amino acid sequences in cavefish. We determined that 12bp deletions in the *flt4* gene, which codes for a vasculature growth factor, caused significant decreases in eye size compared to wild type, along with vascular abnormalities. To better contextualize and visualize these results, *flt4* mutants were crossed with a *fli1:GFP* reporter line. We worked to develop larval fluorescent imaging techniques to image and quantify vascular malformations. Imaging using low melting point agarose and titanium pins to orient larvae proved unfeasible due to scalability. Future technique attempts include methyl cellulose mounts. Because 5 of the 19 genes are vascular-associated, mutants in the *tie1* gene, a tyrosine kinase endothelial-specific receptor involved in angiogenesis, were also screened for defects in eye size and gross morphology. Presumptive loss of function alleles in *tie1* had significantly smaller eyes. These results, along with findings from other groups on cavefish eye vascular abnormalities, suggest that vasculature plays an important role in the evolution of eye development and loss. This model may also provide insight into the mechanisms by which genetic variation is hidden and revealed, potentially improving genetic counseling and disease prediction models in variably-penetrant diseases.

Quantifying the Effects of Fuel Treatments on Subsequent Wildfire Severity Using Geospatial Data Integration and Causal Inference

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Wildfires in the United States have become a widespread hazard that endangers lives and property and degrades regional air quality. Substantial evidence identifies fuel treatments, particularly prescribed burns, as potential land management strategies for moderating subsequent wildfire severity, but accurately assessing the impact of such treatments is doubly constrained. First, we cannot reliably quantify how the type, placement, and frequency of treatments modify wildfire behavior, in large part because treatment records are fragmented. Second, prescribed burns are concentrated in the Southeastern United States, while the largest and fastest-growing wildfires occur in the West, leaving the region of greatest need with the sparsest data. These gaps are consequential as state liability and certification reforms increasingly enable non-federal practitioners to conduct smaller, more numerous prescribed burns. Here, we address whether such decentralized burning outperforms the typically larger federal burns, especially in the West. First, we develop a reproducible algorithm that merges heterogeneous fuel treatment dataset sources, while accounting for uncertainty in attribute data and geometries, and extending readily across private, state, and federal jurisdictions. Next, we build cost functions that quantify wildfire occurrence, frequency, and burn-severity indices in terms of landscape and treatment covariates, including elevation, location, vegetation properties, and distance to road. Finally, we apply differences-in-differences analyses across the conterminous US, while accounting for regional differences, to discern differences in subsequent wildfire severity, quantified by Differenced Normalized Burn Ratio (dNBR), explained by the smaller prescribed burns. Our work provides insights to determine whether a shift toward decentralized burning is warranted.

Targeting Desmoplasia in Cervical Cancer to Promote Anti-Tumor Immunity

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Cervical cancer is the fourth most common cancer among women globally and accounts for hundreds of thousands of deaths each year. Although nearly all cases are driven by human papillomavirus (HPV) infection, which can promote immune checkpoint expression, clinical responses to immune checkpoint blockade remain limited. Desmoplastic remodeling, present in approximately 80% of cervical cancer cases, is associated with reduced immune infiltration, increased metastasis, and higher mortality. Therefore, targeting desmoplasia may improve anti-tumor immunity and enhance responses to immune checkpoint therapies. Previous work highlights infigratinib, a previously FDA-approved fibroblast growth factor receptor (FGFR) inhibitor, as a potential drug to reduce collagen production in cervical cancer co-culture models. To this end, three human cervical cancer cell lines, HeLa, ME-180, and HT-3, were treated with three doses of infigratinib individually and in co-culture with normal human lung fibroblasts. Total procollagen levels in the culture supernatant were quantified over one week. Results show that infigratinib substantially reduces procollagen production in HeLa and ME-180 co-cultures, suggesting that FGFR inhibition may suppress fibroblast-mediated desmoplastic remodeling in cervical cancer. These findings support further investigation of infigratinib as a potential therapeutic strategy to reduce desmoplasia and improve response to immune checkpoint blockade in cervical cancer.

Developing New Clonal Cell Lines to Investigate the Amyloid-β/Tau Axis in Alzheimer's Disease

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Amyloid-β (Aβ) accumulation and tau pathology are hallmark features of Alzheimer's disease (AD), and prior work has shown that the Aβ42/40 ratio drives pathogenic tau phosphorylation in 3D human neural progenitor cell (hNPC) models. This study aimed to develop and validate a novel blue fluorescent protein (BFP)-expressing hNPC line as a reporter tool to study the Aβ-tau axis and associated proteins, adding another model to the existing toolkit for investigating this pathway. BFP localizes to the nucleus rather than the cytosol, enabling visualization of nuclear morphology without DAPI staining. Naïve ReNcell VM hNPCs were transduced with lentiviral vectors encoding APP transmembrane domain mutations (I45F, high Aβ42/40; I47F, low Aβ42/40) linked to BFP expression. FACS-assisted single-cell sorting was used to isolate BFP-positive clonal lines, 10 of which were expanded and differentiated in 3D culture without drug treatment. Protein lysates from 3D culture pellets were extracted, and Western blot analysis was performed to compare phosphorylated tau (p-tau) levels across cell lines. I45F-derived clones are expected to show a higher Aβ42/40 ratio, while I47F-derived clones are expected to show a lower Aβ42/40 ratio. Consistent with the Aβ-tau axis hypothesis, this elevated Aβ42/40 ratio in I45F-derived lines is expected to drive increased p-tau accumulation relative to I47F-derived lines. Non-AD control lines lacking the APP mutations are expected to show minimal p-tau accumulation, further supporting a relationship between Aβ42/40 ratio and tau pathology. If confirmed, this BFP reporter system may expand the capacity of existing 3D AD cell culture models. This allows additional pathway markers to be visualized alongside APP expression, providing a broader mechanism for exploring the Aβ-tau axis to identify therapeutic targets.

The Role of CLOCK in Social Communication, Auditory Sensitivity, and Dopaminergic Function in a Bipolar-Relevant Mouse Model

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CLOCK, a transcription factor best known for coordinating 24-hour circadian rhythms, has also been genetically linked to bipolar disorder, a condition marked by disrupted social behavior, altered sensory processing, and dopaminergic dysregulation, though whether *CLOCK* contributes causally to these non-circadian features remains unclear. Because human and mouse *CLOCK* differ in ways that could affect these roles, we used the huCLOCK mouse model, comparing wild type (WT), Clock knockout (KO), and KO mice rescued with human *CLOCK* (KOHum), to test whether restoring human CLOCK rescues bipolar-relevant behavioral phenotypes. We assessed social communication via ultrasonic vocalizations (USVs) during male-female interactions, auditory function via auditory brainstem response (ABR) testing, and dopaminergic locomotor reactivity in an open field following administration of the dopamine uptake inhibitor GBR 12909, which models manic-like hyperactivity. KO mice showed a marked reduction in USV production relative to WT and KOHum mice, indicating impaired social communication. ABR testing revealed a selective threshold elevation at low frequency in KO mice relative to WT, which was fully rescued in KOHum mice, with no genotype differences at higher frequencies. GBR 12909-induced hyperactivity did not differ across genotypes, indicating that dopaminergic locomotor reactivity is independent of *CLOCK* genotype. Together, these findings show that human *CLOCK* selectively rescues social communication and low-frequency auditory sensitivity while sparing dopaminergic motor function, suggesting that *CLOCK*'s contribution to bipolar-relevant phenotypes is pathway-specific rather than reflecting a general disruption of brain function. This selective pattern, rather than global behavioral dysregulation, may help explain the heterogeneous social and sensory features observed in *CLOCK*-linked mood disorders. Future work will determine whether these deficits reflect cochlear-level changes or central auditory processing differences, and whether they extend to other *CLOCK*-dependent behaviors.

Analyzing the Neural Substrate for Differences in Sociality across Sex and Strain of Mice

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Mentor(s): Maria Fernanda Martignago Cassol
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Across the animal kingdom, there is a wide range of sociality across species. Some animals are extremely social, while others are more solitary. Previously, differences across common strains of laboratory mice, as well as between males and females, have been found in response to social isolation, indicating different levels of social need across diverging genetic backgrounds. These behavioral responses to isolation have been linked to the activity of a population of neurons in the preoptic area (POA) of the hypothalamus. However, the underlying neural substrate responsible for the differences between sex and strain is currently unknown. In this study, we are investigating the role of the neuropeptide receptor NK3R, which showcases differential expression across sex and strain in the POA, in how mice socially interact. We administered senktide, an NK3R agonist, into group-housed C57BL/6J female mice and measured the impact on the mice's behavior. Mice were administered 0.5 mg/kg of either senktide or saline, and were then recorded after 20 minutes with a cagemate. Behavior was quantified using Social LEAP Estimates Animal Poses (SLEAP), a machine learning model that converts video footage to key points tracking each mouse. We used these key points to quantify the time that the mice spent interacting. Preliminary results in group-housed animals suggest that administration of senktide may reduce the amount of time spent interacting. The purpose of this study is to determine the underlying genetic factors underlying differences in social need across genetic backgrounds.

Understanding the Role of Sleep in Emotional Memory Consolidation

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Emotional aspects of memory are preferentially preserved at the expense of neutral details over time, in what is known as the emotional trade-off (ETO) effect. This phenomenon has been demonstrated across a variety of studies, exhibiting how emotional memories can change and evolve. Sleep is known to play a pivotal role in memory consolidation, notably magnifying the ETO effect. Various sleep architecture features, including REM, slow-wave sleep, and sleep spindles, have been implicated in memory consolidation, but their relationship to ETO is not fully understood. Forty-two healthy adults, aged 18 to 50 years old, were exposed to negative and neutral arousing scenes, created from negative (e.g., taxi crash) and neutral (e.g., taxi) objects on neutral backgrounds (e.g., street), to evaluate ETO. After the evening encoding session, the sleep participants received an 8-hour sleep window, followed by a memory test of previously encoded objects 12 hours post-encoding. Sleep participants underwent polysomnography (PSG) to monitor brain activity overnight. Wake participants completed encoding in the morning, followed by a test session 12 hours later. Overnight PSG was used to record and monitor sleeping brain activity, including the duration and percentage of REM, non-REM, and slow-wave sleep. PSG also measured sleep spindle count and duration. Data collection and analysis are in progress, but we expect to observe selective enhancement of negative scenes and objects across both sleep and wake groups, with a more pronounced effect in the sleep group. We also predict a positive correlation between slow-wave sleep and negative object memory alongside other positive correlations of REM sleep, as suggested in related prior studies. With complete polysomnography and emotional intensity evaluations, we hope to develop a stronger understanding of emotional memory processing during sleep.

Optimizing Electrochemical Oxidation of Carboxylates

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Existing synthetic processes to form carbon-carbon bonds often rely on toxic or environmentally harmful reagents. Electrochemical oxidation of carboxylates to yield a carbon-centered radical offers a promising alternative but must occur at low enough potentials to both avoid unwanted electrochemical transformation of solvents or radical-accepting organic substrates and to ensure practicality. In this work, we attempt to decrease this oxidation potential via pairing carboxylate anions with non-coordinating cations, experimenting with different organic solvents, and performing chemistry in water-free, oxygen-free conditions. Using a simple three-electrode system inside a glovebox, we obtained electrochemical data on different electrode-electrolyte pairings. Preliminary results suggest that platinum electrocatalysts in water-free acetonitrile, with carboxylate anions paired to non-coordinating potassium-2.2.2-cryptand counter-cations, can lower oxidation potentials to 0.8 V vs. Ag/AgCl, though the platinum electrode rapidly passivates. Studies are ongoing to mitigate such passivation and to confirm formation of desired products via nuclear magnetic resonance (NMR) spectroscopy and infrared (IR) spectroscopy. Further experiments will seek to validate the importance of water-free environments and to identify the most promising counter-cations, in hopes of providing a usable electrochemical system for more sustainable organic synthesis.

Characterization of Anti-Inflammatory Mechanisms of Lactobacillus Crispatus-Secreted Indole-3-Lactic Acid on T Cells in the Female Genital Tract

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Lactobacillus crispatus-dominant vaginal microbiomes are associated with decreased likelihood of infections, such as bacterial vaginosis (BV), and several negative reproductive health outcomes, including pre-term birth (PTB), spontaneous abortion, and infertility. While the effects of *L. crispatus*-secreted metabolites on immune cells have been well characterized in the gut, the mechanisms by which key metabolites (specifically indole-3-lactic acid, or ILA) reduce inflammation in the female genital tract (FGT) remain poorly understood. This project utilizes both *in vivo* and *in vitro* techniques to characterize the relationship between T cells and *L. crispatus* secreted ILA as facilitated by the aryl hydrocarbon receptor (AHR) and retinoic acid receptor-related orphan receptor gamma (RORγt) pathways. Primary methods include quantification of gene and protein expression for the two transcription factors (qPCR, ELISA, Western Blot) and downstream protein and gene targets (CHIP-Seq, immunoprecipitation, immunohistochemistry), as well as measurement of systemic impact (mouse fertility readouts). The preliminary results of our AHR experimentation indicate that, as in the gut, ILA likely activates and perhaps even engages in positive feedback with AHR: expression of IL6, an inflammatory cytokine, is near zero post-treatment with various concentrations of ILA compared to Pam3CSK4 (Pam), a positive control. Joint treatment with Pam and ILA also cuts IL6 expression from 3000 pg/mL (Pam-only) to 1500 pg/mL, indicating lower inflammation. Additionally, AHR expression is elevated in FGTs dominated by *L. crispatus*, a primary producer of ILA. These results partially confirm that interactions between *L. crispatus* and immune cells are regulated through the AHR-ILA signaling axis, suggesting potential for future therapeutic investigation in pursuit of treatments for adverse reproductive health issues such as BV and disordered fertility.

Cell-Penetrating Peptide Vesicles for Drug Delivery

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Increasing intracellular transport of therapeutic nanoparticles via cell-penetrating peptides (CPPs) has emerged as a strategy to enhance the efficiency of targeted drug delivery. Lipid vesicles are already used to encapsulate therapeutic cargos; however, their cellular uptake is often hindered by unfavorable membrane interactions. Therefore, we hypothesize that conjugating CPPs to the surfaces of lipid vesicles will promote more efficient membrane crossing, enhancing intracellular drug delivery. This study functionalized 50-75 nm lipid DOPC vesicles containing DSPE-PEG-maleimide by conjugating a cysteine-terminated octaarginine peptide (Cys-R8) through a thiol–maleimide reaction. The thiols were coupled to DSPE-PEG-maleimide through a Michael addition, and different ratios (1:1, 1:0.5, 1:0.25, and 1:0.1) of DSPE-PEG-maleimide to CPP vesicles were incubated with HEK 293 cells overnight to evaluate cell uptake. Cell uptake was imaged by confocal microscopy and quantified as mean fluorescence intensity from 20 cells per condition. Ratios 1:0.25 and 1:1 showed statistically significant increases in mean cellular uptake compared to the control group with a one-way ANOVA test ($p < 0.0001$). To further investigate the mechanism of cell uptake, a complementary study was done using endocytosis inhibitors. The results showed that cellular uptake in the presence of cytochalasin D (CD) and filipin was not statistically different from the control without blockers, supporting the hypothesis that CPP vesicles may help increase cellular uptake not only by endocytosis but also by direct translocation into the cell through the membrane, compared to lipid vesicles. These preliminary findings suggest an optimal CPP density of 1:0.25 (without overexposure of fluorescent signal) that can be used in future studies to evaluate different kinds of therapeutics (i.e., mRNA, proteins, nucleic acids) to be delivered into cells with CPP-conjugated maleimide vesicles.

Electronic Structure Across Isostructural Tricobalt Series

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Multimetal active sites appear prominently in both natural and industrial chemical processes. Both the Fischer-Tropsch and Haber-Bosch processes, used for bulk synthesis of essential industrial fuel and fertilizer precursors, rely on heterogeneous metal-based catalysts containing such sites. However, the catalysts themselves are poorly understood, as they can only be observed in operando making it impossible to rigorously characterize how the metals themselves interact. Thus, the Betley Group is pursuing the synthesis and characterization of multimetal clusters with accessible trinuclear metal cores that can serve as a model for these industrial processes. Building from previous work in the Betley Group demonstrating that the one-electron reduction of a neutral triiron cluster (F,tbsL)Fe3(thf) which is supported by a hexadentate, amine-based ligand scaffold leads to loss of a solvent molecule and accompanying rearrangement of the triiron core, I have successfully reduced the structurally analogous (F,tbsL)Co3(py) to yield [K+][(F, tbsL)Co3-], leading to a similar rearrangement and loss of coordinating solvent. Subsequent oxidation of the tricobalt anion in 1,2-difluorobenzene yields the neutral species (F,tbsL)Co3 with no solvent molecule bound, allowing for a more rigorous isostructural comparison across the series. Preliminary examination of the naked neutral tricobalt indicates that it shares the same symmetry as its anionic counterpart, and future research will focus on collecting magnetic and electronic structure data on both the neutral and anionic tricobalt cluster. These studies will thus enable the development of a more complete model of metal-metal interaction in these types of multimetal active site environments, leading to a better understanding of key industrial processes than have thus far been possible and potentially guiding the next generation of transition metal-based catalyst design at a time when energy-efficient fuel production is more important than ever.

Optimization of a Robotic End-effector for Automated Land Restoration

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Land degradation, caused by erosion, nutrient depletion, and desertification, affects 40% of Earth's land, impacting 3 billion people and costing the global economy around 10 trillion USD annually. Indigenous technologies help restore ecosystems through the construction of berms for nutrient and water retention, yet this technique is labor intensive and unsuitable for remote, labor-scarce degraded regions from which people have had to emigrate. There is currently no large-scale automated solution. Hence, this project aims to improve a robotic end-effector initially prototyped as the senior thesis of Toluwaniase Ademola (2026), which simultaneously tills and plows soil to form semi-circular berms, by making it rover-agnostic, optimizing the berm-digging path, and decoupling tilling and plowing. This is a prototype design driven endeavor with on-site testing to optimize the final product. We 3D-printed a prototype, which controls the plow's angle with a linear actuator, and mounted it on top of a mobile robot (Clearpath Jackal) to conduct tests on a soil bed and on a test site in Hadley, MA. We measured the dimensions and compaction of the resulting berms alongside current consumed by the Jackal's wheels. Through the first tests in the soil bed, we found out the robot can form berm-walls 6 inches wide and 6.5 inches tall measured from the lowest point. Additionally, through ROS2 (Robot Operating System) we observed wheels lose traction when the motors consume around 1.8 Amps each. This showed the Jackal can excavate considerable berms, but it will need to perform several passes accompanied with plow-angle variations (of 10°). It will be valuable to acquire another rover to compare the results obtained and try multi-robot interactions. Consequently, the team will focus on deciding which rover to acquire, machining the end effector in aluminum extrusion, incorporating reinforcement learning, and developing a tool-changing mechanism to incorporate tilling.

Characterizing the Interaction Between ENL and CHCT

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Chromatin remodeling is a process that changes how DNA is bound to histones and it directly controls gene expression. This process is regulated by interactions between ATP-dependent remodelers and accessory factors, and disruption of these interactions contributes to cancer and neurodevelopmental disease. Yet many regulatory interactions remain undefined. I investigate a previously uncharacterized interaction between the transcription elongation factor ENL and the C terminus of the chromatin remodeler CHD1 (CHCT), identified by AlphaFold screening. I expressed and purified ENL and CHCT from insect and E. coli systems, respectively, obtaining crystallization-grade milligram quantities of each construct. Preliminary size exclusion chromatography shows an elution shift consistent with direct binding, providing initial experimental support for the AlphaFold model. Together, these results motivate further investigation into the affinity and structural basis of the complex. I will next quantify binding by fluorescence polarization and determine the structural basis of the interaction by X-ray crystallography using CHCT and a 20-mer ENL peptide spanning the predicted binding region. This work will define how a transcription elongation factor directly engages an ATP-dependent chromatin remodeler.

Interpreted Simulation and Analysis of Rule-Based Models with PyKappa

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Computational models have experienced increasing favor as tools for predictive and explanatory study of experimental results. Modelers often reach for agent-based models, which specify systems in terms of local interactions between discrete particles; complex behavior emerges in aggregate as these rules are applied through time. But without imposing any particular form on these rules, simulations can become inefficient. This issue may be ameliorated by restricting the possible agent-agent interactions through an artificial chemistry. Rule-based models are a subclass of agent-based models which do exactly this. Our work concerns the implementation of software architecture around Kappa, an existing rule-based modeling language. PyKappa is our implementation of the Kappa runtime in Python's interpreted environment. It allows users to simulate and analyze these models while remaining entirely within the Python ecosystem. Users may also inspect the system as it simulates and disrupt it as needed, bypassing the need for an intervention language within Kappa itself. The package has been written with the hope that scientists who wish to contribute to the ecosystem or modify the Kappa language find the code simple enough to do so. The adoption of rule-based models has been stymied by several practical considerations. PyKappa solves many of these problems. It is written in a language already familiar to many programmers, works across platforms, and requires only that users learn the basic syntax of Kappa rules. Given students' increasing familiarity and interest in computation, it is also plausible that the increasing accessibility of rule-based models present a new opportunity for the physical sciences to welcome the computationally minded.

Investigating the Causal Role of Chitinase-3-like Protein 1 (CHI3L1) in Cardiovascular Disease Using Mendelian Randomization

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Increased circulating levels of Chitinase-3-like Protein 1 (CHI3L1) have been associated with inflammation, atrial fibrillation, heart failure, and other cardiovascular diseases in observational studies. However, observational studies alone cannot determine whether CHI3L1 directly contributes to disease development or only reflects the underlying disease processes. Recent studies found that CHI3L1 may have a protective effect on heart failure. This project used Mendelian randomization (MR) to validate and extend initial findings by evaluating the causal effects of CHI3L1 on multiple cardiovascular disease outcomes. Genetic instruments associated with CHI3L1 were identified from a European proteomic genome-wide association study of 30,931 participants, which served as the exposure dataset. Summary statistics from genome-wide association studies of heart failure (139,533 cases), atrial fibrillation (180,000 cases), and dilated cardiomyopathy (9,365 cases) were harmonized with the exposure dataset. Causal estimates were obtained using inverse-variance weighted MR, which combines the effects of multiple genetic variants into a single causal estimate. Sensitivity analyses were performed to evaluate the strength of the associations. Higher levels of CHI3L1 were associated with a lower risk of heart failure and atrial fibrillation, potentially indicating a protective causal effect. However, there was no significant causal association observed between CHI3L1 and dilated cardiomyopathy. These findings suggest that CHI3L1 may have a causal, protective effect in the development of heart failure and atrial fibrillation instead of serving only as a biomarker of disease. Further research is needed to clarify the biological mechanisms behind these associations and to determine whether CHI3L1 can be a therapeutic target for cardiovascular disease.

Characterizing Light-dependent Phase Shifts in the Zombie Fungus Entomophthora muscae

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To accommodate daily recurring change, nearly all organisms show cyclic variations in their behaviour and physiology controlled by endogenous clocks. Many behaviour-manipulating parasites also exhibit daily timing, but it remains unclear whether this is circadian clock-driven. A key feature of circadian clocks is their ability to integrate light signals from the environment to temporally organise cellular processes, physiology, and behavior. Depending on when it's provided, a light pulse can change the timing, or phase, of a circadian output. To study the effects of light on parasite-dependent outputs in the context of a host-parasite interaction, we utilised Drosophila melanogaster infected by the fungus Entomophthora muscae, which controls the timing of death of its host, restricting it to near-sunset. Recent work with clock gene mutants revealed this gated pattern of mortality is host-independent, with infected flies dying every 21 hours in the absence of light cues. Here, we leverage light pulses to probe the phase-shifting properties of the fungal clock and its effects on the timing of host death, to test whether this death-gating mechanism is truly circadian. For all trials, flies were exposed to *E. muscae*, incubated under 12:12 L:D white light, loaded into tracking arenas 48-hours post-exposure, and released into constant darkness (DD). Behaviour was monitored for 120 hours. We applied one-hour white-light pulses every 2 hours across the third day of infection, except for the baseline DD condition. Time of death was measured as time of last movement and used to calculate the magnitude of the death-time delay or advance relative to the baseline. Preliminary results indicate that a light pulse advances time of death when given in the late night, and delays death when provided in the early night. These findings provide the first characterisation of a light-dependent death resetting mechanism in *E. muscae*-infected flies.

Analysis of Superluminous Supernova 2025

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Superluminous supernovae (SLSNe) are among the most luminous stellar explosions known, yet the physical mechanism powering their extreme brightness remains unresolved. Two models currently dominate explanations for hydrogen-poor SLSNe (SLSN I): the magnetar model, in which a rapidly rotating, highly magnetized neutron star deposits rotational energy into the ejecta through magnetic dipole radiation; and the circumstellar medium (CSM) interaction model, in which the ejecta collides with material previously shed by the progenitor star. This project presents a photometric and spectroscopic analysis of SN 2025afcr, an SLSN I whose light curve exhibits three distinct brighter bumps instead of the expected smooth decline. Using photometric data of optical and near-infrared wavelengths, we model the resulting light curve with Modular Open Source Fitter for Transients (MOSFiT) to compare magnetar- and CSM-powered fits. We analyze spectra for blueshifted absorption features that indicate ejecta velocity alongside emission signatures typical of CSM interaction. We further compare 2025afcr against existing SLSN catalogues, including other multi-bump events such as SN 2019ujb, and examine its host galaxy environment. Preliminary results show no clear emission-line signatures of CSM interaction, suggesting the magnetar model may better account for the observed bumps, though this question remains open. Because identifying the mechanism behind SLSN luminosity bears directly on our understanding of neutron star physics and massive star death, resolving this question for multi-bump events like 2025afcr helps clarify which physical processes generalize across the broader SLSN population.

Frequency Stabilization Cavity Transfer

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Laser cooling is a technique in which lasers are used to cool atoms down to the milikelvin level, which can then be used for quantum simulation, atomic clocks, or studying reactions at ultracold scales. In atomic laser cooling it is necessary for the lasers used to be stabilized to within a certain frequency range matching the state transitions of the atoms to cool them. In our laser cooling of Yb atoms, we require the use of a 556 nm laser stabilized to the kHz level, in addition to a 399 nm laser stabilized to the MHz level. While it is necessary to use a high-cost ultralow-expansion (ULE) cavity to stabilize to the kHz level, it is possible to stabilize the other laser to the MHz level without such a cavity. We follow the established method of frequency stabilization using a transfer cavity, in which a Fabry-Perot cavity is used with both a stabilized and unstabilized laser directed into it. Scanning the length of the cavity results in transmission peaks from the lasers, which are then used with a PID feedback loop to stabilize the unstabilized laser by using two stabilized transmission peaks for reference. Current work has focused on designing the optical path, aligning the cavity, detecting transmission peaks, and testing the code logic for peak detection, normalization, and feedback control. Once implemented, this system should provide stable MHz-level frequency stabilization for the 399 nm laser without requiring an additional ultrastable cavity. By lowering the cost of frequency stabilization, this method may broaden access to advanced laser-cooling experiments involving multiple lasers without having to use additional expensive ULE cavities.

Regulatory Pathways Linking Intercalated Disc Integrity to Cardiac Arrhythmia

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Intercalated discs (ICDs) are specialized membrane domains that connect individual cardiac muscle cells called cardiomyocytes (CMs) physically, electrically, and chemically. ICDs serve as crucial structural support for the heart in preserving tissue integrity and signaling hubs for CMs, allowing the heart to maintain coordination and efficiency. The importance of ICDs is underscored by a disease called arrhythmogenic cardiomyopathy (ACM), a genetic disorganization of the ICD characterized by severe adipofibrous remodeling and lethal arrhythmias. Because its intricacies are still largely unknown, learning more about the ICD composition has become essential. Using proximity proteomics, we identified two unknown proteins located in the ICD micro-environment: COBLL1 and EPS15L1. By utilizing genetically modified mouse models, we studied both proteins' function in the heart. Successful generation of the mouse models was verified by PCR genotyping. RNA and protein expression levels were measured utilizing RT-qPCR and Western blotting respectively to assess KO efficiency. The heart was phenotyped measuring morphological parameters and performing histological characterization of the cardiac tissue to measure the percentage of fibrosis and immune cell infiltration. Current results support that mice depleted of COBLL1 and EPS15L1 developed pathological cardiac remodeling characterized by interstitial fibrosis, immune cell infiltration, and increased lung weight/body weight ratio. Understanding the role of COBLL1 and EPS15L1 in ICD function can provide a basis for further studies on heart development and arrhythmogenic diseases. This research will allow future investigations to focus on molecular mechanisms underlying ACM, contributing to a more comprehensive understanding of its pathology.

Tracking the Immune Response in Zebrafish

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When the body detects a potential threat, it protects itself via the immune response. A delicate balance of pro-inflammatory and anti-inflammatory activity is critical to blocking the spread of a detected pathogen, or healing an injury, without causing excessive damage to native cells. When this process malfunctions or activates unnecessarily, an excessive pro-inflammatory response may attack the body's own tissues, resulting in autoimmune conditions like rheumatoid arthritis, type 1 diabetes, and multiple sclerosis. The goal of this project is to define the location and timing of these two counteracting responses and identify how they modulate the activity of immune-active macrophages and neutrophils. A potential trajectory is that the site of infection triggers a pro-inflammatory response, which then spreads throughout the bloodstream until anti-inflammatory activity neutralizes it to suppress the global inflammatory response and protect distant tissues from excessive damage. As a transparent model organism, zebrafish allow for the tracking of cellular activity through live imaging. By raising transgenic zebrafish with fluorescent reporters for pro-inflammatory cytokines TNF-α and IL-1β, anti-inflammatory neurotransmitter acetylcholine, and activity marker cAMP, we can track immune cells' behavior in real time. This project will thus help corroborate or redefine this proposed model of inflammatory regulation by illuminating where, when, and how various cells are working to modify it. In the future, this knowledge will lay the groundwork for studies of more specific autoimmune conditions; once we can establish a baseline of what a healthy immune response should look like, we can recognize where this response goes wrong, and, ultimately, why.

Mechanism and TransTAC-Mediated Cell-Specific Delivery of a Bivalent BET/ATR Inhibitor for Metastatic Osteosarcoma

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Osteosarcoma is a rare but aggressive malignant bone tumor that most commonly affects adolescents and young adults. Despite recent advances in treating early-stage disease, lung metastasis is often present at diagnosis, underscoring the urgent need for new treatments for metastatic patients. This study aims to elucidate the mechanism of action of JNB-06-069, a highly potent bivalent compound that couples a BET (*Bromodomain and Extra-Terminal motif family proteins*) inhibitor, which suppresses oncogene expression, with an ATR (*Ataxia Telangiectasia and Rad3-related protein*) inhibitor, which disrupts repair of DNA strand breaks, leading to the accumulation of DNA damage and subsequent apoptosis. In the patient-derived cell line OS186, JNB-06-069 was found to be more potent than combination treatment with the individual inhibitors. Data from immunoprecipitation followed by mass spectrometry suggest that JNB-06-069 may induce a ternary complex consisting of the two proteins bound to the linker drug. Protein quantification assays indicate that this may induce endoplasmic reticulum stress, thereby triggering the unfolded protein response to halt translation, possibly due to the ternary complex being sensed as a misfolded or unfolded protein. This is corroborated by immunofluorescence data indicating increased formation of stress granules in JNB-06-069-treated cells as compared to the combination-treated cells, which may further amplify and overwhelm the endoplasmic reticulum stress response beyond a recoverable threshold, leading to apoptosis and contributing to JNB-06-069's heightened cytotoxicity. Building upon these findings, we seek to develop a Transferrin Receptor-Mediated Targeting Chimera (TransTAC) strategy to selectively eliminate osteosarcoma cells through exploiting their high cell surface expression of CADM1. This TransTAC will incorporate a second binding motif targeting the transferrin receptor, enabling receptor-mediated endocytosis to selectively deliver JNB-06-069 into CADM1-positive cells. This research provides a foundation for translating JNB-06-069 into a clinically viable, targeted therapy for metastatic osteosarcoma.

Too Much Of A Good Thing: Dynamics of PMN-MDSC in Colitis-associated Colorectal Cancer

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Intestinal inflammation in inflammatory bowel disease is shaped by immune responses involving neutrophils and cytokines. Notably, chronic colonic inflammation is a major risk factor for colorectal cancer. This relationship motivates investigation into how immune effectors influence colorectal cancer progression, a process typically restrained by adaptive immune responses, particularly cytotoxic antitumoral T cells. Within the tumor microenvironment, neutrophils often acquire polymorphonuclear myeloid-derived suppressor cell (PMN-MDSC) functions that promote immunosuppression and tumor progression. Unpublished work from our laboratory identified the antiviral cytokine IFN-λ as a key regulator of PMN-MDSC activity that exacerbates tumor growth. However, whether IFN-λ-dependent regulation of PMN-MDSCs in colitis-associated tumorigenesis depends exclusively on disruption of T-cell effector function remains unclear. We used the ApcMin/+ mouse model of colon cancer combined with dextran sodium sulfate (DSS)-induced experimental colitis to investigate this question. To determine the dependence of IFN-λ-linked PMN-MDSC activity on T-cell responses, we depleted both CD4+ and CD8+ T cells in vivo. Preliminary findings suggest that protection from tumor growth in PMN-MDSCs lacking IFN-λ responsiveness is abolished following T-cell depletion, indicating that PMN-MDSCs suppress antitumoral CD4+/CD8+ T-cell adaptive responses. Flow cytometric analysis of colon tumors, spleens, and intestinal lymph nodes will identify key immune populations and inflammatory pathways associated with IFN-λ and PMN-MDSC-mediated inhibition of T-cell activity. Overall, this work aims to define how PMN-MDSCs regulate immune control of tumor growth through CD4+/CD8+ T-cell-mediated adaptive immunity. By defining these mechanisms, this work may identify therapeutic strategies capable of limiting inflammation-associated colorectal cancer progression.

TDP43 Mislocalization in Mouse Olfactory Epithelium

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TDP43 (TAR DNA-binding protein) is an endogenous and essential RNA- and DNA-binding protein that regulates gene expression, RNA processing within the cell nucleus, and cellular stress responses. The cytoplasmic mislocalization and aggregation of TDP43 is hypothesized to trigger activation of immunostimulatory genomic double-stranded RNA (dsRNA) that activates pattern recognition receptors (PRRs), which results in increased cellular inflammatory processes and subsequent neuronal death. Previous experiments on 12- and 18-month-old mice of the TDP43 ΔNLS (IMSR_JAX:014650) x OMPivt (IMSR_JAX:017754) mouse line found advanced degeneration in mature sensory neurons of the olfactory epithelium. The olfactory system is orderly, allowing for identification of circuitry by position of cells. Additionally, the absence of connections between the olfactory epithelium and the olfactory bulb and brain allows for a clear understanding of how degeneration spreads from the peripheral nervous system to the central nervous system.Previous studies have theorized that mice younger than 4 months old lack pathology because stem cells rapidly regenerate and compensate for degeneration. Questions remained unanswered at the youngest age at which mice display pathology. This project investigates modeling TDP43 mislocalization in the olfactory system of mice and searching for spatial coincidence with dsRNA at 4 months old with the TDP43 ΔNLS x OMPivt model. Mice are euthanized at 4 months old, and brains are sectioned and stained using immunohistochemistry. Stained samples are then imaged for target biomolecules olfactory marker protein (OMP), TDP43, nuclear DNA, and dsRNA in the olfactory epithelium. Previous research suggests a high possibility of coincidence of TDP43 ΔNLS and dsRNA in the cytoplasm. These results would clarify the timeline of diagnosis for human patients, utilizing a four-month marker of pathology. Additionally, the interactions between TDP43 ΔNLS and dsRNA can be further investigated in other diseases of the nervous system. With an understanding of these biomolecules, further work into drug rescue can be pursued.

Sensitive Small Molecule Dyes for Multicolor Electron Microscopy

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Proper understanding of biological functions requires integrating molecular information with ultrastructural connectivity. However, no existing electron or fluorescence microscopy method can image ultrastructural detail with precise localization of biomolecules. Cathodoluminescence (CL) enables simultaneous imaging of biomolecule localization and cell ultrastructure. In this technique, the electron beam directly excites small molecule dyes and detects their luminescence, while concurrently visualizing cell ultrastructure via heavy metal stains. However, the low photon yield of conventional fluorescent dyes under electron-beam excitation limits the resolution and sensitivity of CL imaging. This project aims to identify dyes with better CL sensitivity and brightness. For this, polystyrene (PS) beads were loaded with fluorescent dyes that have high photostability and blue absorbing. We loaded ATTO 425, Coumarin 102, JF549 dyes in PS beads. Tetrahydrofuran (THF) was used to swell the beads, allowing the dyes to diffuse into them. Dilution and washing with water removed the solvent and caused the beads to shrink, retaining the dye. Beads containing different dye concentrations were imaged by CL, and the photon count per dye molecule was estimated. ATTO 425 produced a high CL signal, with a photon count of 4 photons per molecule, suggesting that it may be a suitable dye for future use with CL. Further experiments will be carried out to quantify its sensitivity within biological samples. HaloTag ligand-labelled dyes will be introduced to Vibrio cholerae and imaged with CL to measure photon count. These findings provide evidence that brighter dyes can be found to improve sensitivity and resolution of CL imaging, improving the quality of information obtained when imaging cells.

Formalizing the Kontsevich-Segal Axioms in Lean and Verifying Basic Classes of Quantum Field Theories

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Quantum field theory (QFT) underlies modern particle physics and ranks among the most experimentally successful frameworks in science, yet it still lacks a fully rigorous mathematical foundation. Axiomatic QFT seeks to close this gap by recasting the theory in precise mathematical terms, and the recently proposed Kontsevich-Segal axioms offer an especially promising formulation. They characterize QFTs through a class of allowable complex metrics that interpolate between the Euclidean and Lorentzian regimes while guaranteeing positivity of energy. I am formalizing these axioms in Lean 4, a proof assistant and programming language, so that the definitions and theorems of the framework can be stated and machine-checked with complete precision. My immediate goal is a faithful encoding of the framework's statements. I render its definitions, axioms, and theorem statements in Lean building on the Mathlib library, deferring the deepest analytic constructions still absent from Mathlib, such as nuclear spaces, inverse limits of topological vector spaces, and completed tensor products, and treating them as named and fully documented assumptions rather than unproven gaps. Each result is organized in a formal blueprint whose dependency graph makes the logical structure of the theory explicit and auditable. In parallel, I plan to verify by hand that well-understood theories, such as two-dimensional conformal field theories, satisfy the axioms, giving the formalized framework concrete examples to test against. By rendering a leading candidate framework for rigorous QFT in machine-checkable form, this work turns a promising set of axioms into a precise and auditable object, and it maps out exactly which mathematical foundations must still be built to complete the program

Construction and Calibration of a 3D-AOD-based Optical Device

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A principal tool in ultracold molecular labs is the optical tweezer (a tightly focused laser) used for trapping molecules, generally constructed using acousto-optic deflectors (AODs). Most modern tweezer systems only permit molecular control in the 2D plane (the lateral directions). This leaves researchers with a critical block on the way they can arrange molecules, as well as image them. However, the 3D-AOD system (recently developed at the California Institute of Technology) acts as a focus-tuning lens providing full three-dimensional control (lateral and axial directions) of the molecules. Using their design as a basis, the goal is to reconstruct and calibrate a system to aid the research of molecules in the Doyle Lab's calcium monofluoride (CaF) experiments.Using the physics underlying the 3D-AOD design, an optical system combining a double-pass AOD block with a diffraction grating in the Littrow configuration was constructed. The laser was imaged at 29 different distances across four distinct radio frequency (RF) frequencies, individually passed through the device. The images were then analyzed using a computer program to calculate values for the beam waist, focal-length positions, and theoretical Raleigh ranges for each respective frequency. The four frequencies utilized were within 85 MHz-120 MHz. The experimental data for each frequency across all distances roughly corresponded to a Gaussian distribution. The beam waist remained between .029 mm and 0.037 mm, and its position decreased from 7.05 cm to 6.67 cm. The data analysis reveals that the beam successfully propagates through the optical device. The roughly constant waist size and the shift in its position reveal that the device behaves as an axial scanner and that focus-tuning is achievable. Next steps now include constructing an interferometer to demonstrate that a focus-tunable lens has been built, and recreating the device as a CAD design for easy implementation into future experiments.

Characterizing Regeneration Specific Enhancers in Axolotl Limb Regeneration

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While humans have limited tissue regeneration capacity, axolotl salamanders can fully regenerate entire limbs after injury. However, regulation of necessary genes in axolotl limb regeneration remains poorly understood. This study investigated the role of enhancers, distant DNA sequences that play a role in controlling expression of regeneration specific genes, during injury response. Candidate enhancers were determined by assessing peaks of accessible chromatin close to key regeneration genes using ATAC-seq datasets. Genetic constructs with candidate enhancers driving GFP under a minimal promoter were injected into axolotl zygotes and directly into adult axolotl limbs. The injected embryos were screened for successful integration of the construct to begin a transgenic line of axolotls, enabling the study of enhancers during development and regeneration. To quickly assess activity of candidate enhancers, injected limbs were amputated and imaged for 28 days to assess fluorescence, and regenerating limbs were collected once fluorescence was observed. We expect activity of promising enhancers such as Peak 2, an accessible DNA sequence near several important regeneration genes, to associate with distinct cell types, such as muscle cells and their progenitors. To assess this, HCR-FISH will be used to probe for myofibroblasts and satellite muscle cells using *PAX7*, a gene regulating muscle stem cells. We will then observe the colocalization of enhancer activity with muscle cells to determine which cell types are turning on enhancer activity. These results uncover a broader understanding of gene regulation in the regenerating axolotl limb by characterizing enhancer elements in the axolotl genome, which may shed light on why humans are not able to regenerate limbs and offer more opportunities to improve human regenerative capacity.

Selectively Targeting Melanoma Using Bispecific Antibodies Against Integrin Beta-2 and the Melanacortin-1 Receptor

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Melanoma is an aggressive malignancy. While checkpoint inhibitors have profoundly improved outcomes, for metastatic disease, the 5-year survival rate remains below 40%, highlighting the need for improved therapies. Antibody inhibition of integrin β-2 (ITGB2) has been shown to reduce melanoma growth in cell and animal models, but ITGB2 is broadly expressed. Therefore, selective targeting of ITGB2 in melanoma or other tumor cell lines may not be viable with monospecific antibodies. To overcome this challenge, we aimed to create a bispecific antibody (bsAb) that may selectively target ITGB2 on melanoma cells through parallel binding to the melanocortin-1 receptor that is often elevated in tumorigenic melanocytes, increasing avidity of and selectivity. I designed and cloned bispecific antibodies using "knob" Fc domain fused to a previously validated ITGB2 binder that pairs with our other expression construct: a "hole" Fc domain fused to one of three different types of MC1R binding heavy chain only antibodies. Including controls, we expressed and purified an ITGB2 binding antibody, two MC1R binding antibodies, and three bispecific antibodies. All three types of bsAb will be tested for binding with flow cytometry on wild-type melanoma cell lines, ITGB2 knockout cells, MC1R knockout cells, and dual knockout cells. Through comparison of binding of our bsAb with homodimeric versions of the anti-MC1R or anti-ITGB2, we expect to see an increased avidity and specificity for the WT melanoma cells. Successful purification and validation will allow for future testing of efficacy in animal models of melanoma.

Phylogenetic Inference with Stochastic Context-Free Grammars

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Ancestral sequence reconstruction (ASR) is the inference of ancestral protein or DNA sequences from the sequences of their descendant (extant) species. It requires first performing a multiple alignment on the extant sequences, followed by the construction of a phylogenetic tree, and is paramount to understanding the evolution of protein structure and function. Currently, methods for ASR follow two major paradigms: a non-parametric maximum parsimony (MP) approach, and a probabilistic approach including both maximum likelihood (ML) and Bayesian methods. Here, we propose a method using stochastic context-free grammars (SCFG), a probabilistic model for the formation of strings of symbols from an alphabet. In particular, we implement the inside-outside algorithm, a generalization of the forward-backward algorithm for hidden Markov models, to derive the posterior probability of sequence residues for each site in the alignment and at each of the tree's internal nodes. Compared to existing methods, our approach demonstrates optimal theoretical efficiency, with linear time complexity in relation to the number of extant species used in constructing the tree. Moreover, we formulate an expectation maximization (EM) algorithm by iterating this procedure, obtaining re-estimated transition probabilities for residue substitutions along each branch. From these updated probabilities, we aim to infer new information about, but not limited to, the evolutionary model's parameters, the tree's branch lengths, and time reversibility. Other future steps include applying our SCFG-based framework to merge conflicting tree topologies.

Pheomelanin-Induced Oxidative DNA Damage as a UV-Independent Driver of Melanomagenesis in MC1R-Deficient Melanocytes

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Melanoma is the deadliest skin cancer, and melanoma risk reflects not only ultraviolet (UV) exposure but the type of pigment melanocytes produce. Individuals with red hair and fair skin almost always carry loss-of-function variants in the melanocortin-1 receptor gene (MC1R), have the highest melanoma risk, and synthesize predominantly pheomelanin (red-yellow pigment) rather than photoprotective eumelanin (black-brown pigment). Pheomelanin not only offers weaker UV protection, but its synthesis is also a pro-oxidant process that can damage DNA without sun exposure, partially by generating the same mutagenic cyclobutane pyrimidine dimers (CPDs) caused by UV radiation. How pheomelanin synthesis produces this UV-independent damage, and whether it can be modulated pharmacologically, remain unknown. Here, we developed models and tested if shifting melanocyte pigment production toward pheomelanin is sufficient to generate CPDs in the complete absence of UV exposure. We used SK-MEL-30 melanoma cells (darkly pigmented) alongside two isogenic lines to modulate pigment content: MFSD12-knockout (pheomelanin-deficient) cells and a tyrosinase-knockout (pigment-null) line, to isolate the contribution of pheomelanin specifically. We manipulated the eumelanin and pheomelanin levels by treating the cells with the melanin precursor L-DOPA and the pheomelanin precursor cysteine, and we modulated cysteine availability and redox state with erastin, cysteamine, and N-acetylcysteine. We quantified UV-independent CPD levels by immunohistochemistry, ELISA and flow cytometry using an antibody that recognizes the CPD adduct on DNA. This research aims to directly link a defined pigment and redox state to pheomelanin-driven, UV-independent DNA damage and show which interventions raise or lower it. Our findings would help explain the intrinsic melanoma risk of red-haired, MC1R-variant individuals and support the development of new antioxidant-based strategies to reduce baseline DNA damage in these high-risk populations.

Speech and Visual Cue-Based Human Engagement Analysis for Prompting Robot Interaction

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Recent advances in human-robot interaction have expanded the use of robots in public spaces, serving as waiters, personal assistants, and receptionists. However, many existing systems rely on fixed interaction strategies and rigid voice commands, responding similarly to all users rather than adapting to individual social cues. This research addresses that limitation by developing an autonomous mobile robot that uses computer vision (CV) and speech-to-intent inference to tailor its approach behavior to each individual's apparent willingness to engage. The system uses the open-source MediaPipe CV framework to detect humans and analyze body language and gestures. It also feeds transcribed speech to a large language model that infers underlying intent without relying on hardcoded phrases. Based on a calculated visual engagement score and speech intent, a TurtleBot3 robot decides whether to switch between states of approaching, following, or ignoring an individual. The accuracy of the algorithm is assessed by observing the robot's behavior when an actor performs predefined gestures showing varying levels of engagement, such as crossed arms versus an open chest, as well as when different phrasings of the same command are spoken. Ongoing work includes learning model parameterization to improve generalizability across humans with varying physical characteristics and speech patterns. To do this, the algorithm is to be re-trained on several different human actors to ensure consistent engagement assessment by the robot. By enabling robots to infer human receptiveness in real time during an interaction, this work could improve user comfort and foster trust in a service robot, therefore facilitating the deployment of robots in a wide range of public spaces and scenarios.

Comparative Network Analysis of Intracellular and Extracellular Recordings from the Same Neuronal Population Using a CMOS Microhole Electrode Array

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Extracellular recordings often capture electrical activity from multiple nearby neurons, making it difficult to determine which signals originate from the same neuron. In contrast, intracellular recordings provide signals from a single neuron in direct contact with an electrode but are typically limited to a small number of cells. Extending this comparison across large neuronal networks remains a significant challenge. This project develops an experimental protocol for identifying neurons that first produce extracellular signals and are later recorded intracellularly using a complementary metal-oxide-semiconductor (CMOS) microhole electrode array with 4096 electrodes to record activity from a mammalian neuronal network. Extracellular activity is first recorded across all electrodes and processed using the spike sorting package Kilosort4 to identify putative neuronal units. Spike-triggered averaging (STA) is then used to reconstruct the spatial electrical footprint of each neuronal unit by averaging extracellular signals using spike times from that unit as triggers. Intracellular access is subsequently obtained at selected sites through electroporation while extracellular recordings continue across the remaining electrodes, allowing direct comparison between STA images generated from intracellular and extracellular spikes. Preliminary results show cases in which STA images generated from intracellular and extracellular spikes coincide, suggesting that both signals originate from the same neuron. These findings suggest that sequentially recorded extracellular and intracellular signals can be paired to the same neurons, allowing network analysis using both recording modalities, which has not previously been demonstrated. The current contribution focuses on developing the STA-based analysis pipeline for spike-sorted extracellular neuronal units and applying it to direct comparison with intracellular STA measurements. Ongoing work includes increasing the number of intracellular recording sites and identifying additional matched intracellular and extracellular STA pairs to support systematic cross-modal analysis.

Investigating the Neurogenic Potential of Putative Rejuvenating Endothelial Cell-Secreted Factors on Adult Neural Stem Cells

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Although rates of neurogenesis slow dramatically after development, some human neural stem cell (NSC) populations are retained into adulthood. The reactivation of these populations, where cells exit quiescence (a non-proliferative state), could inform potential therapeutics. Previous work in the lab characterizing heterochronic parabiosis pairs, where the circulatory system of a young and old mouse are surgically joined, shows that factors in young blood rejuvenate the brain. These factors could cross the blood brain barrier (BBB) and work directly on the brain, or they could act on the surrounding vasculature, inducing BBB endothelial cells (ECs) to release neurogenic factors into the brain. The lab performed intercellular communication analysis to identify NSC receptors and EC ligands putatively involved in rejuvenation, and this project aims to screen their neurogenic and therapeutic potential. To begin, we selected four factors with established roles in neurogenesis and neuroprotection: platelet-derived growth factor-B, pleiotrophin, prosaposin, and vascular endothelial growth factor-C. I defined the proliferative window of adult mouse NSCs cultures to determine the optimal time and density to observe any changes in proliferation. I also established a protocol to study NSC reactivation where removing growth factors from basal proliferation media is sufficient to induce quiescence. Preliminary data suggests each factor is sufficient to maintain a similar rate of proliferation to the basal media. I have also applied the factors to quiescent NSC cultures. This will allow us to evaluate whether they induce cells to exit quiescence. I will expand on my findings from mouse NSCs and explore their translational potential. Adult human NSC populations have been shown to persist even in neurodegenerative disease states, such as Alzheimer's disease, and could have neuroregenerative capabilities. While more fetal in nature, human iPSC-derived cortical brain organoids may be able to reveal whether the factors' therapeutic effects translate to human cells.

Identifying Conserved Residues Required for Emw1-Mediated EFT2 Folding

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Eukaryotic elongation factor 2 (EF2) is a highly abundant, multi-domain translation factor that drives ribosome translocation along mRNAs during protein synthesis. In unpublished work, the Denic lab identified Emw1 as an essential and evolutionarily conserved chaperone dedicated to EF2 folding in budding yeast. AlphaFold predicts that Emw1 is a large, highly elongated solenoid of alpha helical repeats that initially captures an EF-2 folding intermediate via a conserved binding site (EBS). Consistent with this view, Emw1 mutants with crude EBS deletions caused the appearance of misfolded EF2 aggregates in the cell. Unfortunately, in some cases, these deletions led to undesirable effects on Emw1's structural stability in the cell. To better dissect the mechanistic role of Emw1 binding to EF2, I am systematically introducing point mutations at conserved, charged positions in the EBS. Thus far, I have generated a panel of Emw1 point mutants and plan to test their phenotypic consequences soon using complementary cell growth, microscopy, and protein-protein interaction analyses. Beyond the scope of the PRISE internship, I plan to make reciprocal EF2 charge mutations in its predicted Emw1 binding site; my expectation is that these changes will help restore EF2 folding in cells carrying Emw1 EBS point mutants. By better defining the molecular interface between Emw1 and EF2, my work will advance the still limited understanding in the field of how cells assist folding of complex, multi-domain proteins.

A Machine Learning-Guided Framework for Combinatorial Antibiotic Screening

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Drug-resistant bacteria contributed to nearly 5 million deaths in 2019. Streptococcus pneumoniae ranks as the third leading bacterial cause of death and causes the highest number of deaths among children under five years of age. Antibiotic combinations have shown promise against resistant pathogens, but the sheer number of drug and dosage combinations makes exhaustive experimental screening infeasible. To facilitate computational screening of drug combination efficacy using machine learning, we generated a comprehensive bulk RNA-seq dataset of Streptococcus pneumoniae exposed to three drug combinations across four dosages and three timepoints. We developed a two-step framework for combinatorial antibiotic screening consisting of 1) a regression model that predicts bacterial survival using gene expression profiles, and 2) a generative autoencoder that predicts gene expression profiles in response to specified drug combinations and doses. Training on single-drug treatments and 25% of the combination treatments enabled accurate prediction of the remaining 75% of combination datapoints. Preliminary results from the autoencoder further suggest promising architectures capable of generalizing to unseen drug combinations. Together, these findings demonstrate that the majority of drug and dosage combinations can be accurately predicted using only single-drug data and a minimal set of combination RNA-seq profiles, providing a scalable computational platform to accelerate antibiotic combination screening.

Neural Computations of Parental Care: Deciphering the Internal State Cues and Environmental Cues that Shape Parenting Behavior in Mice

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Parental care in mice depends on the nervous system's ability to integrate internal physiological state with external, environmental information, yet how molecularly defined neurons in the hypothalamus accomplish this integration remains unclear. This thesis addresses two components of the computation. The first examines how neuropeptide and hormone receptor signaling shapes the medial preoptic area neurons that regulate distinct parenting behaviors. Because this requires linking neural activity recorded during parenting to the molecular identity of the same neurons after the fact, I developed a computational pipeline that registers in vivo one-photon calcium imaging data to postmortem MERFISH transcriptomic data. Unlike recently reported multimodal registration platforms, which rely on specialized optomechanical hardware to physically align tissue planes across imaging sessions, this pipeline is purely computational: it uses blood vessels, an anatomical feature already present in standard preparations, as shared landmarks, then propagates cell correspondences outward with a neighbor-geometry spider-web algorithm. Because it needs no custom equipment, any lab with paired calcium imaging and MERFISH datasets could adopt it directly, and I am packaging it into a standalone application so other groups can run the registration without writing custom code. Validated against manually matched neurons, the pipeline achieved 98.5% accuracy with a median error of 3.7 micrometers and complete one-to-one coverage, enabling receptor and neuropeptide profiling of functionally characterized preoptic neurons. The second component investigates how environmental context modulates parenting: preliminary data show that fathers, unlike mothers, reduce pup care in an unfamiliar cage. Using cFOS mapping across the hippocampus, cortex, and brainstem in mothers and fathers tested in home and foreign cages, I will identify candidate regions that convey contextual information to the hypothalamus. Together, these aims combine molecular, neural, and behavioral data to move beyond identifying parenting circuits toward understanding how the brain computes care from internal state and external context.

Understanding How the Principles of Evolutionary Developmental Biology Scale Down to Brain Circuits

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Evolutionary forces are fundamental to the structure and function of the brain. While evolutionary changes in macrostructures and gross anatomy are well-documented, only now do we possess the sophisticated tools required to study these changes at a microscopic level. This study explores how evolution reshapes physical neural wiring across development to drive different survival behaviors. Using high-resolution, electron microscopy, we are capturing detailed images of brain tissue to map out the ”connectomes” (complete wiring diagrams) of the predatory worm Pristionchus pacificus across its lifespan. We will measure how its synapses and neural connections change as it grows from larvae to adulthood, and directly compare these maps to existing developmental data from the bacteria-eating worm Caenorhabditis elegans, which split from a common ancestor about 200 million years ago. We expect that comparing these timelines side-by-side will reveal the exact developmental windows where neural wiring diverges between the two species. By bridging evolutionary biology and physical brain wiring, this work provides a clear window into how small changes during growth allow a nervous system to adapt and produce entirely new survival behaviors.

Comparing Automated EEG Artifact Removal Pipelines for Reliable Resting-State EEG in Children Across Laboratory and Clinical Settings

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Electroencephalography (EEG) is a non-invasive, low-cost neuroimaging tool used to characterize brain activity, and, recently, there has been growing interest in utilizing resting-state EEG (rs-EEG) as biomarkers predictive of developmental outcomes, including neurodevelopmental conditions and language delays. However, for EEG-derived measures to serve as clinically meaningful biomarkers, rs-EEG must be scalable and accessible in its acquisition. A promising approach is to collect EEG in primary care clinics, but it remains unclear whether these data yield comparable representations of neural signals to data collected in highly controlled laboratory settings. To address this need, automated preprocessing pipelines have become increasingly crucial for scalable EEG processing and analysis, but previous research suggests that preprocessing choices may significantly influence signal decoding performance in the same individual. Therefore, it is crucial to compare performances across commonly used automated pipelines for rs-EEG data collected in different recording environments, such as the clinic and laboratory. 33 individuals, including infants and adults, completed two 5-minute rs-EEG recordings at the laboratory and the primary care clinic waiting room. To compare performance across pipelines, EEG recordings from the laboratory and clinic for each participant underwent separate artifact correction using the HAPPE, HAPPE+ER., and RELAX-Jr pipelines. Ultimately, this work will help inform practices for scalable rs-EEG preprocessing and facilitate the development of reliable EEG-based biomarkers for neurodevelopmental research and clinical applications.

Pyk2-Mediated Synapse Elimination via Liquid-Liquid Phase Separation

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During brain development, neural circuits undergo refinement, a process where active synapses are stabilized while inactive synapses are eliminated. This refinement is essential for circuit function, and its disruption has been linked to conditions such as autism and schizophrenia. A central open question is how inactive synapses are selectively eliminated. Prior work identified two tyrosine kinases, Pyk2 and JAK2, as activity-dependent signals present at inactive synapses that drive their elimination. Pyk2 is necessary and sufficient for synapse elimination and acts upstream of JAK2, which is required to eliminate the axon. This raises two key questions: how does Pyk2 eliminate a synapse, and how does it subsequently activate JAK2? Pyk2 has an intrinsically disordered region that allows it to self-assemble into dynamic, selective membrane-less compartments (condensates) through liquid-liquid phase separation (LLPS). The presynaptic active zone, the protein scaffolding complex involved in neurotransmitter vesicle release, is also organized through LLPS. We hypothesized that Pyk2 condensates disrupt active zone structure to eliminate synapses, and that LLPS also enables Pyk2's activation of JAK2. Testing revealed two active zone proteins, Liprin-α and Munc13, co-condensate with Pyk2. Pyk2 condensates also displace Liprin-□ from the membrane, where it normally functions to support vesicle release. Kinase-inhibited Pyk2 retains these effects, suggesting condensate formation, not kinase activity, drives active zone disruption. Further, both Pyk2 kinase activity and condensate formation are necessary for JAK2 activation: kinase-inhibited Pyk2 failed to activate JAK2, and condensate-deficient Pyk2 similarly failed despite normal autophosphorylation. Consistent with a direct role of condensates in signaling, activated JAK2 colocalizes with Pyk2 condensates. This work reveals that Pyk2 uses phase separation to induce synapse and axon elimination, and may inform therapeutic strategies for neurodevelopmental conditions linked to abnormal synaptic refinement. Further work will test kinase-dead and condensate-deficient Pyk2 mutants in vivo to assess effects on synapse/axon density.

Characterizing Mechanical-Immune Crosstalk Driving Tendon Regeneration in Adult Zebrafish

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Tendon injuries affect over 30 million individuals each year yet remain among the most challenging musculoskeletal conditions to treat due to their limited regenerative capacity. Current treatment approaches combine surgical repair and rehabilitation; however, post-surgical scarring fails to restore the native tissue architecture required for proper force transmission, and injury heterogeneity complicates the development of personalized rehabilitation. Emerging evidence suggests that physical activity ('loading') promotes healing by facilitating immune cell recruitment to the injury site. However, whether clinically prescribed post-injury immobilization ('unloading') disrupts these regenerative immune responses remains unknown, limiting our ability to define the mechanical conditions that support healing. To address this, our group leverages adult zebrafish, which, unlike mammals, fully regenerate their maxillary superficial tendons (MSTs) following acute injury. We hypothesized that unloading via localized Botulinum Toxin B (BoNTB) injection impairs regeneration by attenuating injury-site innate immune cell recruitment. Zebrafish expressing fluorescent reporters for tenocytes, neutrophils, and macrophages received either BoNTB or a saline control prior to acute MST injury. Using multiphoton microscopy, we tracked healing from 1-7 days post-injury (dpi) and quantified gap closure and neutrophil/macrophage abundance at the injury site. Finally, we treated a subset of fish with both BoNTB and pro-inflammatory mediator prostaglandin E2 (dmPGE2) to assess whether inflammatory stimulation could restore regeneration despite unloading. Consistent with our hypothesis, BoNTB treatment increased gap distances at 7 dpi and reduced neutrophil and macrophage recruitment at their respective peaks at 1 and 3 dpi. Remarkably, dmPGE2 rescued both phenotypes. These findings identify innate immune cell recruitment as a key mechanistic link between mechanical loading and tendon regeneration and highlight the potential of the FDA-approved drug dmPGE2 to overcome unloading-induced regenerative deficits. Ongoing work includes evaluating tendon biomechanics following dmPGE2 treatment, and resolving the specific macrophage and neutrophil subpopulations associated with regeneration.

Leveraging Somatic Driver Mutations for Single-Cell Phylogenetic Tracing of Clonally Expanded Brain Macrophages in Alzheimer's Disease

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Alzheimer's Disease, one of the most prevalent neurodegenerative disorders, is increasingly recognized as immune-mediated. Recent studies have identified somatic driver mutations in subsets of brain immune cells that cause pro-inflammatory phenotypes, suggesting that genetically distinct populations of microglia-like brain macrophages contribute to neuroinflammation and disease progression. However, the developmental origin of the brain immune cells that harbor somatic driver mutations remains poorly understood. Preliminary work in our laboratory identified shared driver mutations in matched patient blood and brain microglia samples. Although these shared mutations suggest a hematopoietic origin for mutant microglia-like brain macrophages, they cannot definitively establish the developmental relationship between individual cells. This project will expand ongoing lineage reconstruction studies using single-cell whole genome sequencing to address this question. Here, we refined a pipeline beginning with identification of cases with clonally expanded microglia and culminating in the ultimate selection of single nuclei from these donors for phylogenetic tree generation. Candidate somatic driver mutations identified by targeted panel sequencing were successfully validated by high-depth bulk amplicon sequencing in matched blood and brain samples, demonstrating strong agreement with the initial panel sequencing and enrichment in sorted microglia. Following identification of cases with validated clonal mutations in microglia, individual nuclei were isolated using flow cytometry before whole genome amplification. These nuclei were genotyped to enable sequencing of the ideal ratio of mutant and wildtype cells to yield data for a maximally resolved tree. This work will establish a framework for using naturally occurring somatic mutations as markers for lineage relationships in neurodegenerative disease and could reveal a novel therapeutic window for intervention by targeting clonal somatic mutations in blood. Future studies will supplement these data with genotype-resolved functional profiling to continue investigating pro-inflammatory phenotypes that result from acquired driver mutations and elucidate how clonal genetic changes contribute to neuroinflammation in Alzheimer's disease.

Developmental Foundations of Predictive Processing

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Comprehenders use contextual information to predict upcoming input, facilitating later word recognition and processing. Prior research with adults demonstrates that predictive processing is flexible and modulated by contextual support, but it remains unclear how these mechanisms develop in early childhood. Our work investigates whether children aged 54–78 months utilize adult-like predictive strategies, specifically whether contextual reliability modulates their predictive engagement. In an EEG study, participants are presented with trials featuring a prime–target pair consisting of two words followed by an image. They are asked whether the image matches either of the words they heard, ensuring sustained engagement. We controlled the semantic relatedness of the two words (e.g., salt–pepper would be related while clown–pizza would not) and artificially manipulated the proportion of related trials in the presentation list (either 20 % related or 80% related). From this data, we analyze neural responses to critical target words to assess the magnitude of semantic priming and compare the effects across low– and high–relatedness conditions. More specifically, we are assessing the amplitude of the N400, an Event-Related Potential (ERP) characterized by a negative voltage deflection that peaks roughly 400 milliseconds after encountering a meaningful stimulus. The amplitude of the N400 is correlated with the lexical predictability of a word; the more unexpected a word is given the context, the greater the N400. Thus, if prediction is a flexible, strategic mechanism, we expect larger semantic priming effects in high-relatedness contexts compared to low-relatedness contexts. By analyzing how these priming effects unfold across the experiment, we determine whether children initially engage prediction by default and subsequently modulate their engagement of this mechanism based on cue reliability, mirroring adult patterns. This study offers insight into the developmental trajectory of predictive processing, illuminating whether flexible predictive processing is established during early childhood or undergoes significant maturation across development. These findings will advance our understanding of how young children integrate context to facilitate learning and communication. Further studies might investigate prediction mechanisms in children younger than 54 months.

Identification of a Non-Invasive Biomarker for the Assessment of Disease Severity in Pediatric Moyamoya Patients

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Moyamoya is a rare cerebrovascular disease characterized by progressive narrowing of the internal carotid arteries and their proximal branches. Moyamoya-related stenosis increases the risk of transient ischemic attacks and ischemic strokes in affected children. Despite its infrequency in the general population, this disease is responsible for approximately 20% of cerebral arteriopathies in children with acute stroke. Monitoring vessel stenosis and disease severity in moyamoya patients often requires angiography and magnetic resonance imaging (MRI). While a handful of non-invasive biomarkers have been proposed to detect the disease in pediatric populations, few investigations, if any, have assessed whether non-invasive biomarkers can convey disease severity in place of these established imaging techniques. In this study, we sought to identify a biomarker that can reliably predict the degree of vessel narrowing in pediatric patients with unilateral moyamoya. Plasma samples were obtained from 16 patients age $\leq$ 17 with unilateral moyamoya. These samples were analyzed by an independent proteomics service, and abundance profiles were obtained for 2,925 distinct proteins. We then reviewed patients' imaging records and graded disease severity using two ordinal scales, Suzuki grade and ivy sign. Using Spearman's rank correlation coefficient, we identified 238 candidate proteins for predicting Suzuki grade from plasma samples. Further statistical testing is needed to isolate the most accurate biomarker for Suzuki grade from this cohort of candidate proteins. After isolating the highest-performing biomarker, we plan to quantify reference ranges of relative protein abundance for each degree of the Suzuki grading system. Further analysis will also be conducted on the proteomic dataset to identify potential biomarkers capable of predicting ivy sign in patients with unilateral disease. Ultimately, the isolation of a single biomarker for Suzuki grade and ivy sign could improve prognostic reliability and potentially reduce the need for more invasive and costly imaging among patients with moyamoya disease.

Establishment of a Naturalistic Reward-threat Assessment Paradigm: Cricket Hunting in Mice

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Novel stimuli often require animals to balance innate threat assessment with learned value when determining appropriate behavioral responses. In mice, encounters with crickets initially produce avoidance, but following experience with cricket consumption, some animals rapidly transition toward successful hunting. The mechanisms underlying this rapid behavioral shift and its variability across individuals remain largely unknown. We sought to quantify and characterize this transition as a framework for investigating how innate and experiential information interact to produce value-motivated behavior. A 10-day cricket (*Gryllus sigillatus* or *Gryllus bimaculatus*) exposure procedure was performed on a total of 18 naïve, food-restricted mice. Behavioral trajectories were extracted from videos using the animal position tracking machine learning model DeepLabCut and analyzed to quantify approach, retreat, and hunting behaviors across experimental days. Behavioral analysis revealed that both cricket species produced transitions from avoidance to successful hunting, although this switch was variable rather than universal, with individual mice demonstrating differences in hunting success and learning behavior. The ratio of approach to retreat behavior did not consistently explain transition outcomes. Segmented mixed-effects regression suggested that the immediate behavioral shift following transition was more strongly associated with hunting success than gradual behavioral changes across exposure phases. Individual trajectory analyses further demonstrated substantial variability in approach behavior prior to switching. These findings establish a quantitative behavioral framework for studying rapid value acquisition and motivate future investigations into the neural mechanisms underlying this transition, including ventral striatal activity measurements following behavioral switching.

Biophysical Characterization of Tau Family Microtubule-Binding Domains in Invertebrates

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The tau family is a large group of proteins defined by their use of a shared domain to bind to and modulate the properties of microtubules, a highly conserved cytoskeletal filament. This microtubule-binding domain consists of tandemly repeated stretches of amino acids. Our lab previously observed that the repeat for vertebrates is typically thirty-one amino acids long, while the repeat for invertebrates is thirty amino acids long. Despite the equal binding efficacy of both consensus vertebrate and invertebrate binding domains, shortening vertebrate repeats by removing a residue diminishes microtubule-binding ability. We aim to understand how invertebrate tau proteins, but not their vertebrate counterparts, can efficiently bind to microtubules with shorter repeats. We identified unique features of the invertebrate repeat, including a tryptophan in position 10 and a valine in position 16, and compared the microtubule-binding affinity of consensus invertebrate repeats with sequences without these features. We attached labeled microtubules to a surface and flowed in a buffer containing our GFP-tagged proteins, which we imaged by confocal microscopy. We also tested binding under more physiological conditions by using frog egg extract to simulate the cytoplasm. Our preliminary results indicate that switching the tryptophan to a vertebrate-specific phenylalanine prevents the protein from binding at lower concentrations, while switching the valine to a vertebrate-specific cysteine prevents binding at all protein concentrations tested in the assay (1nM to 5uM). It appears that while both amino acids contribute to microtubule-binding for invertebrate tau proteins, the valine may have particularly important interactions for binding. In future experiments, we can test whether changing the cysteine to a valine in a vertebrate 30-residue repeat improves its binding and whether the valine is sufficient for short-repeat binding. We can then better understand the mechanism by which tau repeats attach to microtubules and how each sequence evolved its features.

Phototunable Modeling of Rheological Extracellular Matrix Heterogeneity

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Lesions such as fibrotic tissues and tumor microenvironments are commonly associated with the dysregulation of extracellular matrix deposition and crosslinking. These changes produce irregularities in the mechanical properties of tissues, including viscoelasticity, a measure of tissues' solidlike and fluidlike behavior under applied stress. While deviations from baseline viscoelasticity have been observed to disturb critical immunocyte behaviours and functions—for instance, by impeding the migration of T-cell-priming dendritic cells—current models used to investigate these disturbances are limited to mechanically homogeneous biomaterials, which fail to capture physiologically accurate patterns and variations in tissue viscoelasticity. The dearth of standardized, rheologically nonuniform in vitro tissue models has left the physiological basis underpinning mechanoimmunological changes poorly understood. This project aimed to develop and experimentally validate a phototunable, collagen-based model for spatially resolved variations in matrix viscoelasticity. We present a collagen-based matrix model displaying photoadjustable crosslinking behavior following strain-promoted azide-alkyne cycloaddition. Oscillatory and stress-relaxation rheometry coupled with selective UV exposure reveal stable but photoreversible increases in matrix viscoelasticity following chemical crosslinking. We then pattern functionalized collagen containing human and murine dendritic cells into areas of variable viscoelasticities via two-photon polymerization. Live cell imaging of the encapsulated dendritic cells reveals substantial reductions in cell motility under elevated crosslinking conditions. If viscoelasticity-associated changes in cell migration phenotypes can be faithfully recapitulated, the model may provide a viable platform to further investigate the biological implications of viscoelastic matrix heterogeneity. Integration of more sophisticated and morphologically complex viscoelasticity patterns into the model, as well as additional computational modeling to elucidate long-term cell-to-fibril and fibril-to-fibril force transmission effects, offer further opportunities for physiologically representative mechanical studies.

Discovering the Specific Mechanism Behind DEPP1-Mediated Mitochondrial Autophagy

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The mechanisms by which skeletal muscle loss occurs in severe diabetes remain incompletely understood. The Wyant Laboratory previously discovered that upregulation of the novel protein C10orf10 (DEPP1) is both necessary and sufficient for fasting-induced muscle atrophy and autophagy. Studies using C10orf10/DEPP1 knockout (KO) mice and transgenic mouse models (e.g., GFP-LC3/RFP) generated on a C57BL/6 background provided strong evidence supporting the hypothesis that DEPP1 is a key downstream mediator of FoxO transcription factor signaling during fasting-induced muscle atrophy. In a pilot study, I used confocal microscopy in C2C12 myoblasts and found that DEPP1 predominantly localizes to mitochondria. Based on this observation, I hypothesized that DEPP1 promotes muscle atrophy through a previously unknown role in mitochondrial biology. To test this hypothesis, I generated a DEPP1 mutant lacking its predicted mitochondrial targeting sequence to determine whether mitochondrial localization is required for its function. Confocal imaging and western blot analyses demonstrated that deletion of this domain attenuated mitophagy under catabolic conditions such as starvation and hypoxia, indicating that mitochondrial localization is essential for DEPP1-mediated activity. I also sought to identify proteins that associate with DEPP1 using co-immunoprecipitation and proteomic analysis. I have not yet identified strong or reproducible interacting partners, which may reflect transient or weak protein-protein interactions under the experimental conditions tested. To define the function of DEPP1 at mitochondria, I am performing confocal microscopy-based colocalization studies in C2C12 cells by labeling mitochondria and lysosomes with fluorescent markers in both wild-type and DEPP1 knockout cells. Preliminary results indicate that loss of DEPP1 reduces mitochondria-lysosome colocalization, suggesting impaired mitophagy. In parallel, I am quantifying mitochondrial DNA (mtDNA) copy number by quantitative PCR to assess mitochondrial abundance and turnover. Together, these experiments will provide mechanistic insight into how DEPP1 regulates mitochondrial homeostasis and contributes to skeletal muscle atrophy under catabolic conditions.

Constructing Odd Cycles for a Class of Fano Problems

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Enumerative geometry studies the set of solutions to certain geometric problems, such as its cardinality when it is finite. This question can be specified to identify the symmetries and constraints among the solutions. In particular, Jordan in 1870 proved that each problem has a Galois group and calculated this group for some examples. Interesting as an object of its own, Galois groups of enumerative problems also inform other properties about the problem, such as the solvability and reality of solutions. This paper investigates enumerative problems of counting 2-planes on a degree d hypersurface in n-space, called (2, $\mathbb{P}^n$, d) Fano problems. Specifically, we modify Harris' technique of constructing a special fiber with exactly one point with multiplicity, aiming to exhibit an odd cycle in the Galois group. This builds upon and refines the result by Hashimoto-Kadetz in classifying Galois groups for other problems. Our construction suggests a similar approach for the remaining classes of Fano problems.

A Mathematical Analysis for Linear and Random-Feature Conditional Diffusion Denoisers

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Diffusion models generate samples by training neural networks to denoise Gaussian corrupted samples. Beyond their practical effectiveness, there is one theoretical property: the minimum value of their loss is tightly linked to mutual information (MI), known as Information-Minimal Mean Square Error (I-MMSE) relationship. Specifically, the mutual information between a signal and a context variable can be exactly expressed by integrating the difference of the unconditional and the conditional denoising loss. This relationship allows us to estimate MI in cases previously unreachable. Here we studied this relation analytically when the function approximators are constrained in two classes of functions. For the linear denoiser we derive that the unconditional loss reduces to a trace involving the signal covariance shrunk by the noise level, and the conditional loss involves canonical correlation between signal and context. For the nonlinear case, we analyze random-feature denoisers whose inputs are projected via a linear mapping then passed through a fixed nonlinearity. Feature means become a Gaussian-smoothed nonlinearity; the loss takes an explained-variance form in feature covariance and signal-feature cross-covariance. We validate these formulae on CIFAR-10 and uncover a Gaussian-equivalence phenomenon. Hermite contributions of third and higher order vanish, and the random ReLU denoiser is entirely its linear and quadratic structure. The random-feature denoising loss thus is written as an explained-variance functional that differs from the linear-denoiser only by an orthogonal projection onto the span of the features. The random-feature loss is therefore never below the linear loss. When the feature width is at least the signal dimension unconditionally (e.g. width of 8192 against dimension of 3072), and at least the signal-plus-side dimension conditionally, nonlinear denoiser reproduces the linear one. Only in the underparameterized regime, where feature width is smaller than signal dimension (e.g. width of 512), does the random-feature nonlinearity strictly underperform the linear denoiser.

Dopaminergic Mechanisms of Social Dysfunction in Transgenic Rat Models of Autism Spectrum Disorders

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Social communication, observed in humans and many other social species, is fundamental to survival and wellbeing. Impairments in social communication are a defining feature of autism spectrum disorder (ASD), yet the underlying neurophysiological mechanisms remain poorly understood. Dopamine (DA) signaling has been implicated in reward and motivation, and neuroimaging studies have reported decreased phasic striatal DA release in adults with ASD. In rodents, ultrasonic vocalizations (USVs) are a primary mode of social communication. Appetitive 50 kHz USVs signal positive affect and elicit social approach behavior, whereas aversive 22 kHz USVs and lower frequency pain squeaks elicit defensive responses such as freezing. Previous studies have shown that 50 kHz USV playback elicits phasic DA release in the nucleus accumbens (NAc) in mice, while recent work suggests that DA signaling in the tail of the striatum (TS) promotes threat avoidance. However, the roles of NAc and TS DA signaling during social communication, and whether ASD-associated mutations alter these responses, remain poorly understood. In this study, we utilized transgenic rat models of ASD that show social behavioral deficits, combined with fiber photometry, DANNCE, a 3D kinematic tracking system, and an empathy paradigm that captures both social transfer of fear and other-oriented comforting behaviors. Observer ASD rats, or wildtype (WT) control littermates, interacted with a WT demonstrator rat in an open field before transfer to a partitioned transparent cage, where the demonstrator received footshocks eliciting aversive USVs and pain squeaks. Later, rats underwent a similar paradigm with no demonstrator in which shocks were replaced with audio playback. DA signals in NAc and TS were recorded simultaneously via fiber photometry during all behavior sessions and analyzed offline. ASD-associated changes in DA responses to aversive and appetitive social calls may reveal circuit-level mechanisms underlying ASD-relevant social dysfunction.

Top-Down Modulation of Vision by Prefrontal Brain Circuits

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Neural activity in the primary visual cortex (V1) is shaped by top-down projections from higher-order cortical regions, yet the circuit mechanisms underlying this modulation remain incompletely understood. The medial prefrontal cortex (mPFC), which regulates cognitive flexibility, emotional processing, and reward-related behaviors, has recently emerged as a potential modulator of visual processing. Our previous work suggests that nonspecific suppression of mPFC activity impairs visual acuity, potentially through vasoactive intestinal peptide-positive (VIP+) interneurons. However, the distinct contributions of the dorsomedial (dmPFC) and ventromedial (vmPFC) subregions remain unknown. This project investigates the anatomical and functional connectivity between the dorsomedial and ventromedial subregions and V1 in adult mice. A retrograde Cre-expressing virus was injected into V1, while a Cre-dependent GFP was delivered to either the dmPFC or vmPFC to selectively label top-down projections. Connectivity is characterized by using slice microscopy and whole-brain imaging. To examine functional consequences, visual evoked potentials (VEPs) are being recorded during selective suppression of dmPFC or vmPFC activity. Anatomical, electrophysiological, and behavioral findings will be integrated to define the distinct contributions of dmPFC and vmPFC pathways to top-down regulation of visual cortical function. Data collection and circuit characterization are currently ongoing. Based on previous findings, selective suppression of prefrontal projections is expected to reduce visual selectivity at higher spatial frequencies, supporting a role for cognitive circuits in sensory processing. A behavioral assay will be developed to evaluate the role of these pathways in visual perception and visual learning.

Therapeutically Modulating Cytotoxic CD8+ T Cells in Alzheimer's Disease

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Alzheimer's disease (AD) is a devastating brain disorder with no cure. Emerging evidence suggests that peripheral CD8+ T cells migrate into the brain and exacerbate neuroinflammation and neurodegeneration in AD. To understand the neuroimmune interactions between T cells and brain-resident cells and mitigate their cytotoxic impact on neurons, we isolated human T cells from whole blood and treated them with a panel of FDA-approved drugs for 24 hours. We then measured drug effects using both flow cytometry and confocal imaging of treated T cells in chemokine□containing 3D microfluidic systems that model neuroimmune interactions. We found that specific inhibitors in our panel significantly reduced T cell infiltration via blocking the chemokine-chemokine receptor axis relative to untreated controls, either through direct antagonist action or through indirect inhibition through other cell signaling pathways. Future research is needed to determine whether or not these drugs work not just within our ex vivo systems but also in vivo models of AD, such as 5xFAD mice.

A Temporal Single-Cell Atlas of the Aging Mouse Hypothalamus

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Aging coincides with the degradation of core circadian processes, including sleep and metabolism, which are governed by the hypothalamus. How aging reshapes the temporal dynamics of the underlying brain circuits remains poorly understood. Here, we characterize age-related changes in neuronal and transcriptomic activity in the hypothalamus across circadian time. Using single-nucleus RNA sequencing, we constructed a temporal atlas of the aging female mouse hypothalamus. We profiled hypothalami from young, middle-aged, and old (12, 52, and 76 weeks) female mice at four time points across the 24-hour cycle. In total, we analyzed 1,339,901 high-quality nuclei mapped to a reference atlas of 66 hypothalamic cell types. Using differential expression analysis and cell type prioritization, we identified the neuronal populations and pathways most associated with age-related transcriptional change. Preliminary results suggest vasoactive intestinal peptide (VIP)- and agouti-related peptide (AgRP)-expressing neurons show the largest age-associated changes in transcriptomic activity. Both populations show diurnal oscillations in young and middle-aged mice, with reduced or absent rhythmicity in old mice. Ongoing analyses will quantify these changes in periodicity using a cosinor regression across cells pseudobulked by neuronal subtype. A decrease in amplitude across age would indicate circadian disruption. VIP neurons reside in the suprachiasmatic nucleus (SCN), the brain's master circadian pacemaker, while AgRP neurons regulate feeding behavior under circadian and SCN regulation. Loss of temporal patterning in the VIP and AgRP populations may represent a mechanism linking hypothalamic aging to metabolic decline in the body. Resolving these changes at the single-cell resolution offers a candidate roadmap of specific brain cell types and pathways that could be targeted to preserve circadian and metabolic health in aging.

Cost-Effectiveness of the Judicialization of Health in a Brazilian Context

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The right to healthcare in Brazil is enshrined in the 1988 Constitution, establishing a legal foundation for healthcare judicialization, a process whereby citizens may contest insurance denials in court by suing their state government. Critics contend that this judicialization system disproportionately facilitates securing access to high-cost treatments that extend drugs beyond their indicated use cases while diverting scarce state-level funding from broader public and population health initiatives that may yield greater benefits on a societal level. In this study, we evaluate the cost-effectiveness of all 6,370 cancer medication cases from 2019-2026 across the 26 states of Brazil. We further assess the distributional equity implications of the healthcare litigation system across income groups using extended cost-effectiveness analysis (ECEA) modeling. Although the majority of cases result in payouts of less than US$20,000 in total, we find that a small number of medications account for a disproportionate share of rapidly increasing judicialization costs while struggling to meet the Brazilian cost-effectiveness threshold of approximately US$8,000 per quality adjusted life year (QALY). These key drivers of judicialized healthcare spending can account for more than one-quarter of state-level judicial healthcare expenditures despite only addressing a small fraction of cases, with individual awards approaching or exceeding US$200,000. We seek to expand this work to medications acquired through the litigation system for additional disease areas and compare the impact of judicialization on the Brazilian system with that in other Latin American countries, including Colombia and Costa Rica, where healthcare litigation is similarly prevalent.

Creating an FKBP-FRB Acute Recruitment System for Lipases to Lipid Droplets and Golgi Apparatus

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Lipid droplets are highly regulated monolayer subcellular organelles that function as the primary triglyceride and fat storage sites within the cell. Current methods for studying lipid droplet degradation rely on starvation of cultured cells to upregulate endogenous lipolysis and lipophagy pathways. However, there are currently limited ways to acutely control the degradation of lipid droplets. Therefore, the objective of this project is to develop an assay that rapidly recruits lipase proteins to lipid droplet surfaces. To create this system, we used restriction enzyme cloning to generate plasmid constructs encoding tagged lipases, including ATGL and DDHD2, and tagged organelle markers for lipid droplets and the Golgi apparatus. These constructs were fused to FKBP or FRB, protein domains that dimerize in the presence of rapalog, a small-molecule inducer. Cells were co-transfected with the corresponding FKBP- and FRB-tagged constructs, such as ATGL-FKBP and lipid droplet-FRB. Upon rapalog addition, the FKBP-tagged protein is rapidly recruited to the FRB-tagged organelle marker. Recruitment was then evaluated using confocal microscopy. We successfully generated the lipase and organelle-targeting plasmid constructs. Following rapalog treatment, recruitment was highly efficient, with confocal microscopy showing strong colocalization of lipases with the targeted organelles within five minutes of induction.

Investigating FAST p13-Mediated Cell–Cell Fusion Through Genome-Wide CRISPR Knockout Screening and APEX2 Proximity Labeling

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Fusion-associated small transmembrane (FAST) proteins are a class of short (100–200 amino acids), nonstructural proteins derived from fusogenic reoviruses that mediate direct cell–cell membrane fusion through interactions with host cytoskeleton. The Khalil lab's synthetic immune cell fusion (sICF) platform harnesses the FAST protein variant Broome orthoreovirus p13 to mediate inducible, programmable, antigen-directed fusion between engineered T cells and target cells for therapeutic payload delivery, e.g., tumor antigen-directed cytotoxicity. Despite the therapeutic potential of FAST proteins, the molecular pathways through which they mediate fusion remain poorly understood. We are conducting two genome-wide CRISPR knockout screens to identify genes required for p13-mediated fusion in fusogenic effector cells and in target cells. Jurkat T lymphocytes were engineered to express p13 under the control of doxycycline-inducible αCD19 sICF gene circuits. The resulting fusogenic cell line will be transduced with a genome-wide lentiviral CRISPR knockout library to generate a pooled population of effector cells bearing diverse gene disruptions. These cells will be co-cultured with CD19+ NALM6 B lymphocytes as model fusion targets. Effector cells that fail to fuse will be isolated by fluorescence-activated cell sorting and sequenced to identify effector-cell genes required for fusion. In parallel, CD19+ NALM6 B lymphocytes will be perturbed using the same genome-wide CRISPR knockout library and screened to identify target-cell genes required for fusion. To complement this genomic approach, we evaluated proximity-dependent biotinylation using engineered ascorbate peroxidase APEX2 as a potential method for identifying proteins that interact with p13. We found that p13 did not remain functional when genetically fused to APEX2 at the tested sites, providing guidance for the design of future proteomic studies. We anticipate that our findings will help elucidate the poorly understood molecular pathway through which p13 mediates cell–cell fusion.

Automatic differentiation-based inference of rules for multicellular patterning

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During development, cells become arranged into distinct architectures, enabling the formation of tissues, organs, and the overall body plan. This organization requires both the differentiation of cells into defined fates and the rearrangement of cells into their proper positions. Differentiation is now comparatively well understood, but the rules governing rearrangement are not. The differential adhesion hypothesis holds that cells sort according to their relative adhesive affinities, and adhesion-molecule identity and expression level are known to drive sorting and boundary formation. Yet these results remain largely qualitative and confined to two cell types, limiting both our understanding of how morphogenesis produces reproducible form and our ability to engineer tissues with a chosen geometry. Recent high-throughput measurements from the Klein Lab now provide the data needed to study these rules quantitatively and beyond two cell types, assaying 10^4-10^5 spheroids assembled from random combinations of cells expressing different adhesion molecules and yielding paired readouts of spheroid composition and 3D cell position. A statistical framework then allows inferring relative adhesion energies from such data. Here, we develop a framework to generate desired multicellular arrangements based on these inferred adhesion energies. To do so, we build on an automatic differentiation approach found in literature to infer the optimal pair-wise adhesion energies that will drive self-organization of a target structure. We modify the original approach to minimize a maximum mean discrepancy (MMD) loss of the 3D coordinates of cells to a target structure. With this change, we recapitulate experimentally observed rules for two cell types, and demonstrate design of structures with three and four cell types. We then restrict the approach to select only from empirically-observed adhesion energies. By removing the need for configuration-specific loss functions and using empirically-inferred energies, our approach connects statistical inference of adhesion parameters to the rational design of synthetic tissues.

Development and Evaluation of Chiseling for Reliable Subgroup Discovery in Randomized Clinical Trials

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Individual patients can experience substantially different benefits and risks from the same medical treatment. Recognizing this variation and translating it into treatment decisions is a central challenge in precision medicine and can support more effective and efficient allocation of healthcare resources. This project aims to identify clinically meaningful patient subgroups with heterogeneous treatment effects and benefit-risk profiles using participant-level data from randomized clinical trials. To accomplish this, we apply Chiseling, a recently developed statistical framework that increases power to discover such subgroups while preserving valid inference. We analyze data from three randomized clinical trials: the Diabetes Prevention Program (DPP), the Systolic Blood Pressure Intervention Trial (SPRINT), and the Childhood Asthma Management Program (CAMP). Candidate subgroups are defined using baseline demographic, clinical, and behavioral characteristics, and evaluated in terms of both treatment efficacy and adverse outcomes. For example, in the DPP, we examine which patient subgroups have a more favorable benefit-risk profile with metformin than with intensive lifestyle intervention. Although the lifestyle program produced the larger average treatment effect in the original trial, the metformin regimen is generally easier to implement and sustain, potentially making it the better overall choice for patients with comparable outcomes under both treatments. Results will focus on both clinical interpretation and methodological evaluation. Clinically, we will identify patient subgroups whose treatment benefits and harms differ meaningfully from trial-wide averages and characterize them using baseline features. Methodologically, we will compare Chiseling across model classes and feature sets to quantify its power gains, clarify practical implementation choices, and assess its use with flexible machine-learning tools. Together, these analyses aim to produce statistically reliable, interpretable findings that can more directly inform physicians' treatment decisions.

Src Kinase-Dependent CALR Expression for Macrophage Engulfment of Leukemic Cells in Vivo

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Acute myeloid leukemia (AML) is one of the most common leukemias, with nearly 150,000 new cases diagnosed each year. There is an urgent need to develop therapies that target leukemic cells, which drive AML's 30–40% relapse rate. Previous work from this lab demonstrated that macrophages preferentially preserve healthy hematopoietic stem and progenitor cells (HSPCs) while eliminating unhealthy ones through the "eat-me" signal Calreticulin (CALR). However, leukemic cells exhibit reduced surface CALR expression, enabling them to evade macrophage-mediated phagocytosis. A major unmet need is to identify approaches that selectively induce surface CALR on leukemic cells to promote macrophage clearance. A chemical drug screen identified a Src family kinase inhibitor (SFKi) that increases surface CALR on a panel of leukemic cells in vitro without significantly impacting healthy HSPCs. Preliminary confocal microscopy studies examining endoplasmic reticulum (ER)-resident proteins revealed increased formation of ER-derived vesicular structures within the cytoplasm following SFKi treatment, suggesting enhanced intracellular protein trafficking. This study aims to elucidate the mechanism regulating CALR expression in response to SFKi treatment. We will further evaluate the in vivo relevance of this pathway by measuring disease burden in zebrafish genetically engineered to develop leukemia and zebrafish embryos transplanted with human leukemic cells. Collectively, this work seeks to provide insight into the mechanism underlying SFKi-mediated clearance of leukemic cells by macrophages and to evaluate its in vivo therapeutic potential.

Mapping Transcription Factor Regulators of Stability in Human Tregs

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The immune system must constantly distinguish the body's own tissues from foreign threats, and this balance sometimes fails, leading to autoimmune disease. Regulatory T cells, or Tregs, are one of the main safeguards against this failure, suppressing immune responses that would otherwise attack healthy tissue. CD4-positive T cells can differentiate into several types of helper cells depending on the signals they receive, so a central question in immunology is what allows some of these cells to become and remain Tregs rather than adopting a different identity. Despite decades of study, the transcription factors that maintain a stable Treg identity in human cells are not fully understood. This project used single-cell RNA sequencing data from human CD4-positive T cells to search for transcription factors associated with stable Treg identity. Established Treg markers, including FOXP3, IL2RA, and CTLA4, were used to define Treg populations, and gene expression differences between these cells and other CD4-positive T cells were compared to identify transcription factors enriched in Tregs. These expression patterns were then intersected with predicted transcription factor binding sites near Treg-associated genes to prioritize candidates most likely to directly maintain Treg gene expression, rather than merely correlating with it. Final results are not yet available, so this project does not claim that any candidate transcription factor controls Treg identity. However, the analysis has produced a ranked list of candidate regulators for future testing and established a framework for narrowing a large gene expression dataset into specific, testable hypotheses. Future work could compare these candidates across additional sequencing datasets and test whether they affect Treg stability, plasticity, or function through perturbation experiments. This work may help clarify how transcriptional regulation shapes immune tolerance and could eventually inform strategies for improving T-cell-based therapies.

Characterizing the Myogenic and Lysosomal Phenotype of Skeletal Muscle Stem Cells in Cystinosis

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Cystinosis is a rare lysosomal storage disorder characterized by progressive skeletal muscle weakness, yet the cellular mechanisms driving this myopathy remain poorly understood. Previous studies have identified impaired differentiation in cystinosis patient-derived myoblasts, but the broader effects of the disease on skeletal muscle stem cell proliferation and lysosomal phenotype remain unclear. This study investigates how cystinosis alters these processes to better understand the mechanisms underlying muscle degeneration. Primary human myoblasts derived from cystinosis patients and unaffected donor controls were expanded in two-dimensional cell culture and analyzed using immunofluorescence microscopy. Proliferation and myogenic commitment were assessed by staining for myogenic regulatory transcription factors PAX7 and MYOD, respectively. Myogenic differentiation was evaluated using Myogenin staining and quantification of multinucleated myotube formation through fusion index analysis. Lysosomal phenotype was examined using LysoTracker staining. Preliminary findings suggest that cystinosis-derived myoblasts proliferate poorly and exhibit impaired myogenic differentiation compared with unaffected controls. Cystinosis cultures contained significantly fewer PAX7- and MYOD-positive cells, indicating reduced maintenance of the proliferative myogenic population and diminished myogenic commitment. Following differentiation, cystinosis myoblasts generated significantly fewer Myogenin-positive cells and exhibited reduced myotube fusion, with fewer nuclei incorporated into multinucleated myotubes. In addition, cystinosis cells demonstrated increased LysoTracker staining, consistent with lysosomal accumulation resulting from defective lysosomal cystine transport. Together, this work expands previous observations of impaired differentiation by providing an integrated characterization of proliferation, myogenic differentiation, and lysosomal phenotype in cystinosis-derived skeletal muscle stem cells. These findings suggest that lysosomal dysfunction impairs muscle stem cell function and may contribute to the progressive muscle weakness observed in cystinosis. By defining these cellular abnormalities, this work establishes a foundation for future studies investigating how lysosomal dysfunction disrupts skeletal muscle regeneration and for the development of therapies targeting muscle stem cell function in cystinosis.

Mixing in High-Dimensional Expanders and Applications to Pseudorandomness

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In computer science, a graph is a collection of vertices with edges between the vertices. An expander graph is a type of graph with favorable properties, such as being well-connected and sparse. Expander graphs are of high interest due to their relevance to algorithms, complexity, cryptography, and more. Generalizations of graphs to higher dimensions are referred to as hypergraphs, and generalizations of expander graphs are types of hypergraphs called high-dimensional expanders (HDX). Motivated by the role of HDX in many recent breakthroughs across theoretical computer science, there is a lot of work dedicated to a better understanding of high-dimensional expansion. A long line of work is dedicated to trying to generalize results from the graph case to the higher dimensional cases. We know a key lemma about expander graphs, called the Expander Mixing Lemma, which states that the edges of certain d-regular graphs are evenly distributed throughout the graph. We also have a converse to the Expander Mixing Lemma. Currently, both the lemma and its converse have generalizations from expander graphs to high dimensional expanders that are simplicial complexes, but there is an additional logarithmic loss factor in the converse in the hypergraph setting. We explore whether this logarithmic loss is necessary, in particular if it is necessary under stronger assumptions of symmetry or regularity. Furthermore, we explore if the logarithmic loss factor is necessary when considering the related notion of local spectral expansion.

Mechanistic Characterisation of PRC2

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Polycomb Repressive Complex 2 (PRC2) is an essential protein complex that controls gene silencing by modifying chromatin- the packaging material of DNA. Although the complex's catalytic activity is vital for transcriptional regulation, some of the intrinsic allosteric and structural mechanisms that determine how PRC2 is activated and maintained remain unclear. Recent base editor scanning identified a critical functional hotspot at the interface between the EZH2 MCSS and SUZ12 VEFS domains (the MCSS-VEFS interface), where mutations such as EZH2 C260R and SUZ12 N607G impair PRC2 activity and diminish H3K27me3 deposition in cells without reducing protein abundance or subunit assembly. As these mutant complexes assemble normally in vivo, we hypothesise that this interface controls an intrinsic regulatory mechanism required for enzyme function. To investigate how this functional hotspot contributes to wild-type PRC2 architecture in vitro, we express and purify recombinant wild-type and mutant protein complexes (including EZH2 C260R, EZH2 C260A, and SUZ12 N607G). We then use targeted biochemical assays- including testing for allosteric stimulation by trimethylated H3K27 (H3K27me3) peptides- alongside electrophoretic mobility shift assays with reconstituted 185-base-pair nucleosomes to measure how effectively the mutant complexes bind and modify their substrates. We expect our results to show whether this loss of function is driven by mechanisms such as defective nucleosome binding or a broken allosteric activation. By pinpointing why these specific mutations cause the complex to fail, this research will give us a much clearer picture of how wild-type PRC2 functions normally.

A Salp-Mimetic Biohybrid Muscular Pump for Investigating the Design Principles of Biological Pumps

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Muscular pumps have evolved independently in many animals, from vertebrate hearts to free-swimming tunicates such as salps. Although these systems perform the same function (moving fluid through coordinated muscle contraction), the design principles that make them effective remain poorly understood. In particular, it is unclear whether coordinated contraction of circular muscle bands alone is sufficient to generate propulsion or whether additional structures, such as valves, are also required. To investigate this question, we developed a simplified biohybrid model inspired by the salp. The model isolates the muscle-band architecture by removing valve and assembly components, allowing the role of peristaltic contraction to be studied independently. Two-dimensional muscle-band constructs were fabricated by bioprinting a fiber-infused gelatin ink (FIG-ink) scaffold and seeding it with human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs). After culture, contractile behavior, fluid flow, and swimming performance are evaluated under both field and point electrical stimulation. Thus far, the biohybrid constructs have been successfully fabricated and maintained in culture, demonstrating the feasibility of the platform. However, contractile performance has not yet been sufficient for quantitative assessment of fluid flow or propulsion. By providing a simple, controllable platform for studying how muscle architecture drives fluid propulsion, this work lays the groundwork for uncovering general design principles of biological pumps. These insights may inform the future development of biohybrid pumping systems, including engineered cardiac tissues and, ultimately, artificial heart technologies.

Adolescent Gaboxadol as a Sleep-Based Intervention for Social Behavior in a Male C57 Mouse Model of Fragmented-Care Early-Life Stress

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Early-life stress in humans, including neglect and fragmented caregiving, is linked to lasting social difficulties, elevated risk of depression and anxiety, and disrupted sleep during the same developmental period. Disrupting sleep within critical windows can itself cause long-lasting social changes, yet whether enhancing sleep can reverse deficits following early-life stress, rather than sleep loss itself, remains unclear. Our project tests whether boosting deep, non-REM slow-wave sleep during adolescence can improve social behavior in a mouse model of early-life stress. Male wild-type C57 mice underwent a fragmented-care paradigm from postnatal days 2–9, in which limited bedding and nesting over a raised mesh floor drives inconsistent maternal care. Treated mice then received daily 2 mg/kg gaboxadol, a drug that enhances non-REM slow-wave sleep by acting on extrasynaptic GABA-A receptors, across an adolescent window (postnatal days 37–49). Social behavior was measured in a three-chamber assay using EthoVision, scored with sociability and social novelty preference indices (the difference in chamber times over their sum). In an initial cohort of seven mice, sociability was intact: all seven preferred an unfamiliar mouse over an object ($t(6) = 3.58$, $p = 0.012$), confirming the assay works. Whereas untreated mice in this model typically prefer a familiar mouse, treated mice showed a trend toward the novel mouse (novelty index 0.128; six of seven above chance), a large effect in the predicted direction (Cohen's $d = 0.79$) and an encouraging early signal, though not yet statistically significant ($p = 0.083$) in this small cohort . Ongoing work adds a larger, vehicle-controlled cohort and re-tests treated animals about one month after dosing to assess whether any improvement persists. Future studies will examine how enhancing slow-wave sleep might improve social behavior, potentially focusing on dopamine signaling in the ventral tegmental area, a brain reward region.

Characterizing Early, Asymmetric Wound-Induced Gene Expression in the Acoel Hofstenia miamia

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Regeneration, the replacement of missing tissue, is fundamental to animal biology. While human regeneration is limited, some organisms are capable of whole-body regeneration (WBR): regenerating essentially any missing tissue de novo. WBR requires re-establishing body axis pattern, or "polarity"; organisms must identify which tissues require reconstruction and establish their regenerative programs at the appropriate locations (e.g., head fragments regenerating a tail, and vice versa). Across WBR-competent models, polarity is mediated by asymmetric expression of Wnt signaling components. Despite being required for accurate polarity, the mechanisms behind this asymmetry remain incompletely understood. This study characterizes the phenomenology of asymmetric, wound-induced gene expression across injury contexts in the acoel Hofstenia miamia. Animals were sagittally amputated or given incision wounds, with tissue fixed at 0, 3, and 6 hours post-injury (hpi). We performed fluorescent in situ hybridization (FISH) and confocal microscopy to visualize mRNA expression patterns, and qPCR to compare expression across time points and tissue location. In planarians, expression of the Wnt antagonist notum is thought to depend on injury to longitudinal muscle cells along the anterior-posterior axis. Using sagittal amputation to decouple longitudinal muscle injury from wounding, we investigated whether Wnt signaling in Hofstenia relies on an analogous, muscle-injury-dependent mechanism. Symmetric, general wound-response gene follistatin-1 and Wnt target sp5 were visualized across time-points at sagittal wounds, suggesting Wnt activation does not require longitudinal muscle injury. Follistatin-1 expression at incision wounds confirmed minor injuries can initiate the same symmetric wound responses as amputation; additional experiments will examine sp5 expression at incisions to determine whether minor injuries can also activate asymmetric Wnt signaling. Furthermore, qPCR revealed early wound-induced expression of symmetric genes runt and follistatin-1 in sagittal wounds. This characterization will extend to additional generic and asymmetric wound-induced genes (wnt3, pez, egr, tcf-2, brachyury), further elucidating the decision-making processes underlying regenerative patterning.

Mapping the Active Galactic Nuclei, Shocks, and Star Formation in Active Galaxies Using a 3D Diagnostic Diagram

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Supermassive black holes, known as active galactic nuclei (AGN), play a critical role in galaxy evolution by either suppressing or enhancing star formation. Shocks generated by AGN activity are key to resolving this puzzle, but observationally distinguishing these three galactic excitation sources (star formation, AGN, and shocks) remains a significant challenge. To address this limitation, this study utilizes a recently developed theoretical three-dimensional (3D) diagnostic diagram designed to simultaneously disentangle the excitation sources using optical integral field spectroscopy. This study applies this novel tool to the galaxies NGC 1068, NGC 4303, and NGC 1365 using data cubes from the Siding Spring Southern Seyfert Spectroscopic Snapshot Survey (S7). The galaxies were chosen because they have multi wavelength data which can be used for further analysis.Thus far, the research workflow has involved creating two-dimensional (2D) emission line flux ratio maps, velocity maps, and velocity dispersion maps of each galaxy. From these maps, a Baldwin-Phillips-Terlevich (BPT) diagram that uses optical emission line ratios to map energy sources was created, and it clearly highlighted HII (star-forming) regions, AGN regions as well as the AGN-HII mixing sequence. However, the BPT diagram could not distinguish AGN from shock excitation because they produce similar emission-line ratios. To address this, the project implements the 3D diagnostic framework by incorporating velocity dispersion as a third axis. Theoretical models of HII regions, AGN, and shock regions from MAPPINGS version 5.2 were then added onto the 3D diagram. This 3D approach successfully revealed regions of each excitation source. These results will determine the dominant power source in each galaxy, and future analysis will combine this work with X-ray, radio, and infrared data to build a more complete picture of how AGN activity generates shocks. Ultimately, mapping regions of each excitation source will help uncover how these energetic processes interact, contributing to answering the question of how supermassive black holes and galaxies co-evolve.

Computational Methods for Single-Cell Bacterial Transcriptomics

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Bacterial populations display phenotypic heterogeneity in response to stressors e.g. nutrient availability, temperature, oxygen, or environmental toxins. ProBac-seq is a novel probe-based technique that enables highly sensitive scRNA-seq in bacteria, but variable probe-specific hybridization efficiencies with multiple probes associated with each gene introduces technical noise unaccounted for by existing probe-based scRNA-seq analysis pipelines. This project aims to (1) develop and validate an empirical Bayes approach to transforming probe counts to transcript counts, (2) use variational inference to obtain a low dimensional representation of the cell and (3) identify rare gene networks in low dimensional space using independent component analysis (ICA) from ProBac-seq data. We will conduct a computational method-development study using multiplexed ProBac-seq data from E. coli K12 MG1655 grown in LB to OD 0.1 with subpopulations subjected to starvation, high temperatures and antibiotic exposure, as well as simulated cell data. An empirical Bayes model is used to estimate probe efficiency and true transcript counts, which act as inputs to a variational autoencoder to represent each cell in a ten-dimensional latent space. Co-regulated gene networks are then identified via ensemble ICA, which should display differential expression in rare subpopulations. We hypothesize that empirical Bayes methods and variational inference methods will substantially improve the accuracy of predicted transcript counts relative to currently used methods (summation of probe reads). We further hypothesize that ensemble ICA, applied to corrected data, will yield reproducible gene networks corresponding to known regulatory pathways e.g. for drug or heat resistance. These findings would indicate that explicitly modeling probe-level technical noise, over the current assumption of uniform capture efficiency, meaningfully improves detection and interpretability of rare bacterial phenotypes with biological and clinical importance. Beyond ProBac-seq, the approach reveals a generalized template for other probe-capture single-cell sequencing technologies facing similar statistical challenges.

Mosaic Loss of the Y Chromosome Reprograms Fibroblasts During Skin Tumorigenesis

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Skin cancer is the most common form of cancer, with more cases diagnosed annually than all other cancers combined. Biological sex influences cancer susceptibility and progression; however, the underlying reasoning remains unknown. While tumor-intrinsic drivers have been studied, the contribution of fibroblasts, the predominant stromal component of the tumor microenvironment (TME), to sex-specific cancer biology remains unexplored. Although fibroblasts normally maintain tissue homeostasis, they can become tumor-promoting by regulating inflammatory signaling and drive field cancerization, an age-associated process where tissue undergoes progressive changes that promote new tumor formation. One of the most common age-associated somatic alterations in men is mosaic loss of the Y chromosome (LOY). LOY is associated with many diseases, including increased risks of cancer, cardiovascular disease, neurodegeneration, and reduced lifespan. Studies in melanoma also suggest that Y chromosome loss may confer male-specific vulnerabilities to tumorigenesis; however, its direct effects on fibroblasts remain unknown. We hypothesize that loss of the Y chromosome promotes dermal fibroblast plasticity and proliferation, contributing to sex-specific differences in field cancerization and skin cancer progression. To test this hypothesis, we deleted the Y chromosome in fibroblasts using CRISPR-Cas9, with chromosome loss confirmed by fluorescence in situ hybridization (FISH). We will co-culture mosaic LOY fibroblasts with CAL27 squamous cell carcinoma (SCC) cells to determine how LOY stromal cells affect tumor cell behavior. We will perform functional assays, including cell proliferation analyses, to assess changes in fibroblast activation and tumor-promoting activity. Based on our preliminary data, we expect that deletion of the Y chromosome will alter fibroblast activation and proliferation, while shifting male fibroblasts toward a more female-like state. By understanding how sex chromosomes shape fibroblast function, we can establish a link between aging, LOY, stromal plasticity, and skin cancer development, while providing broader insights into how sex chromosomes influence the tumor microenvironment and cancer susceptibility.

Rejuvenating Aged T Cells: Genetic Reprogramming to Restore Function

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Aging weakens the immune system partly by increasing the proportion of senescent T cells, which proliferate poorly and show altered effector function. This decline leaves the body less able to fight infection and cancer while promoting chronic inflammation and autoimmunity. The genetic drivers of T cell senescence remain poorly understood, however, limiting efforts to reverse it. This project asks whether targeted transcription factor perturbation can restore more functional states in senescent human CD8+ T cells. CD8+ T cells, key mediators of immunity, were isolated from blood of two donors aged 75 or older. Rather than using bulk unsorted cells, a CD57+ CD28− senescence-associated population was isolated by fluorescence-activated cell sorting, enriching for the senescent cells of interest so that any effect of perturbation could be attributed to them rather than diluted by non-senescent cells. Sorted cells were cultured and transduced with lentiviral shRNA constructs targeting three candidate regulators of senescence, ZNF124, NR1H4, and DAXX, alongside a non-targeting control and an untransduced condition. Knockdown tests whether these factors causally maintain the senescent state. Flow cytometry then tracked senescence, proliferation, and memory markers, including p16, KLRG1, Ki-67, and CCR7, across timepoints. Preliminary data suggest that knockdown of ZNF124 and NR1H4 may raise CCR7 expression relative to control, hinting at a partial shift away from a terminally differentiated state, though this signal is not yet confirmed across replicates, in part because of limited cell viability. Analysis is ongoing. Future work will repeat these knockdowns with the full marker panel and extend the analysis to proliferation and other measures of immune function. Determining whether knockdown of these regulators reverses hallmarks of senescence could point toward molecular programs that might eventually be targeted to improve immune responses to infection, cancer, and immunotherapy during aging.

HBD Catalyzed Asymmetric Diazenation

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Many of the most important molecules in medicine and biology are chiral, meaning they exist in two mirror-image forms that can behave very differently in the body, and being able to selectively make the desired form (enantioselectivity) is a well-researched goal in chemistry. Diazonium salts (R–N≡N□), most familiar as the reagents behind azo dyes, can also install nitrogen atoms onto other molecules, a strategy known as electrophilic amination. Despite this potential, methods for doing so enantioselectively remain underdeveloped. When diazonium salts react with silyl enol ethers, for example, the products are α-diazenyl ketones bearing a new stereocenter, but controlling the outcome at that stereocenter has proven difficult. This project, based in the Jacobsen group, aims to develop hydrogen-bond-donor (HBD) catalysts capable of controlling this bond-forming step enantioselectively, generating enantioenriched diazene products that serve as versatile precursors to chiral aminoalcohols, α-tertiary amines, etc. To pursue this goal, a family of monomeric, chiral HBD catalysts and diazonium salt substrates were synthesized. Our catalysts were then evaluated in a phase-transfer-based diazenation reaction, in which the HBD both promotes the initial enantioselective C–N bond-forming step and mediates a subsequent kinetic resolution of the minor enantiomer product, with yield and enantiomeric excess (ee) measured across catalysts. Using monomeric HBD catalysts, initial reactions gave unfavorable yields and ee values in the 40-50% range. Future work will focus on synthesizing dimeric catalysts, a scaffold previously reported to reach ee values as high as 96% in related diazenation reactions. In tuning the polarity of the organic phase, the dimeric catalysts were able to achieve these high levels of ee, but at the expense of yield, consistent with a kinetic-resolution model of catalysis. After synthesizing families of dimeric HBD catalysts, our next goal will be to overcome the yield-enantioenrichment trade-off previously observed and rather optimize both.

Leveraging Multi-Omics to Identify Aging and Rejuvenation Oligodendrocyte Biomarkers

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Aging research is critical to addressing the growing prevalence of neurodegenerative diseases. As populations around the world continue to age, aging-related neurodegenerative diseases such as Alzheimer's and Parkinson's are becoming an increasingly important challenge, affecting not only patients but also their families, caregivers, and healthcare systems. Thus, we aim to investigate aging mechanisms to find potential therapeutic targets by finding biomarkers for aging and rejuvenation. Single cell and single nuclei RNA sequencing datasets were used to identify potential biomarkers for various cell types to predict aging and rejuvenation. These datasets included manipulations that caused rejuvenation and/or accelerated aging of the brain: 1) parabiosis where circulatory systems of young and old mice are surgically connected, 2) microbiome depletion achieved using oral antibiotic administration, 3) caloric restriction, and 4) increased exercise. The Rubin Lab utilized the single cell and single nuclei data from these experiments, applying Random Forest (RF) and eXtreme Gradient Boosting (XGBoost) machine learning models to identify cell type specific gene signatures associated with aging and rejuvenation. As white matter is particularly vulnerable to age-related degeneration, oligodendrocyte lineage cells which produce myelin and maintain white matter are examined in this project. Building upon these findings, this study aims to experimentally validate the predicted biomarkers *in vivo* using a heterochronic parabiosis mouse model. Brains from young and old mice that were surgically joined to exchange systemic aging and rejuvenation factors were collected. Specific regions of the brain were cryosectioned and analyzed by immunofluorescence to evaluate the expression of candidate oligodendrocyte aging and rejuvenation biomarkers. Analyzing these biomarkers will improve our understanding of the molecular mechanisms underlying brain aging and may guide the development of future therapeutic strategies for age-related neurodegenerative diseases.

Virtual Reality and Biofeedback for Adolescents with Chronic Dizziness

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Vestibular migraines and persistent postural-perceptual dizziness (PPPD) are common causes of chronic dizziness, defined as dizziness occurring on most days for weeks to months, in adolescents. Nearly half of pediatric patients with PPPD are partially or fully absent from school and often experience symptoms for months or years before diagnosis. Biofeedback (BFB) therapy has been effective in treating vestibular disorders, but does not provide in vivo exposure and a real-world symptom-triggering environment. This pilot study evaluates whether virtual reality (VR) combined with BFB, systematic desensitization exposure-response prevention (SDERP), and cognitive-behavioral therapy (CBT) reduces youths' chronic pain and dizziness. 12 patients aged 13–25 were recruited from the Boston Children's Hospital's Balance and Vestibular Clinic. Participants complete self-reported repeated measures of dizziness and pain symptoms severity, duration, and frequency at baseline, mid-point, and endpoint across a 13-visit treatment program combining BFB, SDERP, CBT, and VR. Patients are exposed to two 360° VR environments at varying intensity levels. These include a grocery store environment and a participant-selected environment like a crowded restaurant, hallway, or movie theater. The pre-treatment and post-treatment data are used to evaluate outcomes. Since the previous BFB, CBT and SDERP protocol has shown significant reductions in pain and dizziness, we anticipate similar or greater reductions with the addition of VR exposure. Patient symptoms, functional outcomes, and VR tolerability variables may vary based on gradual assisted exposure severity and environmental intensity. We hope VR exposure will further reduce patients' fear responses and improve their functioning in symptom-associated places and experiences. Data collection is ongoing. If feasible and well-tolerated, VR exposure offers a scalable way to simulate real-world triggering environments within existing behavioral treatment frameworks for adolescent chronic dizziness. Findings can guide larger study designs and the development of VR tools to improve functional outcomes in this population.

Wiring an Omnivore: Mapping Neural Development in Pristionchus pacificus Across Age

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Connectomes provide a map of how neurons are physically connected, but most complete developmental connectomic work has centered on C. elegans, a bacterial-feeding nematode. This leaves an important gap in understanding how neural wiring develops in related animals with different behaviors and ecological demands. This project examined the neural architecture of Pristionchus pacificus, a nematode that can feed on bacteria and prey on other nematodes, across multiple developmental ages. By comparing neural structure at different points in development, the study asked how the organization of the P. pacificus nervous system changes over time and whether these changes may help support its more flexible feeding behavior. Serial image slices of P. pacificus were manually annotated to identify neurons and reconstruct three-dimensional neural structures. Computational segmentation tools, including 3D U-Net models, were used to assist this reconstruction and reduce the amount of manual tracing required, but the main analysis focused on developmental differences in neural organization. The results showed that neural structures in P. pacificus are not static across age. Instead, the developing nervous system displayed age-dependent differences in neuron shape, position, and connectivity patterns. These findings suggest that the developmental stage is an important factor in understanding the P. pacificus connectome and may help explain how related nematodes adapt their neural wiring to different behavioral needs.

Evaluating the Potential of Small Molecule Forskolin to Maintain Chondrocyte Identity in Patient-Derived Primary Chondrocytes

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Cartilage degradation affects over 250 million people worldwide and is a leading cause of pain and immobility. Primary chondrocytes, the cartilage cells harvested directly from the joint, are a key model for studying cartilage biology as they closely reflect the behavior of native cartilage cells. However, when cultured outside the body, primary chondrocytes begin to dedifferentiate. This entails losing expression of cartilage markers, adopting a different, fibroblast-like morphology, and ceasing production of extra-cellular matrix, a hallmark functional property of articular cartilage. These phenotypic changes present a significant obstacle for maintaining a large quantity of physiologically relevant chondrocytes suitable for experimental modeling. Recently, forskolin, a molecule that stimulates cyclic AMP production by activating adenylyl cyclase, has been found to promote chondrogenicity (chondrocyte identity) in paraxial mesoderm derived from human embryonic stem cells. We seek to investigate if forskolin is able to maintain chondrogenicity in primary chondrocyte culture. To do so, we acquired primary chondrocytes from femoral heads discarded after patient surgery and plated them in chondrocyte media. Half of the plates were cultured in media that was supplemented with forskolin. RNA was collected for RT-qPCR to examine expression profiles following each cell passage. We also created 3-D micromasses by seeding chondrocytes in high cell density spots to examine matrix secretion. These micromasses will be sectioned and stained for cartilage markers using immunohistochemistry. Preliminary morphology results indicate that forskolin-treated chondrocytes better maintain their chondrogenic identity, whereas the untreated group exhibits fibroblast-like morphology. RT-qPCR and histology results will further characterize the extent to which forskolin is capable of maintaining chondrogenicity in primary chondrocytes. If successful, forskolin could provide a simple strategy for supporting the expansion of primary chondrocytes without compromising their identity. As an extension, forskolin might also improve primary-chondrocyte-derived therapies such as Autologous Chondrocyte Implantation (ACI) and Matrix-Induced Autologous Chondrocyte Implantation (MACI).

Developing Ultra-Small, Lightweight Power and Signal Generation for Bio-Inspired Robots

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For insect-scale microrobots, a major barrier to untethered operation is the onboard driving electronics, which must be lightweight and compact yet still produce the reciprocating output actuators required. This project develops ultra-small electronics operating at 1–2 V to drive the low-voltage voice-coil actuators of microrobots, using two complementary approaches. The first is a self-oscillating design that does not require a microcontroller. It is built around a comparator-based relaxation oscillator: a simple circuit that switches itself on and off to produce a steady, repeating square-wave drive signal. Both its frequency and its duty cycle (the fraction of each cycle the signal stays on) can be tuned over a wide range (roughly 0.4 to 136 Hz). We developed and validated an analytical model of the oscillator with simulation and physical implementation. An H-bridge output stage then drives the actuator with a bidirectional, biphasic current waveform at 2 V, on a 7.6 × 3 mm circuit board weighing 18 mg. In an initial proof-of-concept test, this circuit drove a gliding microrobot to flap its wings. The second approach uses a microcontroller for a more complex, programmable drive: a 20 kHz PWM carrier sets each pulse's amplitude while software defines its spike-and-hold envelope, so the waveform can be tuned for each robot. Six channels, each driving its own H-bridge at fixed 60° phase offsets, coordinate the multi-leg gaits of walking robots, such as the compliant-mechanism crawler and the Harvard Ambulatory Microrobot (HAMR).

From Meal Detection to Counterfactual Reasoning in Language-Model Glucose-Forecasting Agents

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Continuous glucose monitors and wearable sensors generate dense physiological histories, but most existing methods for evaluating whether models understand this data test only retrospective questions, such as identifying a trend or computing a statistic from observed readings. These methods do not test whether a model can reason correctly about an intervention, such as a changed meal or insulin dose, and its effect on future glucose, even though meals and insulin can affect glucose in opposite directions. Early work on this project built a pipeline to detect meal timing and estimate macronutrient content from glucose data, which motivated a shift toward directly testing this interventional reasoning in language-model agents, now the project's central focus. The initial phase reproduced an existing meal-detection network as a modular, leakage-aware package, with wider training labels and calibrated decision thresholds, rather than architectural changes, producing the largest gains and reaching an event-level accuracy of 79.9% under subject-held-out validation. The project's current work instead constructs a benchmark that generates quality-controlled counterfactual scenarios from real patient histories in a type 1 diabetes wearable dataset, using personalized physiological simulators fit to each participant as a reference standard rather than as ground truth, mirroring how such simulators already validate control algorithms in closed-loop glucose research. Language-model agents are evaluated on these scenarios both directly and with access to interchangeable forecasting-model tools through a controlled interface, and are scored on whether they respond to each intervened variable in the correct direction and magnitude while leaving unrelated factors unchanged. This design pairs reliable, tool-based computation with a benchmark protocol suited to testing whether agents reason correctly about glucose-relevant interventions rather than repeating observed patterns.

A Scalable Human iPSC-Derived Hematopoietic Platform for Mast Cell Generation

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Mast cells are tissue-resident immune cells that play important roles in allergic inflammation, host defense, and immune regulation through IgE-dependent activation and release of granule-associated mediators. However, primary human mast cells are difficult to obtain in large numbers and have limited long-term expansion capacity in culture, creating a need for renewable human mast cell models. This project aims to generate a scalable human mast cell system by differentiating induced pluripotent stem cell/HSPC-derived cultures toward the mast cell lineage and identifying immortalization strategies that support long-term expansion while preserving mast cell identity and function. We hypothesize that human mast cells derived from iPSC/HSPC cultures can be immortalized in vitro while retaining canonical mast cell markers, granule properties, and functional responsiveness. To test this, differentiating cultures will be monitored over time using flow cytometry for FCER1a and KIT, candidate immortalization factors will be introduced to assess sustained cell growth and marker retention, and mast cell identity will be further validated using staining and imaging assays to examine granule morphology. Finally, IgE anti-DNP sensitization followed by DNP-mediated activation will be used to test whether the engineered cells retain IgE-dependent functional responses. Together, this work seeks to establish a renewable platform for producing functional human mast cells, enabling future studies of mast cell biology, allergic activation, and immune cell engineering.

Investigation of Glia Cells in Young Mice Brains Upon Microbiome Depletion

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The microbiome, the population of microorganisms residing in the gut, is a crucial component of the gut-brain axis (GBA), a bidirectional communication system between the gastrointestinal (GI) tract and the central nervous system (CNS). Gut-derived immune signals have been shown to modulate glia cell (astrocytes and microglia) states in the brain. Together, these coordinate cytokine signalling, synaptic remodelling and debris clearance, leading to context-dependent protective or chronic neuroinflammatory effects. To understand how the gut microbiome influences glia cells in the brain, the Rubin lab performed analysis of brain samples from young mice (2-3 months old) upon microbiome depletion. The single-nuclei RNA (snRNA) sequencing of these samples revealed a shift in the transcriptional signature of various genes in glia cell populations, consistent with their activation states. Of these, we further investigated Gfap and S100β for astrocytes, and Cd68 and Iba1 for microglia. Samples were obtained from mice treated for 30 days with either water as control, or antibiotics (Abx: neomycin, ampicillin, vancomycin, metronidazole) to achieve microbiome depletion. We want to now characterise the morphology and function of these cells in vivo to depict neuroimmune regulation of the brain, modulated by the GBA. To study the effects of microbiome depletion in vivo, we carried out immunofluorescence staining on these brain sections. Antibodies against the aforementioned markers were used to label glia cells and their functional activity and a confocal microscope was used to image sections of the brain. Particularly, we focused on the hippocampus and cortex, quantifying the staining using ImageJ, a software for imaging analysis. Preliminary results reveal increased inflammation in the brain upon microbiome depletion, with increased abundance of the above markers indicating reactive astrogliosis and microglial activation. This work fits into the broader literature regarding the GBA, which proposes it to be the basis for various neurodevelopmental, neurodegenerative and psychiatric disorders. It demonstrates the importance of microbiome maintenance in young mice for supporting brain function, thus providing possible insight about GBA manipulation for clinical treatments.

Counting Real Points on Determinantal Varieties

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Many questions in data science, quantum information, and signal processing reduce to one geometric problem: how many low-rank matrices lie inside a randomly chosen linear family of matrices? The low-rank matrices form a geometric object called a determinantal variety. Over the complex numbers, this count is fixed and equals the degree of the variety, but over the real numbers it can change from one family to the next. Our project pursues three goals: to determine which real counts can occur, to measure how likely each count is when the subspace is chosen at random, and to identify the largest and smallest possible counts. This variety is singular, meaning several rank conditions coincide along a smaller locus inside it, so the classical theorems that count real solutions on smooth varieties do not apply directly. Our first result was that a randomly chosen family avoids this singular locus entirely, which lets us reduce the whole problem to the well-behaved, smooth part of the variety. From there, we combined tools from enumerative geometry, coding theory, and topology to analyze how many low-rank matrices can be found in this portion. We proved that the possible counts form an interval of integers of one fixed parity, and that the maximum equals the complex degree, achieved by an all-real subspace built by degenerating the variety into real linear pieces. We reduced the minimum to an extremal question about subspaces of high-rank matrices, and we found topological obstructions that forbid nonzero counts in some infinite families. Randomness turns out to favor the middle of the count range: for square matrices, the most likely counts cluster around the square root of the matrix size, far short of the maximum, which appears only with exponentially small probability. Future work targets undecided cases and extends the theory to symmetric, skew-symmetric, Schubert, and ladder determinantal varieties.

Metamaterial Solution for MRI-Compatible Deep Brain Stimulation

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Deep brain stimulation (DBS) treats movement disorders such as Parkinson disease, dystonia, and refractory epilepsy, yet patients with DBS implants are routinely denied magnetic resonance imaging (MRI). Inside the scanner's radiofrequency (RF) field, the metallic microwires within the lead act as antennas, concentrating current at the electrode tip and heating nearby brain tissue. To address this, the Bonmassar Lab designed a metamaterial microwire built from two metal segments of differing length and conductivity; the impedance mismatch at their interface partially reflects RF-induced current and reduces tip heating. This project focuses on turning that design into a physical, testable device: fabricating the microwires and integrating them into a complete lead. Fabrication takes place in the cleanrooms at Harvard's Center for Nanoscale Systems and MIT.nano. The two-segment structure is deposited onto a non-conductive, non-magnetic, biocompatible substrate by electron-beam physical vapor deposition, with a titanium adhesion layer and a parylene conformal coating for insulation. Prototyping runs are approaching the theoretical target resistance of approximately 400 Ω, the value that keeps the current generated across the pulse generator's voltage range within safety limits. A complete lead has not yet been assembled. Building one, which includes repurposing commercial clinical DBS leads to house the new microwires, remains the primary near-term goal. Once fabricated, the wires will undergo phantom heating tests at 1.5T and 3T, in both electromagnetic simulation and physical benchtop experiments, followed by biocompatibility and efficacy evaluation. Success could restore safe MRI access for DBS patients, expanding both diagnosis and research into the disorders these devices treat.

Defining the Adhesive Targets of Perineural Invasion in Pancreatic Cancer

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Pancreatic ductal adenocarcinoma (PDAC), the major form of pancreatic cancer, remains highly fatal, with a 5-year relative survival rate of merely 12.5% due to limited treatment and early detection. Its high lethality largely derives from rapid proliferation and metastasis, which recent studies associate with the proximity of tumor cells and neurons within the tumor microenvironment (TME). This tumor-nerve crosstalk, known as perineural invasion (PNI), manifests as the envelopment, invasion, and reprogramming of peripheral nerves and glial cells. Following adhesion, cancer cells invading nerves gain increased access to perineuronal blood vessels and lymphatic networks, promoting vascular invasion and metastasis. Although cancer-cell tropism toward nerves is followed by cancer-nerve adhesion, the protein machinery constructing these interfaces remains poorly defined. To identify candidate mediators, the Hwang lab co-cultured PDAC organoids with dissociated mouse dorsal root ganglia (DRG) and performed spatial optoproteomics through two-photon microscopy and LC-MS/MS analysis to identify proteins enriched at cancer-nerve adhesion points. Among the top candidates were IQGAP1, an intracellular scaffolding protein, and BSG, an extracellular transmembrane protein. Spatial transcriptomics of human PDAC tissue further revealed increasing IQGAP1 and BSG expression with nerve proximity, supporting their potential relevance across experimental models and patient tumors. Our project investigates neuroinvasion in IQGAP1- and BSG-CRISPR knockout (KO) cancer lines by quantifying cancer-nerve contact density in DRG co-cultures. Concurrently, TurboID-based spatial proteomics will identify neuron-expressed interaction partners selectively biotinylated along interfaces containing IQGAP1 or BSG. Candidates will be validated through immunofluorescence co-localization and functional CRISPR-KO assays in 2D and 3D co-cultures. Finally, genetic perturbation and orthotopic transplantation of human and mouse PDAC lines alongside wild-type controls in immunodeficient NSG and syngeneic mice will assess candidate roles in PNI, tumor innervation, and metastasis within primary tumors and distant metastases. If required for cancer-sensory nerve adhesion, candidate disruption should reduce PNI and attenuate PDAC's malignant phenotype.

Multi-Ancestry Genetic Subtyping of Coronary Artery Disease

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Coronary artery disease (CAD), which occurs due to plaque buildup in the arteries of the heart, has been a leading cause of mortality globally for decades. Still, the mechanisms that lead to the onset of disease are incompletely understood. Despite established risk factors of CAD such as hypertension, diabetes, and obesity, there are many groups of patients with seemingly paradoxical phenotypic profiles. For example, South Asian patients with low BMI are disproportionately affected by CAD. This suggests multiple molecular pathways that lead to disease, some of which may be more prevalent in certain ancestry groups. Our study aimed to identify functionally distinct groups, or clusters, of genetic variants causing disease across diverse ancestries by using genome-wide association data from a previously published meta-analysis comprising more than 1.1 million participants. Using the Bayesian non-negative matrix factorization clustering algorithm, 248 CAD-associated genetic variants were grouped based on their associations with 2292 phenotypes. Our preliminary results tested up to 30 possible clusters and converged on 22 clusters as the optimal solution, indicating 22 potential mechanistic subtypes of CAD. Future work will evaluate these subtypes using partitioned polygenic risk scores (pPRS), which use a subset of an individual's genetic variants to calculate disease risk, in approximately 650,000 participants from the Our Future Health database. Analyzing pPRS scores will help determine how molecular phenotypes and disease incidence differ among individuals of different genetic subtypes. Our work will ultimately contribute to determining whether genetic subtypes can improve patient care by improving risk prediction and informing targeted treatment strategies.

Vitamin D Levels and Lethal Prostate Cancer Risk Among Men With High Genetic Risk

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Prostate cancer is one of the most heritable cancers. Vitamin D has been shown to promote apoptosis and inhibit tumor cell proliferation and angiogenesis, yet whether vitamin D affects lethal disease risk among genetically susceptible men remains unexamined. Epidemiologic studies have linked plasma vitamin D levels to lethal prostate cancer, with unpublished data from the VITamin D and OmegA-3 TriaL randomized trial suggesting that vitamin D supplements lower fatal prostate cancer risk by 25%. Our work investigates whether high pre-diagnostic vitamin D status is associated with reduced lethal prostate cancer risk, especially among men with high genetic risk. This prospective cohort study draws on men in the Health Professionals Follow-Up Study (HPFS) who were cancer-free at blood draw (1993-1995). The two variables examined are 25-hydroxyvitamin D, or the main circulating form of vitamin D, split into quartiles, and polygenic risk scores, derived from 451 single-nucleotide polymorphisms. The outcome is lethal prostate cancer, defined as prostate cancer death or metastasis. Logistic regression will be used to estimate odds ratios and 95% confidence intervals, adjusting for metabolic, lifestyle, supplement, medication, and screening covariates. Models will be stratified by polygenic risk score. Data has been pulled from the blood samples in the HPFS dataset, and data cleaning is in progress. If confirmed, these findings would clarify whether vitamin D status offers greater protection against fatal prostate cancer among men at elevated genetic risk to inform targeted prevention strategies. Future analyses will incorporate additional vitamin D-related genes, including CYP27A1, CYP2R1, CYP27B1, GC, CYP24A1, RXRA, and VDR, to refine risk stratification and guide personalized supplementation.

Learning Adaptive Diffusion Timesteps for Image Editing

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One-step diffusion image editing methods achieve real-time performance by carrying out image editing at fixed timesteps. While computationally efficient, methods like ChordEdit use a single fixed timestep for every edit, even though the timestep determines the overall edit strength. Keeping the timesteps fixed at a specific value fails to account for edits that require different strengths and therefore requires dynamic timestep selection. To manage edit strength, we propose using a trained classifier model that incorporates ChordEdit's ChordField pipeline to select different timesteps for different images and prompt pairs. The model, through training on a large image dataset, is designed to predict the optimal timestep for each edit process given source image, source prompt, and target prompt embeddings on SD-Turbo. Our objective is to maximize unedited peak signal-to-noise ratio and masked CLIP-Edited scores to preserve the background and the intended edit. The classifier architecture and training pipeline have been developed, and experiments are underway to evaluate whether adaptive timestep selection improves image editing compared with conventional fixed timestep methods. Three approaches were evaluated on the 700-image PIE-Bench dataset: a vision-language model using in-context learning, a cosine similarity measure, and a task-specific trained classifier. Future work will focus on determining which additional input features can be incorporated to improve timestep prediction accuracy.

Stimuli-Responsive Microscale Carriers for Staged mRNA Lipid Nanoparticle Delivery

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Messenger RNA (mRNA) delivery systems provide an effective and versatile approach to preventive and curative medicine, with applications spanning infectious disease, cancer, and genetic disorders. Building on the programmable nature of mRNA therapeutics, these treatments offer a potent and highly personalizable platform capable of transforming modern medicine. Their clinical success was demonstrated by the widespread deployment of COVID-19 mRNA vaccines, while continued advances in cancer immunotherapy further highlight their therapeutic potential across diverse disease areas. Despite this promise, efficient delivery remains a major limitation of mRNA therapeutics, particularly in solid tumors, where nanoparticle transport and intracellular bioavailability remain major bottlenecks. Prior analyses estimate that only a median of approximately 0.7% of an administered nanoparticle dose reaches solid tumors, while landmark lipid nanoparticle (LNP) trafficking studies suggest that only approximately 1–2% of internalized nucleic acid payload may escape endosomes into the cytosol. To date, most published approaches have focused on optimizing delivery at the nanoscale by modifying LNP formulations. Comparatively less attention has been paid to microscale transport strategies that improve the localization of existing LNP systems before cellular transfection. This project investigates a hierarchical delivery concept that uses a larger vesicular carrier to transport and concentrate conventional LNP-mRNA formulations at the target site. The platform incorporates externally responsive components, including metallic nanoparticles, external fields, and light sources, to facilitate localized accumulation and controlled payload release. These early findings support the feasibility of staged delivery from microscale carriers to nanoscale particles, suggesting that such carrier architectures offer a viable strategy for augmenting, rather than replacing, existing LNP technologies. By decoupling tissue-scale localization from nanoscale cellular transfection, this strategy could open a complementary design space beyond formulation-only LNP optimization, with the potential to improve delivery efficiency and strengthen mRNA-based cancer therapy.

Design of Synthetic Overlapping Genes Using Mutational Fitness and Evolutionary Sequence Data

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Overlapping genes are coding arrangements in which a single DNA sequence contributes to more than one distinct coding region in different open reading frames. First identified in viral genomes, overlapping genes have since been found in all domains of life and present an attractive way to compress genetic information. However, the design of functional overlapping genes remains a challenge, since the constraints imposed by a shared DNA sequence often require substitutions that may not be well tolerated by the encoded products. In this work, we present a computational approach for placing two previously separate coding sequences onto a shared DNA sequence. By integrating deep mutational scanning data and multiple sequence alignments to identify substitutions that preserve fitness, we generate putatively functional overlapping gene designs on a single DNA sequence. We then apply this approach to two orthogonal antibiotic resistance genes: APH(3'), an aminoglycoside kinase, and TEM-1, a β-lactamase. Computational structural analysis indicates that designs preserve the folds of the original wild-type proteins, and protein language models embeddings suggest that designs remain near wild-type in protein space. Top candidates are currently being assayed for joint antibiotic resistance activity in vivo. If validated experimentally, this work would show that empirical fitness data and evolutionary sequence information can be combined to navigate the constraints imposed by overlapping reading frames, which could enable the systematic design of compact DNA sequences that encode multiple functional products.

ASCEND: A High-Throughput Platform for Mapping the Affinity Landscape of Antibody Evolutionary Trajectories

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During an immune response, antibodies improve through Darwinian natural selection: as B cells proliferate in germinal centers, mutations that improve antigen binding are selected for, increasing antibody affinity. While the cellular dynamics of this process are well understood, it remains unclear how germinal centers reliably produce higher-affinity antibodies despite the stochasticity of evolutionary selection. Current models predicting antibody-antigen affinity tend to use additive frameworks; for example, in deep mutational scanning, each base change is assumed to contribute independently to binding. Additionally, previous libraries sample mutations combinatorially or employ random mutagenesis, yielding sequences that fail to reflect naturally evolved trajectories. While powerful, these approaches cannot capture epistasis, and subsequently misattribute phenotypes and the paths sequences take during evolution. Here, we employ a replay design to directly examine natural affinity trajectories, mapping ancestral and extant genotypes to their measured binding phenotypes to reveal patterns of affinity maturation. We build large, custom-designed libraries of B-cell receptor sequences from clonal lineages followed through 20 days of evolution in individual mouse germinal centers. Thus, the platform ASCEND (Affinity Selection and Clonal Evolution in Naive B-cell Development) proceeds in three phases: 1) computational design of representative germinal center libraries; 2) antibody DNA sequence assembly and high-throughput yeast-display phenotyping via Titeseq to quantify each variant's binding affinity; and 3) integration of these phenotypes with phylogenetic and fitness data to build antigenic maps and predictive models of antibody evolution. ASCEND establishes a replicable platform to measure affinity across real evolutionary trajectories, while enabling direct observation of the role of epistasis in antibody affinity. Ultimately, ASCEND may lay the groundwork for rationally guiding B-cell responses toward broadly-protective antibodies and antibody-based therapies.

Entomophthora muscae Light Sensing for Drosophila Infection

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While parasites often develop unique, tailored ways to infect their hosts, the evolutionary role of these traits is not always clear. The pathogenic "zombie" fungus *Entomophthora muscae* infects flies, with infection strategies highly specified to fly physiology. *E. muscae* modulates the behavior of its host by inducing the fly to climb upwards, or "summit," to position it optimally for spore dispersal. However, recent data investigating fruit flies suggest that they fail to become infected by sporulating cadavers if they are not provided light within the first 24 hours of exposure. The cause and purpose for this infection disruption remains unknown. To investigate this phenomenon, we allowed cadavers to sporulate in the dark and observed that spore development is arrested in the absence of light. Primary spores are launched directly from the infected cadaver, and these primaries are known to sometimes fire off a smaller secondary spore before germinating into the fly. Our data finds that secondary firing is likely light dependent, as firing rates are significantly lower in the dark. When light is provided later within the first day, firing rates subsequently rebound. Next, we found that giving spores light in the absence of flies prevents the flies from getting infected later, suggesting that premature light causes secondaries to fire off early, and that secondary formation may be a crucial step for infection. Since the circadian rhythm of the fungus causes summiting and death at sunset, this light dependence may allow spores to lie dormant until the next morning, increasing infection chances by targeting the flies' activity peak. Subsequently, we hope to collect transcriptomic data to investigate the receptors and signaling pathways involved. These results further our understanding of *E. muscae* infection strategies that have arisen from millions of years of co-evolution and illustrate a unique light dependent dispersal mechanism.

A Physical Model of Nuclear Volume Determination and its Effect on Transcription

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The volume of the cell nucleus is correlated with genome size. The physical model we proposed is that chromatin mass sets a minimum nuclear volume at which the nucleus becomes effectively incompressible and import of soluble proteins determines the degree of nuclear inflation above this value. We hypothesized that physiological nuclear volume is regulated to an optimum for effective RNA and DNA production, such that both compression and expansion of the nucleus from this physiological volume reduce transcriptional output. To investigate these hypotheses, we used three main assays, supported by a high-throughput image analysis pipeline capable of processing both 2D and 3D nuclear images using BIOP Cell-pose and StarDist segmentation to quantify signal at the single-nucleus scale. In the first two assays we utilized ethynyl-tagged uridine (EU) substrates and click chemistry to quantify global rates of nucleic acid production and degradation. These assays are predominantly useful as methods development experiments which will later be applied to the inducible HMGB1 cell line. The first assay was a series of EU pulse and pulse-chase experiments on MDCK cells across a range of cell densities over varying pulse and chase durations. This helped develop a live-cell method to investigate the dependence of RNA production and degradation on nuclei under artificially and physiologically applied pressures. In the second assay, EUTP was pulsed into partially and fully permeabilized MDCK and axolotl cells using digitonin or Triton. This assay was used to probe the relative contribution to nuclear volume between soluble and insoluble nuclear components. The final assay directly tested the proposed physical model of nuclear volume determination. We cloned an MDCK line with inducible expression of soluble HMGB1 tagged with GFP to investigate the effects of nuclear inflation driven by high concentrations of soluble nuclear protein. Under both compression and expansion of the nucleus, we found that fluorescence of EU-incorporated RNA decreased, consistent with the proposed optimum-volume hypothesis. This research illustrates that the physical environment cells inhabit can significantly affect intracellular composition, partitioning and behavior.

Direct Synthesis of Formate via the Activation of Bicarbonate with Hydroborane Species in Aprotic Organic Solvent

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Faculty Advisor(s): Daniel G. Nocera
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My work builds upon recent research by Professor Daniel G. Nocera and his team in the Department of Chemistry and Chemical Biology at Harvard University on CO2-reductive reactivity pathways. In their report, the activation of bicarbonate (HCO3-) towards carboxyl transfer led to the formation of carbonyl carbamates. While our group demonstrated HCO3- valorization in aprotic solvents, providing a greener route for the synthesis of industrially relevant polymer precursors, the well-studied and critical CO2-to-formate (HCO2-) utilization process has not been investigated using HCO3- as the primary oxidant. In addition to sustainable CO2 reduction, the removal of HCO3- is crucial for renewable batteries. As we move beyond simple aqueous systems to aprotic ones, the principal goal of this study is to advance our understanding of HCO3- reduction. Thus far, I have investigated HCO3- reduction in aprotic solvents to develop mechanistic insight into these applications, all under mild reaction conditions. While using commercially available Lewis acids or hydroborane reductants, specifically 9-BBN and the green hydrogen transfer source, dimethylamine borane (DMAB), to facilitate the reduction in aprotic solvents, such as pyridine, our results indicate approximately 60% conversion to HCO2- upon treatment with 4 equivalents of DMAB/pyridine at room temperature, without intermediate CO2 formation by Carbon-13 Nuclear Magnetic Resonance. To date, we envision DMAB functioning as a reductant and Lewis acid simultaneously, aiding in HCO3- activation before hydride transfer. My future steps involve translating this process into a sustainable borate-based activation of HCO3- for electrochemical reduction to HCO2- and carbon monoxide (CO).

Framing the Patient: Race, Sex, and Social Description in a Century of Clinical Case Records

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Every entry in the Case Records of the Massachusetts General Hospital opens by introducing a patient through age, sex, and, in many eras, race, occupation, or family circumstance before the diagnostic narrative begins. This opening frame teaches readers how to see a patient and shapes which diagnoses seem plausible. Our work examines how that frame changed across the full run of the Case Records, from their 1923 debut in the *Boston Medical and Surgical Journal* through the *New England Journal of Medicine* to 2025, and asks what these shifts reveal about the entanglement of clinical reasoning and evolving social categories. Drawing on a research license granting full-text access to all 7,102 cases, our work pairs large-scale mapping of when descriptors such as race, sex, occupation, and reproductive history appear in opening sentences with close reading of selected periods: the interwar years, mid-century, the AIDS era, and the machine-learning present. A preliminary analysis of the archive suggests that patterns of patient representation are embedded in the data underlying clinical AI systems. By tracing how the opening frame has organized clinical attention across a century, the project offers a historically and computationally grounded account of how social categories became diagnostic information — and why that history matters for present debates about bias in medicine and its automated tools.

Spectroscopic Characterization of C2H2 Interstellar Ices and Comparison With Astronomical Observations

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Stars form when clouds of gas and dust collapse under gravity, creating a young protostar surrounded by a disk of material that can eventually build planets. Acetylene (C2H2), the simplest alkyne, has no dipole moment, so it can't be detected at submillimeter wavelengths used to find molecules in space, but is identified through infrared observations in the gas phase toward protostars, their disks, and carbon-rich evolved stars. In protostars and disks, C2H2 may be an important building block for complex organics. Known gas-phase reactions cannot explain the amounts observed, so sublimation from icy grains is proposed as the source. Ices are detected through their infrared absorption features, observable with telescopes like the James Webb Space Telescope (JWST). However, little lab data exist on C2H2's infrared signature in realistic interstellar ices, making it hard to confirm its presence or set meaningful upper limits. This project aims to measure C2H2's infrared features when mixed with H2O, CO2, and CO, the main ice components, to generate reference spectra for comparison with JWST observations. We will use cryogenic vacuum systems to recreate low-temperature, low-pressure space conditions and grow interstellar ice analogues. C2H2 will be deposited with H2O, CO2, and CO in a 1:1 ratio and 1:10 dilution, and infrared spectra will be collected from 15 K to 200 K to see how the C2H2 features change with ice composition and temperature. We expect the C2H2 absorption profile to shift measurably depending on the surrounding ice molecule, distinguishing it from pure C2H2 ice. Matching lab and JWST spectra could support direct detection; if not, results may set meaningful upper limits. This project could help determine whether C2H2 ice is a significant source of organic chemistry in star- and planet-forming regions, and help explain the mismatch between observed gas-phase C2H2 and current formation models.

scRNA-seq Analysis of an Accepted Non-Human Primate Heart Graft to Identify Potential Cell Populations for Tolerance

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Following transplantation, infiltration of host immune cells into grafts leads to rejection. Transplantation tolerance refers to the process of inducing long-term acceptance of grafts without the need for continuous immunosuppression by regulating the immune system to a state of donor-specific immune unresponsiveness. The process reduces the risk of rejection but remains poorly understood. Here, we utilized single-cell RNA sequencing (scRNA-seq) to analyze cells from an accepted heart graft in a non-human primate and identify potential cell populations associated with tolerance. By clustering cells with similar gene expression, we reduced the dataset from 18 clusters to 9 distinct cell types that describe the heart graft. From these cell clusters, we measured the expression of cell markers that serve as regulatory signals facilitating tolerogenic programs. We found that in the accepted heart graft, there is significant expression of the markers *TGFβ*, *RBP7*, and *IL33* in endothelial and smooth muscle cells, with average z-scaled expression values greater than 2 (standard deviations above the mean expression). Aside from myeloid cells, ventricular cardiomyocyte cells also show strong positive expression of tolerogenic markers, such as *CD274*. In analyzing the ligand-receptor communication network between cell populations, we found that there is strong autocrine and intercellular signaling between endothelial and smooth muscle cells, and with myeloid and ventricular cardiomyocyte cells. These findings suggest that endothelial, smooth muscle, and ventricular cardiomyocyte cells may contribute to a pro-tolerant environment in the heart. As this study is limited to a single cell population database of a non-human primate heart graft, future studies incorporating greater sample sizes, different subject species, or various longitudinal points would be necessary to confirm the reproducibility and significance of the study. Nonetheless, this study provides an additional perspective contributing to a more comprehensive understanding of the cellular and molecular mechanisms of immune tolerance.

Does When You Sleep Matter for Memory? Understanding Circadian Timing of Sleep Spindles

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Shift work, overnight caregiving, irregular work or school schedules, and social demands are among the causes that lead people to sleep at times misaligned with their circadian rhythm. This circadian misalignment has been linked to a variety of negative health outcomes, including disruption of sleep architecture, cardiometabolic dysfunction, and impaired memory. Memory impairment is thought to arise in part from disrupted memory consolidation. A key marker of memory consolidation are sleep spindles, transient bursts of activity in the sigma frequency band (11–16 Hz) of the sleep electroencephalogram (EEG). To our knowledge, only a single study (16 participants: 8 younger and 8 older adults) has examined spindles across circadian phase using the forced desynchrony (FD) protocol, which imposes a non 24-hour sleep-wake cycle to decouple sleep-wake activity from the circadian pacemaker. We present the largest FD study of sleep spindles to date using state-of-the-art spindle detection methods. We quantified spindle properties (density, amplitude, and duration) as a function of both melatonin-derived circadian phase and sleep depth in single-channel EEG (C3-A2). By clarifying the relationship between spindle activity and circadian phase, this study provides a foundation for therapeutic approaches that identify the best time for circadian-misaligned individuals to sleep in order to optimize spindle activity.

Investigation of Pyrite Oxidation Using Triple Oxygen Isotopes

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As global temperatures have increased so has the rate of Arctic permafrost thaw, which causes the exposure of sulfide minerals like pyrite (FeS2). These minerals are inactive when encased in ice but become vulnerable to weathering upon thaw. Weathering via oxidation releases iron and sulfur leading to rivers acquiring a "rusted" appearance. This transformation is demonstrably detrimental to downstream ecology yet the mechanisms involved have not been well constrained. This study will combine new triple oxygen isotope measurements with existing elemental data to model weathering and constrain pyrite oxidation pathways. The Alaskan Salmon River watershed is used as a case study from which water samples were precipitated as barite (BaSO2) for isotope analysis. Triple oxygen isotope measurements were conducted using laser fluorination and mass spectroscopy. This involved a series of cryogenic purification and chromatography steps to convert and purify the sample to analyte oxygen gas before isotope proportions were measured in the Thermo Finnigan MAT 253. Triple oxygen isotope measurements will be used to trace the relative contribution of atmospheric oxygen in riverine sulfates, integrated across the watershed. This will provide a fingerprint of the dominant oxidation pathway. The measurements will also be paired with elemental data to constrain oxidation pathways using a reactive transport model. With a constrained oxidation pathway, estimates of the rate of reaction and the potential acid generated per mole of exposed pyrite can be made. A greater understanding of river "rusting" and acid production in the Salmon River watershed is important due to its direct ecological effects on the salmon population, secondary effects further down the food chain and significant impacts on the local communities. In addition, this study has implications for the applicability of sulfate triple oxygen isotopes as a proxy for paleo-atmospheric conditions, as it is commonly used.

Investigating the Mechanisms Linking Skin Barrier Dysfunction to Intestinal Immune Dysfunction

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Staphylococcus aureus colonization and infection are highly prevalent in patients with atopic dermatitis. Patients with this debilitating skin condition have a greater susceptibility to developing inflammatory bowel disease and food allergies, indicating inter-organ communication and a functional axis between the skin and the gut. However, the mechanisms linking cutaneous inflammation to allergic disease and to gut inflammation remain poorly understood. This project investigates how skin barrier dysfunction influences intestinal immune, epithelial, and microbial responses that may increase susceptibility to colitis and allergic gut disease. To model this, we infected mice epicutaneously with *Staphylococcus aureus*, along with mutant strains lacking V8 protease (ΔsspA) or phenol-soluble modulins (Δpsm), and then exposed them to dextran sulfate sodium (DSS) to induce colitis. To elucidate these mechanisms, we use Kaede-photoconvertible mice to track immune cell trafficking from the skin to the gut, in combination with flow cytometry for immunological profiling, transcriptomic analyses of colonic epithelial cells, and metagenomic analyses. Longitudinal body weight measurements, fecal samples, and colitis disease activity index scoring are also collected in mice that have been infected with *S. aureus*. Preliminary results indicate that mice infected with the ΔsspA and Δpsm mutant strains exhibit reduced body weight loss and lower disease activity index scores compared with mice infected with wild-type *S. aureus*. 16S rRNA sequencing data show compositional changes in the gut microbiome, specifically reductions in *Bacteroidales* and *Akkermansia*, following epicutaneous *S. aureus* infection. This suggests S. aureus induces gut microbiome dysbiosis, which exacerbates colitis. However, preliminary flow cytometric analyses of the Kaede trafficking model did not detect clear differences in immune cell migration between the experimental and control groups. A better understanding of the skin-gut axis may explain the clinical association between inflammatory skin diseases and gastrointestinal disorders and ultimately identify therapeutic targets for inflammatory diseases and food allergies.

Acoustic Characterization of Dome-seeing: Bidirectional Acoustic Traveltime Pulser for Index Gradients (BATPING)

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The Legacy Survey of Space and Time (LSST) at the Vera C. Rubin Observatory generates 20 terabytes of astronomical imagery nightly, enabling precision cosmological measurements of dark energy and dark matter. Image quality depends on mitigating dome seeing, a form of wavefront distortion caused by lateral temperature gradients in the telescope enclosure. Correcting this thermal structure to 0.1°C would bring the point spread function within 10% of the diffraction limit. The Bidirectional Acoustic Traveltime Pulser for Index Gradients (BATPING) measures path-integrated air temperature via round-trip travel of ultrasonic pulses without disrupting normal telescope operation. Bidirectional propagation cancels airflow contributions to the measured speed of sound, isolating the thermal signal. Piezoelectric transducers at 40 kHz on a 10-meter baseline would transmit and receive waveforms tailored to the transducers' nonlinear resonant response. Laboratory validation employs a 2-meter benchtop acoustic path with transducers driven by an arbitrary waveform generator and digitized at 384 kHz. After evaluating different waveform parameterizations using a Bayesian optimization algorithm, we found that an amplitude-compensated linear frequency-modulated chirp, with an envelope shaped by the inverse of the measured piezoelectric transfer function, maximizes signal quality. A signal-processing pipeline implementing adaptive window slicing for matched filtering and a full-waveform least-squares shape fit was also developed toward the aim of precision measurement. Our preliminary results demonstrate a per-ping temperature precision of 0.045°C on a 2-meter path, surpassing the 0.1°C target by more than a factor of two, with a traveltime estimation precision of approximately two nanoseconds per measurement. Future work includes the design of a transponder circuit that actively retransmits the pulse after a known delay to eliminate signal attenuation at dome-scale path lengths. We anticipate deployment at the Rubin Auxiliary Telescope dome before the end of 2026, with the longer-term objective of two-dimensional acoustic tomography of the full dome temperature structure.

A Density-Dependent Fusion Deficit in SELENON-Knockout Human Myoblasts

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SELENON-related myopathy is a rare, congenital muscle disease marked by early muscle weakness, spinal rigidity, and respiratory involvement. Selenoprotein N regulates sarcoplasmic reticulum calcium uptake and protects muscle cells from endoplasmic reticulum and oxidative stress. Its loss is thought to drive the progressive muscle pathology seen in patients. Whether Selenoprotein N also contributes to myoblast fusion, the merging of precursor cells into multinucleated muscle fibers, remains poorly characterized, despite fusion being essential to building and repairing the muscle that this disease erodes. This project tests whether loss of *SELENON* alters the capacity of human myoblasts to fuse into myotubes during differentiation, and whether any such effect depends on seeding density. To quantify fusion, this project adapted and retrained MyoFuse. This deep-learning pipeline segments each nucleus and classifies it as inside or outside a myotube based on local myosin heavy chain (MyHC) signal, yielding the fusion index and the percentage of nuclei located within myotubes. Wild-type and C11 SELENON-knockout human myoblasts were differentiated at four seeding densities (50k, 100k, 150k, and 200k), stained for MyHC and actin with DAPI, and imaged across 218 fields. Fusion indices were comparable between genotypes at lower densities (50k and 100k). At higher densities, the knockout showed a deficit: 72.5% versus 80.4% in wild-type at 150k, and 68.5% versus 79.7% at 200k, alongside greater field-to-field variability (SD 9-10 versus 3-4). Because each condition came from a single well, these are preliminary single-experiment trends rather than replicated findings. Still, the consistent direction across higher-density conditions suggests a possible density-dependent role for *SELENON* in myoblast fusion, potentially linked to its calcium-regulatory function and to the muscle weakness seen in patients. Next steps include expanding the knockout clones (C11, C12) alongside wild-type clones, using RNA-seq patient data to characterize the expression of fusion- and growth-related factors.

Probabilistic Modeling of Gait for Assistive Robotics

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Harvard University | Lowell House | Biomedical Engineering | 2028

Wearable devices such as functional electrical stimulation (FES) systems have been shown to improve gait quality in mobility-impaired patients by providing electrical stimulation to activate muscles for walking. To target the numerous small muscles of the lower leg, our lab has developed a singular electrode array that wraps around the leg and is divided into channels, allowing selective activation of different muscle groups to produce specific movements, such as pointing the foot up or down. Commercial electrode designs are not well suited for this application, as they are typically too large, must be placed individually, and often require frequent movement when attempting to target smaller muscles. Previously, our lab has fabricated our electrode arrays in-house by screen printing conductive silver ink onto a polypropylene substrate. While effective, this method is highly time, labor, and resource intensive. The aim of this project is to develop a faster and more flexible fabrication method using an inkjet printer to deposit a printer-compatible conductive silver ink onto the electrode substrate. This approach introduced new challenges, including a higher sintering temperature requirement and issues with ink quantity and adhesion. Through substrate investigation, we found that heat resistance is the most critical property, as warping of the substrate during sintering resulted in the greatest loss of conductivity. Other important properties include the porosity of the substrate and its ability to adhere to silver ink. This investigation is still underway, as we look to test more substrates and printer configurations. If successful, this project would enable more rapid fabrication and testing of new electrode designs, streamlining the development of FES systems for mobility-impaired patients.

Overcoming Defensive Tolerance and the Reprogramming of Immunogenicity to Target Pancreatic Tumors by the Host's Immune System

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Our study seeks to identify new targets for immunotherapies against pancreatic ductal adenocarcinoma. We used a model of spontaneously accepted murine kidney allografts in fully-mismatched donor-recipient strain combinations to understand the mechanism of "defensive tolerance." In this process, cytotoxic CD8+ T cells and pathogenic B cells are reprogrammed to become exhausted cells. We believe that tumors employ a similar mechanism, so we referenced previous research to find genes of interest key to escaping the reprogramming process. This study will be conducted by inducing chimerism in KPC mice (mice that we expect to develop pancreatic tumors). The mice donating immune cells will have the gene of interest, *Fcgr2b*, knocked out in order to test if the lack of this receptor can overcome defensive tolerance. After 3 months, we will assess the size of the tumor. We preliminarily confirmed that chimerism was successfully induced by performing a flow cytometry experiment that indicated both MHC complexes were present, as well as populations of T and B cells with both MHC complexes. To further confirm that the immune system functions successfully as a chimerism, we transplanted 2 skin grafts, one of the bone marrow donor (DBA) and one of an unrelated mouse strain (C3H), onto our chimeric mice. We expect to see acceptance from the DBA skin graft, and rejection of the C3H skin graft. This experiment will allow us to assess our technical ability to induce chimerism in our mouse recipients. With this success, our experiment can proceed to the next step, by inducing chimerism in KPC mice and looking for tumor reduction.

A Benchmark and Pipeline for Memory in Mobile Manipulation

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Robotic systems continue to struggle with long-horizon tasks that require memory: recalling and acting on information across extended interaction sequences. Recent work has attempted to address this gap by incorporating explicit or implicit memory representations into diffusion policy models. However, these approaches still struggle to robustly capture various types of memory and remain largely confined to static, tabletop manipulation settings. In this work, we introduce a benchmark of tasks designed to systematically evaluate various types of memory for mobile manipulation, where agents must reason over changing viewpoints and dynamic environments. To address these challenges, we propose an alternative pipeline that, rather than embedding memory representations within the policy itself, uses an external, explicit, object-centric memory combined with a high-level reasoner (VLM) to assign subtasks to a low-level, memoryless policy. Across our benchmark, we find that latent memory mechanisms solve visual cue memory tasks but fail to recover spatial memory for object locations, whereas an explicit object-centric state representation solves these same tasks reliably. Moreover, combining a VLM planner with a memoryless low-level policy (finetuned $\pi 0.5$) enables execution of multi-step tasks, and offloading spatial grounding from the VLM to a segmentation module (SAM3) improves end-to-end success up to 93%. We further show that memory represented in pixel space fails across viewpoint changes, whereas storing memory as a reconstructed 3D scene representation preserves performance under camera motion; combining this representation with temporal object tracking and inter-object relations (e.g., containment) enables the system to recover spatial memory and occluded objects. These results suggest that separating task-level memory from action generation and separating symbolic reasoning from spatial grounding offers a more generalizable strategy for long-horizon mobile manipulation.

Enzymatic Degradation of the Tumor Glycocalyx Improves CAR-T Cell Therapy for Glioblastoma

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Glioblastoma (GBM) is the most aggressive primary malignant brain tumor in adults. GBM treatment strategies have remained unchanged for decades and primarily involve surgical resection followed by chemotherapy and radiation. The five-year survival rate remains below 10% under this protocol, revealing an urgent need for new therapies. Chimeric antigen receptor (CAR) T-cells are engineered immune cells with custom antigen receptors that enable targeted cancer cell killing. This presents a compelling treatment modality for GBM, which lacks FDA-approved immunotherapies. Currently, CAR T-cell therapy remains ineffective against solid tumors like GBM due to a thick coating of carbohydrates on tumor cell surfaces. This coating, termed the tumor glycocalyx, acts as a biophysical barrier that sterically prevents CAR T-cell killing. We hypothesize that concomitant administration of glycocalyx-degrading enzymes and CAR T-cells can overcome steric hindrance from the tumor glycocalyx to enhance CAR T-cell killing. Analysis of patient GBM transcriptomic profiles (n = 17) revealed hyaluronic acid (HA) and sialic acid (SA) as critical glycocalyx components. High expression of HA (*HAS1*, *HAS2*, *HAS3*) synthesis genes was negatively correlated with immunotherapy response. Furthermore, patients with high expression of HA and SA (*GNE*, *NANS*, *NANP*, *CMAS*, *SLC35A1*) synthesis genes had worse survival compared to those with low expression. Follow-up *in vivo* experiments probed the importance of HA and SA in immunotherapy resistance. C57BL/6 mice (n = 24) implanted with murine GBM were treated with CAR T-cells and PBS (control, n = 8), hyaluronidase (n = 8), or sialidase (n = 8). Compared to the PBS-treated group (median survival 24 days), hyaluronidase-treated (median survival 32 days, $p = 0.0059$) and sialidase-treated (median survival 27 days, $p = 0.0620$) mice experienced improved survival. These results suggest glycocalyx degradation may improve CAR T-cell efficacy and encourage future development of enzyme-secreting CAR T-cells for enhanced glycocalyx penetration.

Characterizing Neuromuscular Junction Regenerative Properties in Gene Therapy-Treated Spinal Muscular Atrophy After Muscle Injury

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Spinal Muscular Atrophy (SMA) is a genetic neuromuscular degenerative condition affecting approximately 1 in 10,000 live births worldwide. The condition is caused by a deletion of the Survival Motor Neuron 1 (*SMN1*) gene and is characterized by general muscle weakness and the progressive atrophy of proximal limb muscles as motor neurons in the spinal cord continuously die. In the last decade, three FDA-approved *SMN*-replacement therapies have drastically improved survival rates for individuals with SMA, yet lasting muscle deficits remain which limit patients' independence and reduce quality of life. It is not yet understood how increasing the levels of *SMN* in patients with SMA affects regeneration of the neuromuscular junction after muscle injury. This project studies the relationship between *SMN*-treated muscle satellite cells and the regenerative capabilities of *SMN*-treated neuromuscular junctions post-injury. This project uses 2-D and 3-D cell culture and analysis including skeletal muscle organoid formation, pharmacological mouse models, and various staining and imaging techniques such as immunofluorescence staining and Fluorescence In Situ Hybridization. While consistent *SMN*-rescuing treatment stabilizes motor neuron death, previous findings of persistent synaptic weakness and immaturities lead us to predict that post-injury regeneration will be challenging and result in diminished synaptic occupancy and altered postsynaptic scaffolding post-injury. Assessing if neuromuscular junction regenerative dysfunction persists in *SMN*-treated models may reveal a lasting and localized vulnerability when the neuromuscular system is challenged by an injury. Further, if regeneration of the neuromuscular junction is incomplete post-injury, understanding if regeneration fails at the nerve terminal, post synaptic terminal or in the muscle fibers themselves can help inform limits of -targeted therapies and open the door to new therapeutic targets beyond the motor neuron.

Impact of LINE-1 on DNA Replication Fork Dynamics in Cancerous, Precancerous, and Noncancerous Cells

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The retrotransposon ("jumping gene") *LINE-1* is frequently reactivated in cancer and is associated with genomic instability. Although its capacity to generate new genomic insertions is well established, its potential effects on DNA replication are not fully understood. This project focuses on characterizing replication-stress signaling and replication fork dynamics in cells with inducible *LINE-1* expression using immunoblotting and single-molecule DNA fiber assays, respectively. The latter will determine whether *LINE-1* acts locally by physically blocking replication forks or globally by inducing replication stress responses. Differentiating between these mechanisms requires visualizing both replication forks and *LINE-1* cDNA on the same DNA molecule, a challenge addressed by adapting a single-molecule DNA fiber assay with fluorescent in situ hybridization (FISH) probes targeting *LINE-1* cDNA intermediates. This technique simultaneously measures replication fork speed, sister fork asymmetry, and replication fork proximity to *LINE-1* cDNA. Three outcomes are possible: (1) local disruption: asymmetric forks and reduced speed near *LINE-1* signals; (2) global slowing: symmetric fork deceleration independent of *LINE-1* proximity; and (3) a dual mechanism: local stalling combined with genome-wide slowing. To date, our project has begun to characterize *LINE-1* activity in noncancerous, precancerous, and cancerous cell lines through Western blot analysis of *LINE-1*'s self-encoded ORF1p and ORF2p proteins, which mediates retrotransposition. Our future work will integrate these findings with DNA fiber-FISH measurements across different cell lines under multiple experimental conditions, including hydroxyurea-induced replication stress. The results may clarify how *LINE-1* alters DNA replication dynamics and why it is a source of genomic instability in cancer. Ultimately, this knowledge may reveal vulnerabilities in cancers with high *LINE-1* activity and suggest therapeutic strategies to target cells under *LINE-1*-driven replication stress.

Revealing Viral B-cell Epitopes with Evolutionary Sequences

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Antigen-antibody interactions are the core of the adaptive immune response. Antibodies bind to regions of antigens called epitopes; thus, accurate epitope identification is vital to vaccine design and therapeutic antibody development. However, current experimental epitope-mapping techniques are expensive and time-consuming, and in silico models are fundamentally biased by existing antigens, which skew their datasets. Consequently, novel antigen epitopes are difficult to predict. Surface-accessible residues on antigens are under evolutionary pressure to escape from germline antibody residues. Since germline residues are encoded on a DNA level rather than obtained through affinity maturation, which varies from person to person, we distinguished between germline-contacting epitopes and non-germline epitopes. Thus, we compiled a comprehensive dataset of experimentally determined B-cell epitopes across 42 WHO priority viruses. Then, we used multiple sequence alignments to calculate the mutability of each epitope from antigenic evolutionary sequences, and assessed the distributions of germline epitope, non-germline epitope, and non-epitope mutability frequency across viral families. As a result, we identified a statistically significant enrichment in mutability for germline-contacting epitopes ($p = 0.03$, Cohen's $d = 0.15$), suggesting mutability as a candidate feature for epitope prediction models. While mutability can establish a good baseline signal for epitope designation, we can improve upon this signal by incorporating structural information from antigen-antibody complexes. Future work should investigate complementary factors that, in combination with mutability, may enable accurate B-cell epitope prediction.

A Taphonomic Study of Exceptional Preservation in the Marjum Formation, Utah

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Ordinarily, the fossil record preserves only the hard or biomineralized parts of organisms. However, specific environmental conditions enable the preservation of additional soft tissues like digestive tracts and integuments, as apparent in the Middle Cambrian Marjum Formation of Utah which preserves a diverse biota of arthropods, sponges, chordates, ctenophores, and vermiform taxa. Most of the recovered fossils come from two main localities, Sponge Gully and the Gray Marjum Quarry, each deposited at a different depth along the same marine shelf environment. Despite both preserving early representatives of modern phyla, specimens sampled from Sponge Gully, a site at a deeper depth than the Gray Marjum Quarry, are generally less well-preserved due to their likelihood of having been transported downslope from the shallower locality. Most sites of exceptional preservation only occur at a single depth, as such, this represents a unique opportunity to study how carcasses were transported prior to fossilization. This study compares specimens collected from both localities to determine which organisms were endemic to each depth and whether Sponge Gully represents a distinct ecological community or consists primarily of material transported downslope from the Gray Marjum Quarry. To do so, specimens collected from the Gray Marjum were photographed under polarized light to enhance the visibility of preserved soft tissues. The images were then analyzed by categorizing preserved tissues into five classes: biomineralized structure, non-biomineralized and highly recalcitrant, non-biomineralized and moderately recalcitrant, labile external tissues, and labile internal organs. Then preservational quality for each species will be compared between both sites. By distinguishing varied soft-tissue preservations in both sites this study aims to improve our understanding of the paleoecology of the Marjum Formation.

A Multi-patched Vision Transformer Study of the Antiferromagnetic Heisenberg Model on a Kagome Lattice

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The study of frustrated quantum spin systems has led to multiple advances in understanding exotic phases of matter. The antiferromagnetic Heisenberg model on the kagome lattice (KAFH), a highly frustrated quantum magnet, has garnered significant interest among condensed matter physicists due to the close competition between candidate phases for its ground state. Recent studies using Density Matrix Renormalization Group (DMRG) and variational methods have yielded conflicting results, including a Z2 spin liquid, a Dirac spin liquid (DSL), and a chiral quantum spin liquid. This study uses a multi-patched vision transformer (ViT) to learn the ground state features of the KAFH model with Variational Monte Carlo (VMC) methods. This approach is motivated by the recent success of the field of neural quantum states, utilizing the expressivity of neural networks to learn ground states of quantum spin systems. The multi-patched ViT, inspired by the mean field theory of the DSL ground state, is physically motivated and incorporates various physically important features related to two types of plaquettes on the kagome lattice, i.e., hexagonal and triangular, and may show an advantage over uniform patch methods. The multi-patched ViT used in this study may therefore achieve energies competitive with those of the state-of-the-art techniques, while being more parameter-efficient and capturing longer-range correlations.

Construction and Characterization of an External-Cavity Diode Laser for Optical Pumping into the X(0 3^1 0) Vibrational State of SrOH

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Laser cooling of polyatomic molecules has created new opportunities for precision measurements and quantum control. The strontium monohydroxide (SrOH) experiment aims to develop an ultracold molecular platform for precision spectroscopy that is sensitive to possible variations in the proton-to-electron mass ratio and other physics beyond the Standard Model. On SrOH, a tunable dye laser was previously used to optically pump molecules into the X(0 3^1 0) vibrational state, but no dedicated laser system currently exists for this transition. This project addresses that limitation by building an external-cavity diode laser (ECDL) resonant with the X(0 1^1 1)→A(0 3^1 0) transition at 466.434125 THz. The project focuses on constructing and characterizing the ECDL into the existing SrOH experiment. The requirements for the laser are to provide narrow-linewidth operation, stable frequency control, and sufficient optical power for efficient population transfer. Characterization includes measurements of optical output power, frequency stability, and mode-hop-free operation before integration with the experiment. Thus far, the diffraction grating feedback has been optimized, reducing the lasing threshold current by approximately 10% relative to the laser diode's typical threshold current. The optical beam path has subsequently been aligned through an anamorphic prism pair, two optical isolators, and a polarizing beam splitter (PBS), with one output fiber coupled to a wavemeter for frequency measurements and another to the experiment. The ECDL has been tuned to within a few MHz of the target frequency. When locked by feeding back on the measured laser frequency, it has been measured to have a frequency stability of approximately ±5 MHz over a 20-minute time period. Future work will integrate an acousto-optic modulator into the beam path after the PBS to enable fast optical switching and align the beam into an optical fiber to the experiment.

Characterizing Vascular Glycosylation Along the Progression of Neuroinflammatory Conditions

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Neuroinflammatory diseases disrupt the brain's vascular barrier, allowing immune cells to infiltrate and damage neural tissue. While immune cell behavior and the proteins that anchor vessel cells together have been studied extensively, little is known about how sugar modifications on these vessel cells, known as vascular glycosylation, change as disease progresses. Because these sugars help regulate vessel permeability and immune cell adhesion, they may represent an important but overlooked driver of blood-brain barrier breakdown. This project uses the experimental autoimmune encephalomyelitis (EAE) mouse model of multiple sclerosis to track how vascular glycosylation shifts across defined disease stages. Brain tissue from EAE mice is being examined using immune cell staining, vessel isolation, lectin and antibody panels, and mass spectrometry-based glycan profiling, then compared against immune infiltration and markers of vessel activation. Our preliminary work has established reliable methods for isolating vessels and imaging immune infiltration in this model, providing a foundation for this analysis. Thus far, staining shows clear immune infiltration in diseased tissue compared to wild-type controls, and the project is expected to reveal how specific glycan changes track with immune infiltration and disease stage in this autoimmune context. Identifying these patterns would clarify how the vascular glycocalyx contributes to blood-brain barrier dysfunction during autoimmune neuroinflammation and lay groundwork for future comparisons with other neuroinflammatory conditions, such as sepsis and Alzheimer's disease, to distinguish shared mechanisms from disease-specific ones.

Transferrin Receptor 1 (TfR1) Antibody Binder Design for Clinical Relevance via Phage Display and Computational Methods

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Transferrin receptor 1 (TfR1) is one of the fastest internalizing receptors overexpressed in cancer cells. These attributes make TfR1 a suitable effector for bispecific antibody modalities, such as the novel transferrin receptor targeting chimera (TransTAC) technology. TransTACs enable highly specific membrane protein degradation by engaging a protein of interest (POI) on the cell surface alongside TfR1. However, the need for a clinically relevant TfR1 binder is required for in vivo antibody testing. We intend to find novel TfR1 binders that work for human, mice, and cyno TfR1 through traditional phage display techniques and computational prediction methods using models such as RFdiffusion or BoltzGen. Finding binders for three types of TfR1 (human, mice, cyno) expands the potential for further antibody designs and ability to find cross-reactive binders that work for TfR1 of various species. For the phage display, we began with the gene cloning process to express the TfR1 ectodomain. We fused the Fragment crystallizable (Fc) tail region of the antibody to the TfR1 ectodomain, resulting in the intended dimer structure for human, mice, and cyno TfR1. Next, we intend to perform phage display by incubating TfR1 ectodomains with a custom therapeutic-grade VHH and scFv antibody library. After three to four rounds of biopanning, we will generate concentrated phage pools ensuring the selectivity of high-affinity TfR1 binders. On the computational side, we intend to create a prediction pipeline in which possible epitopes are selected for binding compatibility and structural conservation across species, allowing us to identify epitopes for cross-reactivity. Potential binders are then simulated through antibody design software. The findings of this project will go towards clinical testing of TransTACs and other TfR1-engaging antibody designs, utilizing mice and cyno cells as animal models, bringing antibody-based therapeutics to patient populations

Redox Regulation of FOSL1 Transcriptional Activity in Glioblastoma

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Glioblastoma (GBM) is a highly aggressive brain cancer with poor patient prognosis despite intensive treatment. GBM cells exist in four cell states, of which the differentiated mesenchymal-like and astrocyte-like states have been characterized by a reductive environment and higher activity of the FOSL1 transcription factor. However, the molecular basis for these characterizations remains unknown. This study aims to elucidate the mechanism by which FOSL1 transcriptional activity is regulated by the cellular redox environment. We induced a reductive environment by increasing the NADH/NAD^+ ratio using the EcSTH system and ran a thermal stability assay and an oligonucleotide pull-down assay to detect changes in FOSL1 conformation and transcriptional activity, respectively. To probe the mechanism by which NADH may affect FOSL1 activity, we ran a co-immunoprecipitation with FOSL1 and the NADH-binding protein CtBP1 to identify a binding interaction, and a luciferase assay to measure transcriptional activity. Preliminary results show that upon increasing the NADH/NAD^+ ratio, FOSL1 undergoes a conformational change and has increased oligonucleotide binding. There is a binding interaction between FOSL1 and CtBP1, and their coexpression increases FOSL1 transcriptional activity. These findings suggest a mechanism in which CtBP1 promotes FOSL1 transcriptional activity through NADH binding. The connection between cellular redox environment and FOSL1 activity provided by this study contributes to our understanding of the metabolic profile of GBM cells and the molecular drivers of GBM cell states. The ability of GBM cells to transition between cell states confers to them adaptability that may be compromised by targeting their redox biology, potentially enabling greater therapeutic efficiency.

Allosteric Modulation of the E3 Ligase Adapter Protein Cereblon for the Treatment of Hematopoietic Malignancies

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Targeted protein degradation (TPD) is a therapeutic modality that leverages the cell's natural proteostatic systems to selectively degrade proteins implicated in cancer. The E3 ligase substrate adapter protein cereblon (CRBN) is frequently leveraged for TPD via small molecule molecular glues including thalidomide and analogs to promote degradation of new substrates (neosubstrates). Degradation of CRBN's neosubstrates drives clinical benefits for patients with a variety of hematological malignancies including multiple myeloma and del(5q) myelodysplastic syndrome. CRBN-targeting molecular glues primarily bind to CRBN's orthosteric thalidomide binding site, with little known about alternate binding sites on CRBN. Discovery and characterization of alternative CRBN binding sites may address major challenges in TPD include overcoming therapeutic resistance, avoiding off-target toxicities, and expanding the repertoire of TPD-degradable protein targets. Recent studies have revealed a novel allosteric binding site on CRBN ligandable by small molecule SB-405483, also known as allosteric cereblon binder (ACB). Engagement of the allosteric site by ACB has been found to cooperatively enhance the binding of orthosteric ligands and alter their neosubstrate degradation profiles. This research aims to perform structure-activity relationship studies on ACB for the development of superior allosteric ligands to promote CRBN-mediated TPD. We first computationally design ligands with high predicted affinity to the allosteric site. Computationally designed ACB analogs are then synthesized using organic synthesis techniques, amending based on introduced functional groups. Synthesized ACB analogs are then evaluated in a variety of biophysical and biochemical assays including TR-FRET to measure in vitro ligand binding affinity, NanoBRET to determine enhancement to orthosteric ligand binding in cells, and neosubstrate-HiBiT degradation assays to indicate how ACB analogs affect degradation of known neosubstrates. Identification and characterization of a superior ACB analog will provide a novel therapeutic avenue for overcoming resistances to orthosteric ligands, mitigating off target toxicity, and expanding the scope of CRBN-degradable neosubstrates.

Extending Semi-Empirical Extended Tight Binding Methods to Periodic Systems for an Efficient SCF Guess

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Accurate simulations of crystalline materials, surfaces, and catalytic interfaces often require self-consistent field calculations, in which the electronic structure is refined iteratively until convergence. The efficiency and reliability of these calculations depend strongly on the initial guess for the electron density. Conventional guesses, such as the superposition of atomic densities, can be inefficient for periodic systems because they do not fully capture the long-range electrostatic interactions and band-like electronic structure present in extended solids. This project extended the semiempirical tight-binding framework used in semi-empirical GFN1-xTB, GFN2-xTB, and g-xTB to periodic systems for the purpose of generating chemically informed initial guesses for higher-level electronic structure calculations. Periodicity was incorporated through Bloch's theorem, while long-range Coulomb interactions were treated using an exact Ewald-partitioning scheme that separates short-range real-space contributions from reciprocal-space electrostatics. This formulation enables the tight-binding guess to account for interactions across the periodic lattice while remaining computationally inexpensive. The resulting periodic xTB-based guess was evaluated primarily on slab systems, which are important models for surfaces, heterogeneous catalysis, and electrocatalytic interfaces. In these systems, improved initial guesses are expected to reduce the number of self-consistent field iterations needed for convergence and to improve robustness in cases where standard atomic-density guesses fail or converge slowly. The method also preserves fractional orbital occupations, allowing it to describe metallic, small-gap, and surface states more consistently within periodic boundary conditions.The results establish periodic xTB-based density guesses as a promising approach for accelerating simulations of materials, surfaces, and solid-state chemical systems, with future work focused on further benchmarking and refinement of density-matrix transfer strategies.

Mining MAM Superantigen Homologs with Protein Language Models to Explore Their Structural Diversity, Binding Modes, and Functions

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Antigen presentation by major histocompatibility complex class II (MHC II) molecules is crucial for the adaptive immune system, and developing a reporter that can detect specific antigen-derived peptide-MHC II complexes would establish a powerful tool in immunology. *Metamycoplasma arthritidis* mitogen (MAM) is a bacterial superantigen that non-specifically bridges peptide-loaded MHC class II molecules and T-cell receptors (TCR), leading to broad, antigen-independent T-cell activation. Recently, MAM was successfully engineered into TRACeR, a reporter that specifically recognizes selected peptide-MHC II complexes without activating the TCR. However, current TRACeR variants remain compatible with only a limited subset of MHC II complexes, highlighting the need for additional MAM-like scaffolds that could serve as generalizable reporters of peptide-MHC II complexes. Given the apparent isolation of MAM, which has so far been identified in only a single species, we explored genomic, metagenomic, and structural databases using sequence-, structure-, and protein language model-based approaches. Tools used include BLAST, HH-suite, Foldseek, PLM-BLAST, Protrek, ESM Atlas, and ESM sparse autoencoder feature-based analysis. Initial searches yielded a MAM-like protein (designated as MAM-B) of identical length as canonical MAM, also found in *M. arthritidis*, with 48.8 percent sequence identity. The N-terminus of MAM-B is predicted to bind to MHC in the same pose as canonical MAM. Further mining with protein language models identified protein candidates sharing sparse autoencoder features with the MAM N-terminal MHC-binding region. Those candidates were found primarily in *Metamycoplasmatota* and *Bacillota* lineages, suggesting that MAM-like scaffolds may extend beyond *M. arthritidis*. Several candidates are predicted to interact with diverse MHC molecules, indicating that they might represent functional MAM-like homologs. Together, these candidates highlight the diversity of the MAM superantigen, opening potential avenues towards naturally occurring peptide-MHCII-interacting scaffolds that lay the groundwork for creating a generalizable reporter of antigen presentation.

HSURV ABSTRACT BOOK 2026

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SCHOOL OF ENGINEERING AND APPLIED SCIENCES RESEARCH EXPERIENCE FOR UNDER-GRADUATES

Exploring the Antimicrobial of Extracting Native Herbal Plants Inhibition against H. Pylori

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University of New Mexico | Biomedical Engineering | 2030

Helicobacter pylori is a bacterial disease that is caused in your stomach lining. It infects over half the world's population, causing gastritis, ulcers, and increasing stomach cancer risks. *H. pylori* lies in its significant role as pathogen and its profound impact on global health. A major problem is the escalating antimicrobial resistance to conventional antibiotic therapies, leading to high treatment failures rates and recurrent infections. To develop and validate microfluidic-based technology devices to help detect this process of antibiotic resistance, specifically we aim to create a microfluidic PDMS(Polydimethylsiloxane) allowing for high-throughput screening of new native medicinal plant antimicrobial compounds. That precisely analyzes *H. pylori's* behavior and resistance mechanisms under controlled environmental conditions. There is potential in using PDMS devices to encapsulate Navajo traditional abstracts for potential drug delivery to help the medicine survive the acidic environment of the stomach where *H. pylori* are located.

Universally Visibility Material

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Conventional optical materials are engineered with fixed geometric, molecular, or photonic anisotropies that determine a single optical function after fabrication, limiting their adaptability. Here, we present a new class of adaptive optical materials, termed Universal Visibility Materials (UVMs), that dynamically reconfigure visibility by exploiting refractive index interactions between structured surfaces and their surrounding environment. Our approach employs scalable laser-engraved or 3D-printed microstructured templates replicated in PDMS, enabling low-cost and readily manufacturable devices. Optical behavior is governed by the interplay of light diffusion from high-curvature scattering regions and optical steering arising from refractive index mismatches at structured interfaces. By introducing fluids with different refractive indices onto the same microstructured surface, we continuously modulate scattering and refraction without altering the underlying geometry, producing multiple programmable visibility states. Depending on the refractive index contrast, devices can preserve transparency from head-on views, glancing angles, all viewing angles, or obscure visibility entirely, while also enabling reciprocal or asymmetric viewing behaviors. These results establish general design principles for programmable visibility using scalable optical geometries and demonstrate a versatile platform for adaptive privacy technologies, secure displays, communication interfaces, and other dynamically reconfigurable optical systems.

Sub-Micron Janus Particle Fabrication using Microfluidics

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A Janus particle is an anisotropic colloid with two distinct domains. This dual-compartment design enables the co-encapsulation of incompatible agents, making Janus particles attractive candidates for combination drug delivery, tissue engineering, and catalysis. However, their consistent fabrication at the sub-micron scale has not yet been demonstrated. Here, we introduce a versatile method for generating sub-micron Janus hydrogels inside microfluidic droplets by varying the concentration of the components in an aqueous three-phase system (ATPS). A binodal curve was constructed to identify ATPS compositions of agarose, gelatin, and polyethylene glycol (PEG) that preserve phase separation while maintaining small drop sizes. Preliminary results suggest that the Janus particles can be made at least an order of magnitude smaller than the vesicles that encapsulate them. By further tuning microfluidic device channel dimensions, drop phase concentration, and inner phase concentration, we expect to gain finer control over Janus hydrogel size and morphology. Together, these results establish a strategy for producing sub-micron Janus particles and provide a foundation for future optimization toward biomedical applications.

Atmospheric Water Harvesting

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Pima Community College/University of Arizona | Electrical Engineering | 2029

Dropwise condensation surface characterizations are critical for the development of new materials to combat water scarcity. Many characterizations, such as the drop size distribution are reliant on the accurate segmentation of droplets. Droplet segmentation is commonly achieved through applying a binary threshold to frames of condensation video. Binary thresholding is only reliable to segment droplets when imaging is performed by expensive camera and lighting equipment and condensation surfaces are homogeneous and pristine. We collected and annotated two droplet segmentation datasets of high quality and low quality droplets and created TileSAM3, a droplet segmentation pipeline that can segment droplets on homogeneous and inhomogeneous surfaces. TileSAM3 extends the maximum number of detected droplets of the Segment Anything Model 3 (SAM3) through repeated inference on hierarchical tiles of images. When evaluated on the Low Quality Droplet Dataset, TileSAM3 demonstrates an Average Precision of 0.571±0.021, which surpasses binary thresholding and other deep learning segmentation models including U-Net, DeepLabv3+, and Mask R-CNN. TileSAM3 enables the analysis of new materials imaged with more affordable equipment and more margin for error.

Holographic Microscopy of Colloidal Particles as Models for Viral and Bacterial Particle Interactions

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Self-assembly and close-range interactions shape many biological systems, but the physical encounters between small particles are difficult to measure directly, especially at nanometer-scale separations and over time. This project investigates colloids, microscopic particles suspended in solution, as simplified experimental models for studying how viral and bacterial particles physically interact. Specifically, this work uses 1.3 μm PSS colloidal spheres and holographic microscopy to measure particle motion in three dimensions with high time resolution. The project builds on prior two-particle measurements in which unexpectedly low diffusion coefficients motivated further study of single-particle motion and better-characterized particle pairs. Samples of colloidal spheres were prepared in glass slides and imaged using laser illumination, which produced holographic fringe patterns as particles moved in solution. For single-particle experiments, these holograms were fit with computational models to estimate particle radius, refractive index, three-dimensional position, and an intensity parameter. The project also developed an approach for future dimer experiments, in which optical tweezers will position two particles near each other before holographic imaging. These measurements are intended to support calculation of energy minima, effective spring constants, and diffusion coefficients. Thus far, the project has recorded and analyzed single-particle holograms while identifying fit quality as a key limitation. Some fits were sensitive to initial parameter estimates, so iterative fitting methods are being explored, where earlier fit results inform later fitting assumptions. Future work will extend these measurements to two-particle systems. By improving how close-range colloidal interactions are measured in three dimensions and over time, this work may help clarify physical principles relevant to viral and bacterial particle encounters.

A Non-Linear Approach to Atmospheric Circulation Regimes and Their Influence on Antarctic Sea Ice Variability

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The Southern Annular Mode (SAM) is the dominant mode of atmospheric variability in the Southern Hemisphere and heavily influences surface winds, temperature, and Antarctic sea ice distribution. This research is an extension of previous research, which applied a convolutional autoencoder (CAE) and hierarchal clustering to analyze nonlinear trends in the Southern Hemisphere mean sea level pressure (MSLP). This regime-based approach identified not only the traditional positive (SAM+) and negative (SAM-) phases, but also a frequently occurring third regime that acts as a transitional pathway between the two phases. This suggests that a nonlinear approach to analyzing atmospheric variability identifies variability that may not be fully captured by typical linear methods, primarily empirical orthogonal function (EOF) analysis. As an extension of this research, we investigate whether nonlinear atmospheric circulation regimes can better explain dominant patterns of Antarctic sea ice variability as opposed to traditional linear analysis methods of SAM. Thus far, monthly ERA 5 data of both MSLP and Antarctic sea ice concentration have been detrended and de-seasonalized to identify their respective anomalies. Primary Component Analysis (PCA)/EOF was then applied to the monthly ERA5 data both MSLP and Antarctic sea ice concentration anomalies to identify their respective leading spatial and temporal modes of variability. After running PCA, Maximum Covariance Analysis (MCA) was then used to identify coupled atmospheric and sea ice patterns that have the greatest shared covariance. This allows us to determine whether there are correlations associated with both atmospheric circulation regimes and Antarctic sea ice configurations. If our hypothesis is supported, then this study will reveal whether a nonlinear approach better identifies correlations between atmospheric circulation and Antarctic sea ice variability within the Southern Hemisphere.

Investigating the Role of El Niño/La Niña and Rice Cultivation on Methane Emissions in Southeast Asia

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Southeast Asia is a major emitter of methane, a potent greenhouse gas responsible for 0.6°C of warming since pre-industrial times, and a top global producer of rice, a major source of methane. The seasonality and interannual variability of methane emissions in the region are uncertain, and the role of rice cultivation practices on emissions is unclear, limiting mitigation opportunities. Here, we utilize the Integrated Methane Inversion to estimate emissions at 25 km □ 25 km spatial resolution using satellite observations of atmospheric methane, applying a Bayesian analytical inversion for five Southeast Asian mainland countries (Cambodia, Laos, Myanmar, Thailand, and Vietnam) during the wet (May-September) and dry (October-April) seasons of 2022-2024. We focus on the effects of La Niña (May 2022-April 2023) and El Niño (May 2023-April 2024) on wet- and dry-season variability, examining how these opposing climatological phases affect the availability of observations, precipitation, and the magnitude of emissions over flooded rice fields. We find that during the wet season, satellite observations are limited by persistent cloud cover associated with shifts in the Intertropical Convergence Zone, with more cloud coverage observed during the La Niña phase. Regardless of phase, emissions are higher during the wet season due to increased inundation and warmer temperatures. Future analyses will quantify the effects of these competing influences on rice emissions across seasons, climatological phases, and interannual variations. We plan to overlay the improved rice emission estimates with 30 m cropping-intensity data to assess correlations between the number of cropping cycles and emission intensity at the local scale. These ongoing investigations will improve estimates of spatial and temporal variability of methane emissions in Southeast Asia and link cultivation practices to strategies to limit global climate change.

Biodegradable Soft Actuator for Crawling Locomotion

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Columbia University | Mechanical Engineering | 2027

Soft robotics has emerged as a promising field;, utilizing the compliance of soft robots provides a unique opportunity to enable bioinspired movement in unstructured environments. Inspired by the peristaltic motion of earthworms and the wave-like locomotion of the tobacco hornworms, this project developed a biodegradable, linear pneumatic actuator for crawling locomotion in unstructured environments. The soft robot prototype uses pressurized air to instigate linear extension. A parametric study was conducted to analyze the effects of actuator wall thickness and corrugation density, with the goal of optimizing actuator geometry for maximum free extension and blocked force. The actuators were designed to operate between 5 - 10 psi to work with a low-power microfluidic controller output. Actuator segments were modeled using CAD software and manufactured using injection molding of gelatin into 3-D printed molds. The final design connected individual actuator modules into a crawling sequence that mimics earthworm-like peristaltic locomotion via a cyclic actuation cycle. Anisotropic frictional surface features inspired by earthworm and caterpillar setae were added to mitigate slipping during the locomotion cycle. Constructed entirely from biodegradable materials, the resulting system could support distributed environmental sensing in remote or inaccessible locations where retrieving conventional robotic systems may be impractical or impossible. Integration with environmental sensors could allow for spatially distributed remote environmental monitoring while reducing time, labor cost, and material waste.

Atlantic Ocean Paleotemperature Reconstruction of the Messinian Salinity Crisis Using Geochemical Biomarker Analysis

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University of Alabama, Tuscaloosa | Chemistry | 2028

The past 6 million years have seen periods of climate variability largely based on natural precessional cycles of the Earth. However, anthropomorphic activity has led to a stark increase of 150 ppm in atmospheric carbon dioxide concentrations since the Industrial Revolution, nearing the 500 ppm peak seen during the Miocene Epoch (23-5.3 million years ago (Ma)). In the interest of modeling the impacts that future climate change may have on global ocean circulation and Mediterranean climate, the Miocene has become a useful time period of study. A particular event of interest in the late Miocene was the Messinian Salinity Crisis, occurring from a gradual drying 6 Ma to a catastrophic reflooding 5.3 Ma. During this dry period, the Mediterranean Sea sequestered significant amounts of salt, while simultaneously ceasing to export warm, salty water to the Atlantic, which feeds the Atlantic Meridional Overturning Circulation (AMOC) in the present day. International Ocean Discovery Program (IODP) Expedition 397 recovered sediment cores proximal to the Straits of Gibraltar that may give an insight to conditions in the area before, after, and during the Salinity Crisis through investigating Glycerol Dialkyl Glycerol Tetraethers (GDGTs), a biomarker with varying levels of branching, cyclization, and length. Produced primarily by Thaumarchaeota and Crenarchaota, marine sea surface temperatures cause these variations in GDGT structure. Reconstruction of these organic molecules found in Miocene sediment samples proximal to the Straits of Gibraltar can be used as a proxy to reconstruct sea surface temperatures and predict how future climate conditions may impact AMOC.

Ibero-African Paleoecology and Fire Activity of the late-Miocene Messinian Salinity Crisis

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The Messinian Salinity Crisis (MSC, 5.96-5.33 million years before present (Ma)), during which the Mediterranean Sea largely desiccated before being reflooded via the Zanclean flood, represents one of the most extreme paleoenvironmental perturbations of recent geologic history. This project uses sediment cores recovered during International Ocean Discovery Program (IODP) Expedition 397, which sampled off the Portuguese Margin, to reconstruct how the loss and restoration of Mediterranean-Atlantic connectivity affected terrestrial Iberian ecosystems. I will measure organic geochemical proxies such as average chain length (ACL) to constrain plant functional type, pentacyclic triterpenyl methyl ethers (PTME) to track grass abundance, and polycyclic aromatic hydrocarbons (PAH) as a fire proxy. These records will be generated at 3-kyr resolution and compared against climate models to test whether current simulations can reproduce an extreme scenario, such as the MSC. The comparison is expected to clarify how vegetation and fire regimes respond to Mediterranean desertification and will show whether MSC proxy records can serve as a reliable benchmark for evaluating model performance under abrupt hydroclimate change. Future work will expand the proxy dataset across other core intervals and refine model-data comparisons, with the broader goal of improving confidence in climate model projections.

A Floating-Point Safe Gaussian Sampler for Differential Privacy on GPUs

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Harvey Mudd College | Computer Science | 2028

Differential privacy protects individuals by adding calibrated random noise to computations, but implementations that assume exact sampling from a continuous distribution can lose their intended privacy guarantees when using inexact finite-precision floating-point arithmetic. When Gaussian noise is naively sampled with floating-point operations, there are gaps between reachable outcomes that can allow an adversary to infer protected data. Existing defenses take several forms, such as manipulating compromised mantissa bits directly, rounding the released value onto a coarse grid, sampling on a discrete integer lattice with base-2 acceptance probabilities, or using arbitrary-precision arithmetic. While these reduce or remove leakage risks, each either constrains the output to a resolution coarser than the float grid leading to a less precise released value, or carries the high computational costs of arbitrary-precision arithmetic. We present a sampler that draws continuous Gaussian noise exactly rounded to a native 32-bit float. The approach samples a standard normal using the Karney rejection sampling method, which needs only comparisons of lazily-revealed random bits, only to the precision each comparison needs. It then proves, using exact integer dyadic arithmetic, that the clipped, scaled value rounds to one specific float. We intend to implement the sampler in the OpenDP library, providing a CUDA implementation so it can run efficiently on GPUs within private machine learning algorithms. Preliminary results suggest the approach provides privacy guarantees for a native continuous Gaussian mechanism while keeping per-sample work on a GPU practical for finite-precision integer operations.

Designable Temperature-Responsive Solar Harvesting across Space, Energy Type, and Storage Release Time

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University of Texas, Austin | Chemistry | 2027

The ability to efficiently harvest and utilize solar energy is of fundamental importance to our sustainability. However, typical solar harvesting and storage approaches are static and single-mode, unable to modulate, on-demand, (i) to where sunlight is directed in space, (ii) to what degree solar photons are converted to electrons, phonons, or chemical bonds, and (iii) for how long converted energy is stored. Here, we introduce a universal, temperature-triggered solar harvesting concept and use it to build devices capable of redirecting, harvesting, storing, and releasing sunlight across space, energy type, and storage release time. Our approach is based on the thermally modulated expansion of gas to expand liquids within cavities lined with refractive and concentrating structures. By tuning the thermal sensitivity of the working fluids and spatial landscape of receiving photovoltaic, thermal, and/or chemical harvesters along the device's focal plane, we can design at which temperatures sunlight is harvested as which combination of energy modes, and for how long it is stored. This general solar harvesting programmability enables new multi-mode energy technologies, including passive beam-steerers for photovoltaics, self-regulating space conditioners for buildings, and indoor climate control systems with memory.

Return to Earth: A Biodegradable Paradigm for Transient Robotics

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Faculty Advisor(s): Robert J. Wood
University of Illinois, Urbana-Champaign | Mechanical Engineering | 2027

As transient robotics continues to emerge for environmental monitoring and ecological applications, the development of biodegradable structural materials with sufficient mechanical performance remains a major challenge. Robotic materials must simultaneously provide high specific stiffness, impact resistance, elasticity, and long-term mechanical reliability while maintaining environmental degradability. Here, we develop biodegradable wood-based composites by infiltrating delignified wood with biodegradable polymer matrices tailored for two distinct robotic functions. Furthermore, variations in polymer chemistry allow for us to prioritize certain attributes, such as the specimen's ductility or resistance to temperature. For a wind-driven tumbleweed rover, delignified Balsa wood infiltrated with a chitosan–glycerol matrix was developed as a lightweight structural rim that combines high specific stiffness with improved impact resistance and moisture-responsive actuation. For a latch-mediated jumping robot inspired by the Trapjaw ant, delignified Birch wood infiltrated with a gelatin–glycerol matrix was engineered as a spring capable of storing and rapidly releasing mechanical energy via transient elastic snapthrough. By controlling the buckling mechanism with a biodegradable mechanical oscillator, we are able to achieve cyclic jumping. The mechanical performance of the developed composites was systematically evaluated using Instron tensile testing and Charpy impact testing to characterize their quasi-static and dynamic behavior, respectively. The materials were subsequently integrated into functional prototypes. Rover performance was assessed through incline, impact, and indoor locomotion experiments, demonstrating robust mobility across diverse environments while maintaining structural integrity. The jumping mechanism in the Trapjaw ant further validates the ability of the biodegradable composite spring to repeatedly undergo large elastic deformation with rapid energy release. This work establishes delignified wood composites as a versatile platform for biodegradable structural materials that bridge sustainable materials engineering and transient robotics, enabling environmentally compatible robotic systems without compromising mechanical performance.

Prism Device

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Conventional solar harvesters typically convert sunlight into either thermal energy or electricity. In contrast, we present a dual-mode solar harvester that dynamically transitions between these outputs based on ambient temperature. This mechanism utilizes the principles of Snell's Law to modulate light refraction at the interface of transparent media. The switching mechanism is driven by thermal air expansion, which displaces water into a micro-channel integrated with lenticular facets. As the water level rises, the refractive properties of the facets are altered, proportionally increasing the fraction of incident sunlight directed toward a secondary harvester. The experimental prototypes were fabricated from acrylic components and bonded with Acrifix. Each device incorporates a multi-cavity architecture featuring Polydimethylsiloxane (PDMS) membranes and narrow apertures designed for precise fluidic control, supplemented by a one-way flap valve. Each assembly comprises 9–12 customized segments, including clear PDMS accessories and anti-fog treated surfaces to ensure optical clarity during testing. These components work in tandem to regulate internal fluid dynamics and secure the optical wedge sheets. To ensure structural integrity and operational consistency, the devices underwent rigorous hydrostatic, thermal (refrigeration), and mechanical endurance testing. These evaluations focused on identifying fluid or pneumatic leaks and assessing the long-term durability of the valve system. Optical performance was characterized under varied thermal conditions to observe shifts in focal point concentration and repositioning. While initial trials utilized water, the experimental framework is compatible with a range of refractive liquids for further optimization.

Liquid-Lined Windows Autonomously Regulate Indoor Temperature and Lighting Through Selective Absorption

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Windows act as gateways for heat and light into a building, regulating energy efficiency and illumination. Static windows transmit both visible solar daylight (VIS) and near infrared solar heat (NIR), but the desire for each component of sunlight is independent and variable. Materials that selectively respond to changes in VIS and NIR, or light and heat, can autonomously regulate light and heat transfer into a building at the window in a multitude of weather conditions. However, typical dynamic windows respond only to one stimulus (light or heat), and those that respond to more than one (light and heat) cannot separate input-output pathways, meaning that different stimuli cannot individually modulate VIS and NIR bands. To improve indoor energy efficiency and human comfort, ideal windows must block VIS at high light intensities, yet block NIR at high temperatures. Here, we report optofluidic windows that independently modulate VIS in response to light intensity and NIR in response to temperature. This decoupling is achieved by designing a pair of devices in which increases in sunlight radiation or ambient temperature individually triggers an expansion of gas, pushing a selectively VIS- or NIR-attenuating liquid into one of two adjacent window cavities. Laboratory experiments reveal orthogonal VIS transmission modulations between 0.9-0.01 for solar intensities between 0-1000 W/m2, and NIR transmission modulations between 0.8-0.05 for ambient temperatures between 21-27 degrees Celsius. Further, we show that the sensitivity ranges for VIS and NIR modulations can be modeled and designed, unlocking fully decoupled specification of indoor optical and thermal tunability.

Zircon-hosted Mineral Inclusions as a Window Into Earth's Infancy

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The crustal composition and processes of early Earth remain uncertain, chiefly due to the scarcity of whole rocks older than 2.5 billion years. Given the scarcity of these rocks, zircons can act as proxies for early Earth processes. This project studies 4.2-3.3 Ga detrital zircon crystals from the Green Sandstone Bed in South Africa. During their crystallization, zircons can trap inclusions of other minerals, which can be used as mineralogical proxies to further our understanding of early Earth conditions. Using EDS (energy dispersive x-ray spectroscopy) and BSE (backscattered electron) detectors on a Zeiss Gemini 360 SEM (scanning electron microscope), we image and chemically characterize these inclusions. So far, we have examined 157 inclusions in 79 zircons, which have been categorized into 12 different phases (quartz, muscovite/white mica, K-Al silicate, feldspar, biotite, chlorite, mafic silicate, apatite, monazite/xenotime, Fe/Ti oxides, titanite, and other). Quartz and muscovite/white mica dominate the inclusion assemblage, each constituting 27% of all inclusions analyzed. Previous studies of Hadean detrital zircons from Jack Hills, Australia have shown similarly quartz and muscovite-rich inclusion distributions, indicating potentially similar sources. Apatite occupies 9% of the inclusion assemblage. Previous studies of Phanerozoic granitoids indicate an inverse correlation between apatite inclusion occurrence and whole rock SiO2 content. As such, the relatively low apatite counts in the GSB zircons are consistent with a felsic source material. Our preliminary results are consistent with the presence of evolved crustal materials as early as the Paleoarchean. These observations can aid in better constraining the onset of crustal processes that are essential to climate stabilization and therefore the habitability of the early Earth. As a future direction, combining inclusion and zircon geochemistry with our assemblage-level observations could help better constrain the nature of the early Earth's crust.

Beyond EOF1: Disentangling Trends in the Southern Annular Mode with a Convolutional Autoencoder

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The Southern Annular mode (SAM) is the dominant mode of atmospheric variability in the Southern Hemisphere (SH) traditionally defined as the first empirical orthogonal function (EOF1) of sea level pressure in the southern mid and high latitudes. However, because EOF analysis is a linear decomposition, it can fail to capture nonlinear circulation regimes or lower amplitude transition states between positive and negative phases of the SAM. Applying a convolutional autoencoder (CAE) to identify prominent SAM phases through hierarchical clustering may therefore offer better insight into SAM dynamics and their regional climate impacts in the SH. Due to anthropogenic forcing mechanisms such as ozone depletion and greenhouse gas emissions, the SAM has become increasingly positive over the past century. Our research seeks to determine whether the positive trend in the SAM reflects an increase in the canonical positive SAM regime, or instead results from shifts in the frequency of nonlinear circulation regimes identified by a CAE. We analyzed spatial and time series reprojection data using linear regressions, cross correlations, and power spectral analysis. Based on this, we assessed variability across monthly, seasonal, yearly, and decadal timescales. Preliminary results from non-detrended CAE outputs show an average 0.158 months/year increase in positive-phase frequency of the SAM since 2000 and an average 0.103 and 0.054 months/year decreases in negative-phase and nonlinear-regime frequency over the same time period, respectively. These preliminary findings suggest that the SAM's positive trend is driven primarily by more frequent occurrence of its positive regime rather than a shift away from nonlinear transition states, offering insight into the mechanisms linking anthropogenic forcing to SH circulation change. More broadly, this work demonstrates the potential of nonlinear machine learning frameworks to complement traditional EOF-based analyses of atmospheric variability.

Developing Materials to Address Marine Fouling on Underwater Structures

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McGill University | Physics | 2027

Marine biofouling is the accumulation of unwanted micro-organisms on submerged surfaces. The fuel penalty resulting from marine fouling on commercial vessels is close to $60B/year and can be 5-10% ($1.5-3B) of production costs in the aquaculture industry. There are also environmental concerns of transporting invasive species, causing disruptions in the local ecosystems. Additionally, the current standard coatings used by the US Navy are toxic copper based anti-fouling paints. Recent field studies show that non-toxic amphiphilic additives incorporated into silicone polymers minimally foul when subjected to a continuous flow growth chamber for 3 weeks at the Naval Research Laboratories. This non-toxic foul-release coating minimizes adhesion of fouling organisms causing them to be easily removed under shear. In this study, we compare the behavior and properties of different loadings of the amphiphilic additives in ocean-like conditions over a 3 week period followed by a week in a high shear flow cell. We characterized the materials and surface wetting properties to further investigate the field study results using AFM, contact angle analysis, release kinetic measurements, FTIR, TGA, and SEM images of the cross section. Preliminary results suggest that a mixture with 10wt% additive is the optimal balance between the foul release and material properties.

Antibacterial Activity of Native American Tea and Herb Extracts Against Helicobacter pylori

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Helicobacter pylori is a gram-negative, microaerophilic bacterium that colonizes the human stomach and infects roughly half of the global population. Through urease-mediated conversion of urea to ammonia, it buffers stomach acid, migrate through the protective mucus layer via flagellar motility, and adheres to the gastric epithelium, driving a disease progression from gastritis to peptic ulcers and, in some cases, gastric cancer. *H. pylori* disproportionately affects Native American communities, with prevalence estimated at 70–90% in some populations compared to roughly 30% nationally. For instance, studies show a 62% infection rate among Navajo adults and gastric cancer incidence 2–3 times higher than the general U.S. population disparities linked to water and sanitation access, healthcare availability, and socioeconomic factors. Standard triple and quadruple-therapy antibiotic regimens are increasingly compromised by rising antibiotic resistance, underscoring the need for new antimicrobial strategies. Traditional Navajo tea and herbs including bear root (Naabį), juniper foliage (Gad), Navajo tea (Deeh), sage (Ts'ah), and yucca root (Táláwosh) have long been used to relieve digestive ailments, yet few have been evaluated using standardized antimicrobial assays. Prior testing of these extracts against the non-pathogenic model organism *E. coli* identified bear root as the most effective of inhibiting bacterial growth. This study extends that screening to *H. pylori*, using standardized extraction, filtration, and refrigeration protocols across varied temperatures and steeping times to identify optimal preparation conditions. *H. pylori* cultures are grown under microaerophilic conditions and challenged with each extract, with minimum inhibitory concentration, minimum bactericidal concentration, and urease-inhibition assays used to characterize each extract's antimicrobial mechanism. In parallel, PDMS microfluidic devices are being fabricated via soft lithography to enable controlled, low-volume assays. The most potent extracts will undergo mass spectrometry to identify their bioactive compounds, with the goal of scientifically validating traditional remedies and identifying novel antimicrobial leads against *H. pylori*.

Amplification by Iteration for Differentially Private Linear Regression

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Linear regression is a canonical primitive in statistical learning, and differential privacy (DP) has emerged as the gold standard for enabling statistical learning while protecting user data. However, designing DP linear regression algorithms that are accurate on average-case data, private on worst-case data, and practically implementable remains challenging. Recent algorithms for private linear regression achieve near-minimax-optimal sample complexity, but their large constants and algorithmic overhead make them poorly suited to realistic deployment. In contrast, gradient-based methods are simple and widely used, yet existing privacy analyses either rely on restrictive assumptions on the input distribution or incur undesirable dependence on iteration complexity, as a result of unnecessary privacy loss stemming from composition. Motivated by privacy amplification by iteration, which enables sharp privacy accounting for iterative optimization algorithms, we provide an analysis of noisy gradient descent acting on regularized linear regression. In particular, we show that amplification by iteration does not outperform composition at the mixing threshold, and are currently exploring novel utility bounds. Furthermore, we extend the amplification-by-iteration framework to finite-precision arithmetic, allowing us to provide a faithful implementation of accounting via amplification by iteration and may be of independent interest. We validate our theoretical analysis with empirical experiments on both synthetic and UCI regression datasets. Finally, we are working to implement our algorithm and privacy accountant in the OpenDP library, providing a practical end-to-end method for private linear regression.

Mediating Bubble Nucleation of Gas Evolving Reactions

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Decompression sickness occurs when dissolved gases come out of solution and form expanding bubbles as pressure decreases, damaging surrounding tissues and potentially causing serious injury. Current treatments primarily address these bubbles after they have already formed rather than preventing their formation. Silicalite-1, a microporous zeolite with nanometer-sized pores and a large internal surface area, has previously been shown to increase the gas-carrying capacity of water by adsorbing dissolved gases within its pore network. These properties make it a promising candidate for influencing the earliest stages of bubble formation, although whether it can alter bubble nucleation remains unknown. This work investigates how silicalite-1 influences bubble nucleation and explores its potential as a material for reducing decompression-related injuries. To investigate this, oxygen bubbles are intentionally generated through electrochemical water splitting in a controlled system. Chronopotentiometric measurements are used to identify the onset of bubble nucleation and compare bubble formation in electrolytes with and without suspended silicalite-1 particles. These experiments evaluate whether silicalite-1 alters bubble nucleation through increased gas diffusion, enhanced dissolved gas storage, or a combination of both mechanisms. In parallel, silicalite-1 is surface functionalized with an N-oxide zwitterionic species to improve suspension stability in aqueous environments relevant to biomedical applications. This surface modification is designed to reduce particle aggregation while maintaining the material's hydrophilic exterior and preserving access to its internal pore network. By integrating electrochemical characterization with materials engineering, this work advances the understanding of how microporous materials influence bubble nucleation while establishing design strategies for stable gas-managing suspensions with potential biomedical applications, including the prevention of decompression-related injuries.

Was Plate Tectonics Active During the Archean Eon? A Paleomagnetic Approach

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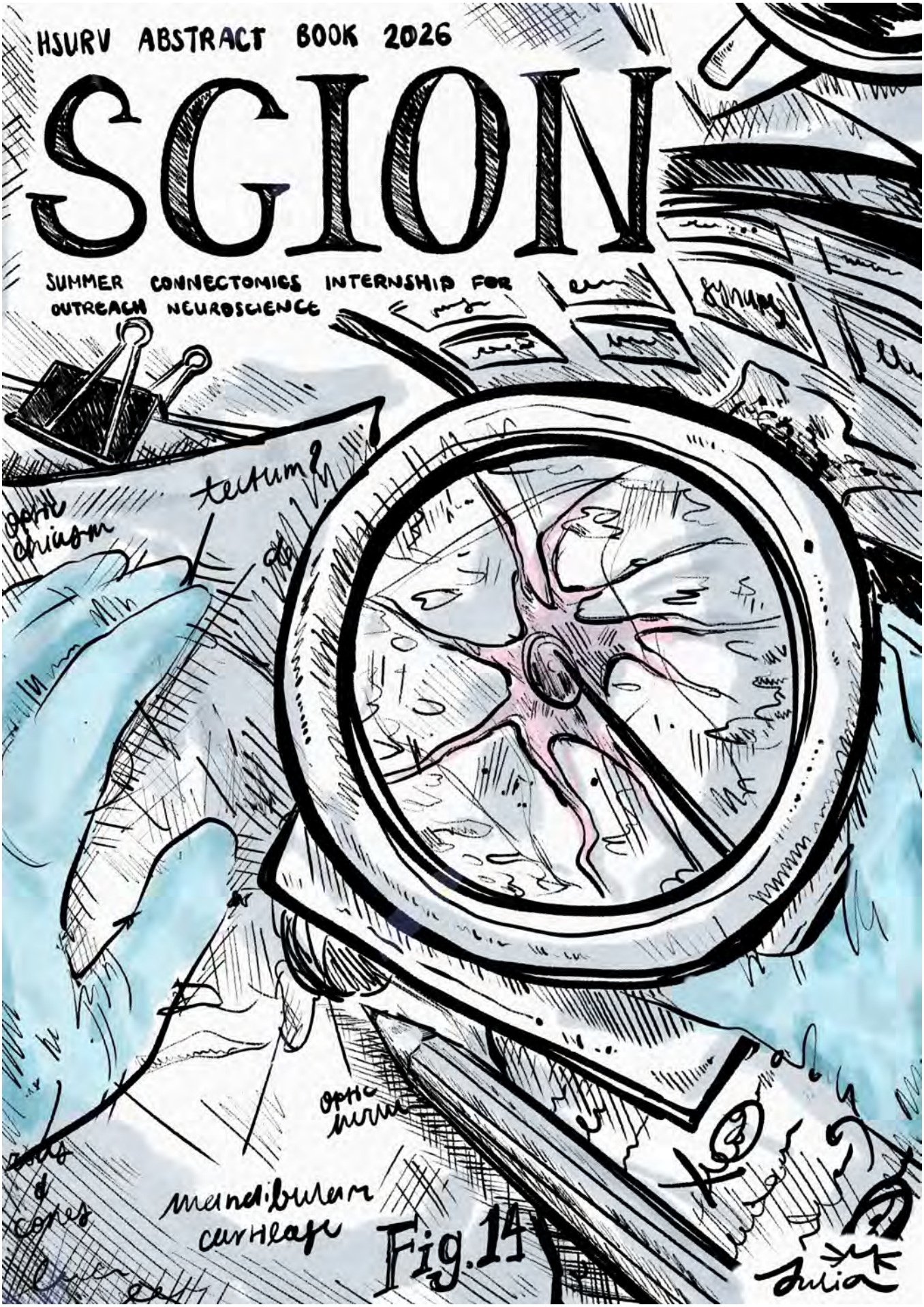
The theory of plate tectonics is the defining concept of modern geology, as it provides a framework for understanding the history and morphology of continental and oceanic crust, as well as the distribution of volcanoes and seismic zones on the modern Earth. While there is evidence that plate tectonics has been active throughout the Phanerozoic, there is no consensus about when it began, nor what characterized the lithospheric regime that preceded it. Determining the nature and timing of the onset of plate tectonics is essential to understanding ancient climate and the development of life, as tectonic processes play an essential role in the modern carbon cycle. This study investigates ancient tectonics through paleomagnetic analysis of 3.1 Ga volcanic rocks of the Sholl Terrane, collected from the Northwest Pilbara Craton in Australia. The orientation of the ancient magnetic field will be determined by measuring the magnetic moment of oriented rock samples in a 2G Enterprises DC-SQuID Superconducting Rock Magnetometer. Through progressive thermal demagnetization past the blocking temperatures of the dominant ferromagnetic mineral phases, the characteristic remanent magnetism (ChRM) component will be isolated. ChRM orientations will be used to define a paleomagnetic pole for the Northwest Pilbara Craton at 3.1 Ga. This will be compared to paleomagnetic poles from adjacent units to quantify the extent of apparent polar wander (APW) and evaluate the possibility of mobile-lid tectonics in the Archean.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Visual Evidence for Self-Stationarity Mechanisms in Larval Zebrafish

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Larval zebrafish rely on optomotor and optokinetic reflexes to orient their eyes and swim in the direction of visual motion for stability in flowing water. This reflex can be misleading since visual motion caused by the fish's turning looks identical to motion caused by movement in the environment, and the brain must distinguish between the two. It remains unclear which neurons and circuit mechanisms allow the brain to use stationary objects to override this turning reflex when self-motion is not occurring. Visual information enters the brain through retinal ganglion cells (RGCs), which carry signals from the eye to downstream visual processing centers. In larval zebrafish, a population of RGC axons project to arborization field five (AF5), a region within the pretectum known to contain visual motion information. There, RGCs form synapses with bistratified tectal cells, neurons with dendrites arranged in multiple layers within the optic tectum. This project aims to identify the neural circuit that suppresses the turning reflex during self-generated visual motion by mapping connectivity from the retina through the tectum to eye-movement motor output. Finding this circuit would clarify how the visual system resolves conflicting motion information. Using electron microscopy, RGCs projecting to AF5 on the left side of the brain were identified, along with their postsynaptic bistratified tectal cell partners. These tectal cells were grouped using a clustering algorithm based on morphological features and synaptic connectivity from RGC inputs. Comparing the resulting clusters across brain hemispheres to identify bilaterally conserved cell types, and tracing downstream neurons will determine which clusters connect most directly to eye-movement motor neurons. This will help distinguish between two candidate circuit models: a dedicated stationary-pattern pathway versus a combined motion-stationary pathway.

Futility-Induced Passivity Circuit in Larval Zebrafish

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Faculty Advisor(s): Mariela Petkova
Brandeis University | Molecular & Cellular Biology | 2029

When an animal's actions repeatedly fail to produce their expected consequences, it can adapt or abandon the behavior. To understand this behavior, larval zebrafish were placed in a virtual-reality assay. Visual feedback was manipulated to control the animal's perception of its movement and to attempt to induce futility-induced passivity in two conditions: closed-loop and open-loop. Under closed-loop conditions, forward optic flow reverses when the fish moves its tail, signaling movement and causing the subject to continue attempting to swim. Under open-loop conditions, visual flow advances regardless of tail movement, and the subject progressively stops attempting to swim. It has been proposed this switch is governed by the following circuit: noradrenergic medulla-oblongata neurons (NE-MO) and locus coeruleus neurons (LC) encode a motor-error signal triggered when optic flow does not change, which is integrated by a build up of calcium in astrocytes and ultimately drives motor suppression, while serotonergic dorsal raphe (DRN) neurons are engaged during optic flow reversal to inhibit the NE-MO and LC neurons. Using prior lab efforts to build a larval zebrafish connectome, the relevant populations of neurons were isolated in electron microscopy data, using morphology and connectivity to properly label each population. Currently, an additional twenty neurons have been contributed to the LC population, an additional thirty-two neurons have been contributed to the NE-MO population, and an additional thirty-six neurons have been contributed to the DRN population. To find the connectivity, the found identified neurons were used to create a pathfinding code tracing the connectivity between 5HT-DRN, NE-MO neurons, and LC neurons individually. By determining the paths between the identified neurons, the hypothesized circuit and the mechanism behind futility-induced passivity can be tested.

Motor Neurons: Muscular Control and Locomotion in the Larval Zebrafish

Student: Aditi Joshi
Mentor(s): Yasuko Isoe & Juan Carlos Tapia
Faculty Advisor(s): Mariela Petkova
Brandeis University | Molecular & Cellular Biology | 2029

Animals exhibit a variety of movements by controlling muscle activity. The neurons that control movement are classified into two broad categories: primary and secondary motor neurons. How the signals from motor neurons to muscles produce muscle contraction is known in general, but the coordination of motor neuronal activity and muscle activity still remains unknown. Our project aims to verify the size principle, a foundational concept of neuroscience. The size principle hypothesizes that smaller secondary motor neurons execute smaller, more precise movements, while the bigger primary motor neurons are recruited for the activation of faster, more powerful muscular units. By studying EM images of a larval zebrafish, we mapped neuromuscular junctions of individual axon collaterals to muscle units. Via calcium imaging, a gradient was constructed to understand whether forceful movements are driven by activation of primary and secondary motor neurons, and delicate movements only by secondary. Thus, a three-dimensional map of neuromuscular junctions will allow us to compare different mechanisms of action and the neural circuitry involved with three specific behaviors that employ muscles in the fish trunk (myotomes 2–5): "c-escape", "forward swim", and "big turn." Studying the discrete pairs of command neurons (Mauthner, nMLF and MiV neurons, respectively) and motor neurons associated with each of these behaviors would enable us to deduce whether individual pathways corresponding to command neurons and behavior exist. The Labeled Line Theory suggests that distinct pathways exist for the processing of distinct sensory information. Finding these motor out pathways would allow us to evaluate whether a Labeled Line-adjacent description is applicable to how these motor circuits operate. Our project aims to investigate whether distinct command circuits are responsible for specific movements and behaviors, with the aim of understanding and being able to better treat neuromuscular disorders such as ALS, which involves deterioration of neuromuscular junctions.

Synaptic Organization of Visual Threat Processing and Escape Behavior in Larval Zebrafish

Student: Geair Justice
Mentor(s): Clemens Riegler
Faculty Advisor(s): Mariela Petkova
Dartmouth University | Neuroscience | 2029

Visually evoked escape in larval zebrafish requires the transformation of retinal information about an approaching threat into a rapid motor command, yet the synaptic organization of this pathway remains poorly defined. This project will use neuronal tracing in a larval zebrafish connectomics dataset to reconstruct circuits linking retinal and pretectal or thalamic inputs to optic tectal neurons and downstream hindbrain reticulospinal populations. We hypothesize that distinct pathways carry expanding-edge and dimming information into the tectum, where local inhibitory neurons and periventricular projection neurons integrate these signals to control escape probability, direction, and habituation. We will specifically test whether dimming-sensitive pathways provide inhibitory input that suppresses loom-responsive circuits after repeated stimulation, and whether tectal outputs diverge onto fast Mauthner-associated and slower non-Mauthner escape pathways. The expected outcome is a synaptic circuit model explaining how visual threat features are integrated, adapted through experience, and converted into distinct escape commands.

Visual Evidence for Stationary Behavior in Larval Zebrafish

Student: Audrey Lin
Mentor(s): Vickie Wang
Faculty Advisor(s): Mariela Petkova
Brandeis University | Neuroscience | 2029

Visual processing enables animals to distinguish self-motion from self-stationarity, a difference essential for survival and stable behavior. In larval zebrafish, stationary visual patterns suppress rotational optomotor (tail) and optokinetic (eye) responses, such that pairing a moving stimulus with a stationary one reduces eye turning. However, the neural circuitry underlying this suppression remains unclear. This project investigates the circuit mechanism for suppression, focusing on visual processing cells in the optic tectum that receive input from retinal ganglion cells (RGCs) projecting to arborization field 5 (AF5), a region known to encode directional, whole-field motion used to drive optomotor and optokinetic behavior. A population of bistratified tectal cells connected to AF5 RGCs are hypothesized to mediate this suppression. Because RGC input onto these cells is excitatory, suppression of rotation must arise from how strongly the bistratified cells are driven, not from their direct inhibition. Two candidate models were considered: stationary input alone may excite bistratified cells enough to suppress rotation, or suppression may instead require combined excitatory drive from both motion and stationary input. These two models predict distinct populations of bistratified cells with different input profiles, motivating a search for structurally and synaptically distinct cell types. Using connectomics, bistratified tectal cells on the right side of the brain were clustered computationally, using code to group cells by synaptic input similarity and morphological features. These clusters will be compared to their left-side counterparts, given expected bilateral symmetry in circuit architecture. Distinguishing these subtypes will help determine which input combination drives suppression. Future work will trace candidate bistratified cells downstream to eye motor control modules to confirm their causal role, extending these findings to other vertebrates and illuminating a shared strategy for resolving self-motion from conflicting visual stimuli.

Investigating Dorsal Raphe Neural Circuits Underlying Futility-Induced Passivity in Larval Zebrafish

Student: Safaa Mohammed
Mentor(s): Marc Duque Ramirez
Faculty Advisor(s): Mariela Petkova
Harvard University | Biomedical Engineering | 2029

Amid persistent failure, various organisms switch from actively struggling to overcome the situation to becoming passive toward it. Larval zebrafish have provided a model for studying this transition in the context of their swimming behaviors. When placed in two different virtual-reality swimming environments with consistent visual flow, fish respond in different ways. In a closed-loop environment, the fish receives visual feedback to indicate progress and feels stabilized. In contrast, an open-loop environment provides no visual feedback as the fish swims; the fish speeds up its swimming in a final attempt to stabilize before registering its actions as futile, shifting to a passive state by slowing down or stopping. Prior studies have identified noradrenergic neurons in the medulla oblongata (NE-MO) and locus coeruleus (LC) driving this transition. NE-MO and LC neurons register swim failures, and evidence of this accumulates in glial astrocytes. The glia have been proposed to relay signals downstream to another population of neurons that potentially lead to motor suppression. However, when a fish receives visual feedback indicating swimming progress, a population of serotonergic neurons in the dorsal raphe nucleus (DRN) is activated, which are hypothesized to inhibit activation of NE-MO and LC neurons. Using connectomic datasets constructed from electron microscopy images of the entire larval zebrafish brain, we are identifying putative NE-MO and serotonergic populations of the fish, based on morphological features and input and output connectivity. To date, we have identified fifty NE-MO neurons to contribute to a fuller map of the noradrenergic population. By identifying these populations, we will test if an inhibitory relationship exists between the serotonergic populations in the DRN and NE-MO. In addition, we will use calcium activity mapping in the same animal to investigate an inhibitory effect by the serotonergic neurons in the dorsal raphe area on the noradrenergic NE-MO and LC neurons.

Synapse-Resolution Connectomic Reconstruction Reveals Structural Organization of Vagal Sensory-Relay-Motor Circuitry in Larval Zebrafish

Student: Nicole Samaan
Mentor(s): Kristian Herrera
Faculty Advisor(s): Mariela Petkova
Princeton University | Biomedical Engineering | 2029

The vagus nerve is anatomically distinct from other brain regions in that it innervates numerous organs and functions distributed throughout the body rather than concentrated in one location. While its systems-level organization is broadly characterized, the neuron-by-neuron architecture of the vagus nerve remains unidentified. Using a synapse-resolution connectome reconstructed from electron microscopy of a 6-day-old larval zebrafish brain, we are tracing the full sensory-relay-motor circuitry of the vagus nerve to produce the first granular map of its neurons and synapses. This map allows us to address whether the symmetry or asymmetry of a given bodily function is mirrored in the underlying neural circuitry that governs it. We hypothesize that circuits governing bilateral functions (e.g., respiration) exhibit bilateral neural organization, while circuits governing ipsilateral organ functions exhibit correspondingly lateralized organization. Testing this relationship requires first completing a manual reconstruction of relay neurons and their synaptic connections to motor neurons and target muscles and organs, followed by computational and statistical analyses of branching and symmetry patterns, including evaluation of the size principle within vagal motor pools. Reconstruction is ongoing. So far, we find high levels of symmetry in vagal motor neuron synapses that are downstream of bilateral relay neurons that innervate the gill arches, a function requiring bilateral synchronization. Additionally, we find low to moderate levels of connectivity overlap between vagal relay neuron partners. Establishing this relationship would clarify a fundamental organizing principle of brain-body communication and provide a framework for interpreting future vertebrate connectomic datasets, with implications for biomedical approaches to neural and physiological dysfunction.

Understanding the Role of the Vagus Nerve in Synchronizing Visceral Function

Student: Devnah Trivedi
Mentor(s): Kristian Herrera
Faculty Advisor(s): Mariela Petkova
Columbia University | Biomedical Engineering | 2029

The vagus nerve drives crucial communication across the brain-body axis, regulating functions including respiration, circulation, and digestion. Certain functions, such as swallowing, require bilaterally coordinated muscle contractions, yet the synchronization of these contractions across the left and right sides of the body remains largely unstudied at the neural level. The objective of this study is to characterize the symmetry of the vagal nerve system across various functions in the body. Specifically, we aim to determine the extent of symmetry across a set of bilateral relay neurons, which have been previously identified as conveying sensory input to vagal motor neurons on both sides of the body. Using the whole-brain electron microscopy dataset of a larval zebrafish, we identified 176 bilateral relay neurons and their vagal motor neuron (VMN) outputs. This study aims to reconstruct each VMN to its neuromuscular junction in the periphery and record the locations of synapses. The synaptic locations of the right and left VMN outputs for each relay neuron will be compared to analyze the extent of symmetry. Further analyses will quantify the extent of symmetry across multiple body systems. Overall, our neural reconstructions of the vagus nerve will serve as a ground-truth model, enabling comparisons with pathological states to better understand and treat dysautonomias.

HJURV ABSTRACT BOOK 2026

SHARP

SUMMER HUMANITIES AND ARTS PROGRAM

Musical Mythmaking: Imagining Dixie Through Confederate Song

Student: Anthony Borrelli
Mentor(s): Blake Spitz
Faculty Advisor(s): Kristine Greive
Harvard College | Winthrop House | Music & Anthropology | 2029

The American South is not simply a region, but a myth ingrained in the minds of the American people. Images of idyllic plantations, chivalrous gentlemen, and untroubled slaves toiling happily in Dixie have long plagued popular portrayals of the South, warping the region's indisputably troubled history of chattel slavery and racial violence. Seeking to uncover the origins of this mythology, this paper examines one of the South's most important ideological and political tools: its music. Through in-depth analyses of Confederate sheet music and songsters located in Harvard University's Houghton Library, this paper analyzes how white Southern songwriters fabricated and promoted a romanticized depiction of the South through song. For this task, this work draws on two crucial frameworks of Confederate musical nationalism, tracing how, in the process of constructing a new nation, Confederate songwriters idealized the Southern landscape, glorified Southern honor and gallantry, and effectively erased the institution of slavery. In doing so, this paper deepens existing scholarship on the musical formation of Dixie, complicating a body of work that engages primarily with songs composed in New York's Tin Pan Alley after the war. Rather than focusing on Northern postbellum material, this paper exposes how musical depictions of the idyllic and nostalgic South were previously developed and distributed during the Civil War, by the South itself. As a result, this research not only fills in existing gaps in Southern musicological works but also challenges prevailing perceptions of the American South that continue to stunt national reconciliation and mask antebellum realities.

In Our Own Words: Reimagining Queer Lives in the Archive

Student: Kalani Clark
Mentor(s): Jenny Gotwals
Faculty Advisor(s): Lauren Kaminsky
Harvard College | Cabot House | History & Literature | 2027

Queerness has existed long before we developed the language to articulate and categorize it. The word "queer" itself carries a complex history—historically wielded as a weapon of hatred, it is now often regarded as a reclamation of power and identity. In Our Own Words spotlights the stories and lives of queer people whose collections are held in the Schlesinger Library. The featured materials invite viewers to think critically about gender and sexuality, while situating the struggle for queer liberation within the broader ongoing pursuit of human rights and collective freedom. They reveal how movements for equality and liberation are inseparable from the personal: desire, expression, everyday intimacy. These individual histories are essential evidence of queer survival and resistance, proof that resistance takes shape in organized collective action just as much as in a private letter between partners. Together, they make space for queer histories that are too often excluded from the historical record, affirming that the fight for queer liberation has always been connected to the broader struggles for dignity, recognition, and the fundamental humanity of all people.

Works in Progress Podcast

Student: Thalia Ferro
Mentor(s): Kat Nakaji
Faculty Advisor(s): Bree Edwards
Harvard College | Pforzheimer House | Art, Film, & Visual Studies | 2028

Harvard University's ArtLab is a center for interdisciplinary creative research that supports artists, faculty, and students as they develop new work across disciplines. During the summer, my research focused on pre-production for the next season of ArtLab's Works in Progress podcast, an interview series that explores creative practice and artistic research at Harvard. My work included identifying potential guests, conducting background research on artists and faculty, reviewing past projects, and developing interview questions that highlight creative process, interdisciplinary collaboration, and the role of artistic research within the University. Through this research, I gained a deeper understanding of the ways Harvard supports creative inquiry across its schools and departments. The project contributes to ArtLab's broader mission of making artistic research more visible by documenting the ideas, people, and institutional resources that foster creative experimentation. The podcast serves as a public resource that introduces students, faculty, and the broader community to the diverse opportunities for artistic practice and collaboration available across Harvard and at ArtLab in particular.

A Creative Exploration of the Detroit Broadside Press Broadsides, 1965-1975

Student: Gabrielle Greene
Mentor(s): Blake Spitz
Faculty Advisor(s): Kristine Greive
Harvard College | Leverett House | History | 2027

This project directs its focus on the poetic works published by the Broadside Press in Detroit from 1965-1975, situated within the context of the Black Arts Movement (BAM). In response to an analysis of this poetry and its significance within the Movement itself, the project includes a creative component: the transformation of the researcher's original poems into the visual styles of the broadsides, such as colors, images, and sizing, as well as the poem themes. During the Black Arts Movement, Black artists published thousands of poems invigorated by a sense of liberation, self determination, and hunger for justice. Moreover, the poetry of the Press serves as a focal point to analyze how Black poets during this time were shaping Black identity and experience through poetry within the context of concurrent racial violence and political progress. The project involves the Broadside Press broadsides from 1965-1975 in the Woodberry Poetry Room of the Houghton Library, with a strategy of investigating Black identity and experience by tracking visual components and themes through individual poems. The visual components are an invitation for the broader Black public to engage with an art form that might have seemed inaccessible to them in past artistic movements. They also strengthen the written significance of the poems. The poems themselves represent key themes including but not limited to Black consciousness and culture, commentary on racial injustice and violence, as well as Black womanhood. The broadsides in the BAM offered a radical and accessible response to the poetry of the Harlem Renaissance. In a contemporary period, and inspired by the broadsides, the researcher's poetry aims to confront Black identity and experience through their work within the context of modern politics through themes including but not limited to: nature, familial memories, and place-based associations.

Capturing the Universe: The History Telescopes at Harvard from the American Revolution to the Space Race

Student: Nina Jasanoff
Mentor(s): Joshua Gorman
Faculty Advisor(s): Hannah Marcus
Harvard College | Adams House | Social Studies | 2028

Telescopes have long offered humans a means to understand the universe. With such a long history, however, pinpointing the precise contributions of individuals and institutions is often a challenge. This project uncovers Harvard's role in the history of telescopes from the American Revolution to the Space Race. It first chronicles the formation of Harvard's telescope collection, noting why some instruments still exist today while others are absent. This research also highlights the contributions of previously overlooked members of the Harvard community like the female computers who worked at Harvard College's Observatory. Finally, this work discusses the history of Harvard's global connections, including early international expeditions and the establishment of satellite observatories around the world. This research also examines how museums can simultaneously engage both children and adults. To achieve this, the project considers how objects may be organized so that the functions and uses of different telescopes are clear to viewers before they learn about individual instruments. In order to find objects for the exhibit, I met with curators at the Collection of Historical Scientific Instruments (CHSI), local astronomers, and the directors of other Harvard collections. I also found information on specific instruments by looking through the CHSI database and files in the collection's library. This project will culminate in an exhibit at the Collection of Historical Scientific Instruments opening in Fall 2027. Ultimately, the exhibit will help museum goers learn about Harvard's role in the history of telescopes while accommodating audience members of any age and level of knowledge. The exhibit will also underscore the enduring importance of telescopes as a tool to help humans understand the world we live in.

Modals Under Discussion: Equivalence Classes in Many Worlds

Student: Moeka Koyama
Mentor(s):
Faculty Advisor(s): Kathryn Davidson
Harvard College | Quincy House | Molecular & Cellular Biology | 2027

Humans routinely reason over possibilities asking what *must*, *might*, or *could* happen. Consider someone deciding how to escape a forest: although there may be countless possible routes, people do not appear to reason over every possibility in equal detail. Instead, they seem to ignore distinctions that are irrelevant to the task at hand. In linguistics, canonical theories treat modal expressions, such as *must*, as quantifiers over sets of possible worlds, known as the modal base. While recent work in psychology has investigated how individuals may cognitively represent and compute over these large spaces of possibilities, this leaves open the question of how such reasoning remains computationally tractable. To leverage linguistic insights, we propose that in a discourse, the question which the interlocutors are attempting to answer, question under discussion (QUD), provide a principled way of determining which distinctions between possibilities are relevant and which can be ignored. Formally, this induces equivalence classes over the modal base, allowing modal evaluation to proceed over QUD-relative alternatives rather than individual worlds. To test this hypothesis, we collect data on truth-value judgments of modal statements under different QUD. From this, we predict modal judgments to be sensitive to QUD-induced equivalence classes rather than the distribution of individual worlds within those classes. If confirmed, these results would suggest that the objects of modal quantification are QUD-relative alternatives rather than worlds simpliciter, providing a novel insight into the granularity of information structure in modal semantics.

Latin Meets The Last Kingdom: An Epic Wiki for The Poem of Walter

Student: Henry Levenson
Mentor(s): William Barthelmy
Faculty Advisor(s): Jan Ziolkowski
Harvard College | Leverett House | History | 2028

The *Waltharius*, or the Poem of Walter, a medieval Latin epic working syncretically across classical, Christian, and Germanic traditions, remains largely unknown outside of specialist circles, despite its immense potential as a Latin teaching tool. Most existing commentaries on the *Waltharius* are hidden behind language gaps, paywalls, or dense scholarly jargon. The *Waltharius* Wiki, which began around 2009, resolved some of these issues by providing a free, open access commentary on and translation of the text. By 2026, however, the site design had become outmoded and much of the commentary needed serious revision. To make the site a valuable contemporary resource, we consulted the over 180 years of literary and historical scholarship on the poem since its first critical edition by Jacob Grimm—sources on everything from Old High German onomastics to the design of medieval weaponry—and wrote a new commentary on the entire text. We then redesigned the user interface and added completely new resources to the Wiki for the study of the poem: dozens of illustrations and images of historical manuscripts and artifacts, a reformatted scansion guide, an introduction to the poem, and a user guide for the Wiki itself. During a time of rising interest in medieval studies, updating the Wiki has made the *Waltharius* more accessible to a fresh audience interested in the language and culture of the Latin Middle Ages. The updated Wiki will allow students to take in and take part in the centuries-long conversation surrounding the *Waltharius*.

In Our Own Words: Reimagining Queer Lives in the Archive

Student: Jaila Mabry
Mentor(s): Jenny Gotwals
Faculty Advisor(s): Lauren Kaminsky
Harvard College | Cabot House | History & Literature | 2027

Queerness has existed long before we developed the language to articulate and categorize it. The word ”queer” itself carries a complex history—historically wielded as a weapon of hatred, it is now often regarded as a reclamation of power and identity. In Our Own Words spotlights the stories and lives of queer people whose collections are held in the Schlesinger Library. The featured materials invite viewers to think critically about gender and sexuality, while situating the struggle for queer liberation within the broader ongoing pursuit of human rights and collective freedom. They reveal how movements for equality and liberation are inseparable from the personal: desire, expression, everyday intimacy. These individual histories are essential evidence of queer survival and resistance, proof that resistance takes shape in organized collective action just as much as in a private letter between partners. Together, they make space for queer histories that are too often excluded from the historical record, affirming that the fight for queer liberation has always been connected to the broader struggles for dignity, recognition, and the fundamental humanity of all people.

Profs and Politics

Student: Katie Martin
Mentor(s):
Faculty Advisor(s): Doris Sommer
Harvard College | Currier House | History & Romance Languages & Literatures | 2028

Profs and Politics is an in-progress book project meant to shed light on the undeniable pattern of good, identifiable teachers rising to political power within Latin America. The evidence of the *profe*, the affectionate title given to educators, in government is overwhelming, but has not been collected in written form. We have perused scholarly and periodical archives to prepare overviews of potential *profe* figures, from primary school educators, to athletic coaches, or anybody who bears this title by their constituents—compiling information on their roots as educators and politicians, seeking to convey the pathway between. We have studied figures from Hipólito Yrigoyen of Argentina to José Mujica of Uruguay—presidents, to middlemen, to local leadership. We have found a myriad of leaders that will serve as evidentiary jumping points, but the exact format in which they will be presented is still to be determined. Together, these profs provide an optimistic and achievable path forward for Latin America, providing a political vocabulary applicable within and beyond the region. Breaking free from the inundation of mortally pessimistic scholarship on Latin America, Profs and Politics justifies and promotes the humanistic education of young citizens, shedding light upon the foundation of good democracy.

Retrieving the Past to Imagine the Future: A Historical Mapping of the Arts and Humanities at Harvard

Student: Lauren Mitchell
Mentor(s): Lauren Kaminsky
Faculty Advisor(s): Sean Kelly
Harvard College | Dunster House | History of Art & Architecture | 2028

Recent years have shown a marked decline in student interest and concentrators within the Arts and Humanities at Harvard College. Although the number of concentrators has been steadily decreasing over the past twenty years, the broader shift away from the inter-disciplinary expectations of a traditional liberal arts curriculum has been unfolding for well over a century. This project investigates how the curriculum has evolved from a broad liberal arts model to its current structure, specifically examining the historical factors that may have contributed to the declining role of the humanities. Drawing on archival materials, including syllabi, course catalogs, oral history interviews, op-eds and editorials, the project traces the evolution of Harvard's curriculum from 1869 to the present. Resources such as course outlines, student notes and evaluations, and materials uncovered from the University's archives, suggest that the decline in the humanities was not solely due to changing student interests, but rather a long-term shift in the expectations for pre-professional career tracks and the shift away from the cohesive liberal arts framework that once encouraged interdisciplinary exploration. The project's findings argue that strengthening the path into each discipline by creating broad and wide-ranging introductory courses while allowing students a greater balance between specialization and general education will reinforce engagement within the humanities.

Retrieving the Past to Imagine the Future: A Historical Mapping of the Arts and Humanities at Harvard

Student: Jules Sanders
Mentor(s): Lauren Kaminsky
Faculty Advisor(s): Sean Kelly
Harvard College | Winthrop House | History & Literature | 2028

Since the 2008 financial crisis, Harvard University has noted a steep decline in the number of students enrolling in arts and humanities courses and concentrating in arts and humanities disciplines. Recently, Harvard has experimented with new introductory humanities courses emphasizing common threads in humanistic inquiry across disciplines, including storytelling, language, and translation. In order to better understand the history of arts and humanities education at Harvard, over 500 syllabi, reading lists, assignments, course reviews, Harvard Crimson articles, and oral testimonies from 1896 to 2020 were catalogued and evaluated. Focusing on the postwar decades, from which the greatest quantity of records was available and during which Harvard's humanities departments matured into recognizable forms, researchers determined that introductory disciplinary courses, rather than introductory interdisciplinary courses, have historically most effectively compelled students to study the humanities. Full-year divisible sequences surveying German, Italian, Russian, and English literature, all conducted in English but expecting substantial time commitment, were traditionally offered by their respective departments but have since lapsed out of course rotation. These courses, however, often attracted upwards of fifty students each and functioned as comprehensible gateways into departments that students today rarely encounter. Analysis of the archival material suggested that departments in the arts and humanities (especially Classics, English, Germanic Languages & Literatures, Slavic Languages & Literatures, and Romance Languages & Literatures)should consider reverting to an older model of instruction, offering intensive introductory survey courses strongly recommended for students to complete before they move on to advanced courses. Higher-level instruction may then assume a common disciplinary language without the need to retread introductory content.

Latin Meets The Last Kingdom: An Epic Wiki for The Poem of Walter

Student: Silvia Siegel-Yousef
Mentor(s): William Barthelmy
Faculty Advisor(s): Jan Ziolkowski
Harvard College | Mather House | English | 2028

The *Waltharius*, or the Poem of Walter, a medieval Latin epic working syncretically across classical, Christian, and Germanic traditions, remains largely unknown outside of specialist circles, despite its immense potential as a Latin teaching tool. Most existing commentaries on the *Waltharius* are hidden behind language gaps, paywalls, or dense scholarly jargon. The *Waltharius* Wiki, which began around 2009, resolved some of these issues by providing a free, open access commentary on and translation of the text. By 2026, however, the site design had become outmoded and much of the commentary needed serious revision. To make the site a valuable contemporary resource, we consulted the over 180 years of literary and historical scholarship on the poem since its first critical edition by Jacob Grimm—sources on everything from Old High German onomastics to the design of medieval weaponry—and wrote a new commentary on the entire text. We then redesigned the user interface and added completely new resources to the Wiki for the study of the poem: dozens of illustrations and images of historical manuscripts and artifacts, a reformatted scansion guide, an introduction to the poem, and a user guide for the Wiki itself. During a time of rising interest in medieval studies, updating the Wiki has made the *Waltharius* more accessible to a fresh audience interested in the language and culture of the Latin Middle Ages. The updated Wiki will allow students to take in and take part in the centuries-long conversation surrounding the *Waltharius*.

Spatially Visualizing Papal Correspondence: A Geodatabase of Communications to and from the Most Important Pope of the Late Roman Empire

Student: Phu Ta
Mentor(s): Reed Morgan
Faculty Advisor(s): Michael McCormick
Harvard College | Quincy House | History | 2028

As the leader of Latin Christendom from 590-604 CE, Pope Gregory the Great played a critical role in the transition of Europe from the fall of the Western Roman Empire to the start of the medieval period. During his 15-year reign, Gregory maintained a network of correspondence throughout the Mediterranean and beyond, writing to monarchs, bishops, and nobles. Fortunately, hundreds of his letters survive to this day in a collection known as the Register. While archival research and written sources, now allied with archaeology, remain well-established methods of historical research, in recent years, historians have increasingly deployed digital methods. This project incorporates one such digital feature, known as Geographical Information System (GIS) Mapping. By using GIS to develop a geodatabase of Gregory's letters from the Register, this project attempts to develop the spatial dimensions of and visualize trends in Gregory's communications by analyzing numerous factors such as location, seasonality, gender, class, and subject matter. This will be done within the framework of Mapping Past Societies, a Harvard-created digital resource that enables spatial and temporal analyses of world civilizations. While the results of this project are still in progress, the compilation of the data has largely been completed, and the early stages of visualization have begun. Through the visualization process, we expect to find patterns regarding seasonality, gender, class, and subject matter, providing implications for Gregory's priorities as a Pope. It will also delineate and explore the key role that networks of communication played during this period of far-reaching change in Europe. By integrating the disciplines of the social sciences and humanities with spatial analysis, GIS allows historians to reveal undiscovered facets of the human past that may otherwise go unnoticed through traditional methods of historical research, providing a new dimension that can supplement archival and other written forms of evidence.

The Poetry of José Garcia Villa and the Philippine Cold War

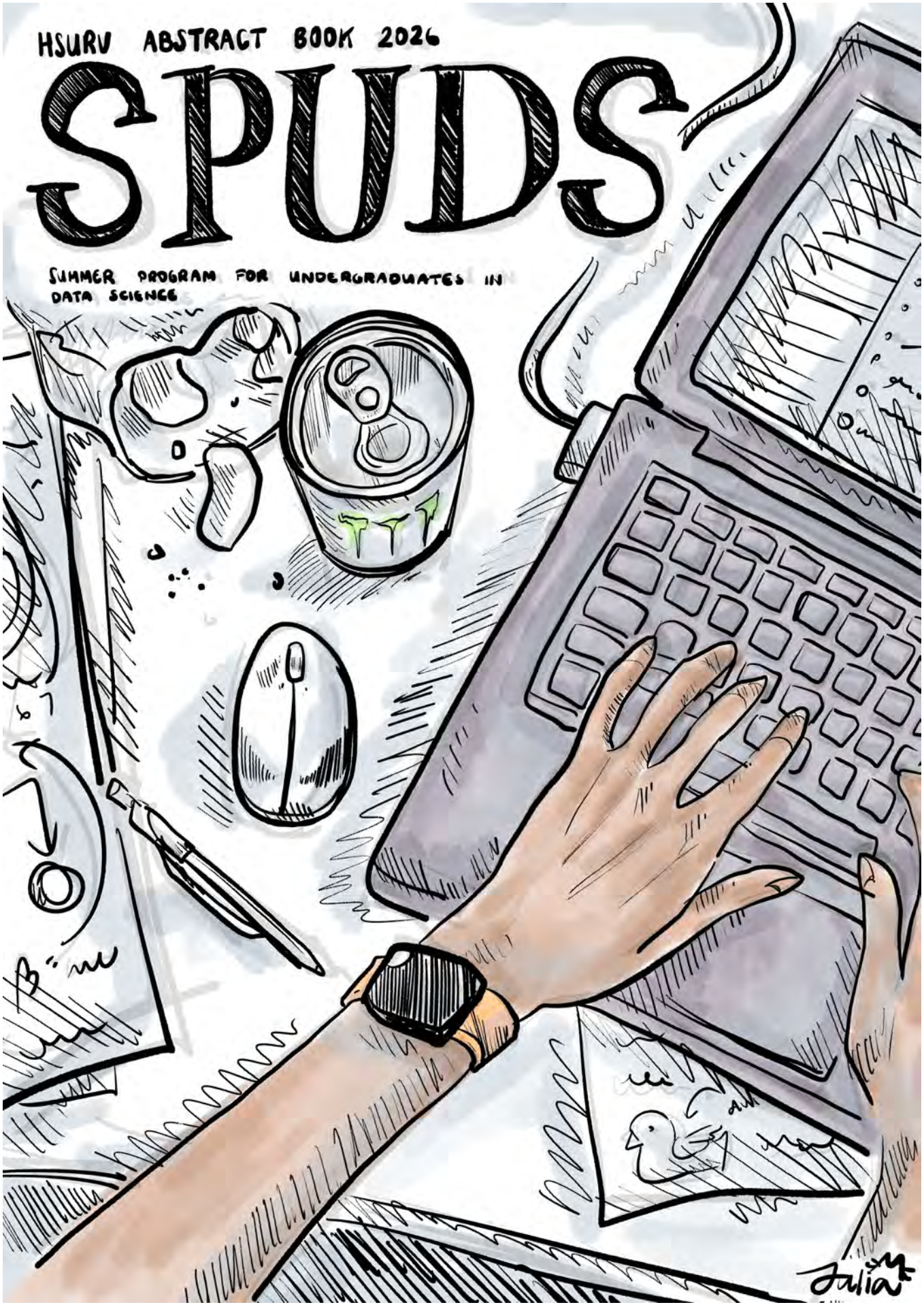
Student: Christian Topinio
Mentor(s): Blake Spitz
Faculty Advisor(s): Kristine Greive
Harvard College | Kirkland House | History & Literature | 2027

This project examines the papers and work of Filipino-American poet José Garcia Villa (1908-1997) within the context of the Cold War and the Ferdinand Marcos regime. The bulk of his creative work being done in the 1930s and '40s, his poetry is deeply experimental and reflects on love, divinity, and desire; moreover, he was a prominent literary critic who wrote extensively on Philippine literature while also being accepted in American modernist circles. However, although much scholarship on Villa has focused on this creative period, there has been a relative lack of scholarly attention which has focused on Villa's output and life after 1950, where the status of Philippine writing in English was hotly contested and co-opted into larger debates on Philippine nationalism during the Cold War. Thus, using his understudied archival papers at Harvard University's Houghton Library, this project argues that Villa's emerging status as a writer in the Philippine canon was embedded within these historical processes. I examine how the context and reception around his 1959 return to the Philippines as well as his poems in Poems in Praise of Love (1962) attempt to rationalize and engage with Villa's emergent status in the Philippine literary canon despite his decades-long residence in the United States. Moreover, I consider Villa's activities during the Marcos dictatorship as one in which he had to mediate his personal disagreement with the regime while being positioned as a Philippine national figure. Ultimately, this project intervenes in an understudied period of Villa's life and poetics, demonstrating the assumptions and processes which made him part of the Philippine literary canon and asking how art in diaspora may play a role in nationalist and state ideologies.

HSURV ABSTRACT BOOK 2026

SPUDS

SUMMER PROGRAM FOR UNDERGRADUATES IN DATA SCIENCE



Linear Riesz Learners for Causal Inference

Student: Jolene Cao
Mentor(s): Salvador Balkus
Faculty Advisor(s): Nima Hejazi
Harvard University | Eliot House | Statistics | 2029

Causal inference increasingly addresses complex scientific questions requiring specialized estimands and estimation methods. Because the identifying statistical parameter of many causal estimands can be expressed in a common bounded linear functional form, they are amenable to being expressed in terms of Riesz representers, a general class of nuisance functions that provides a unified approach to formulating estimators in causal machine learning. Traditional reweighting estimation approaches that derive analytical forms of inverse probability weights and substitute estimated nuisance functions can yield conservative variance estimates and suffer from numerical instability, particularly in high-dimensional settings subject to empirical positivity violations. Riesz learning is an emerging framework that directly estimates Riesz representers by minimizing the Riesz loss function, but few R packages support this relatively new methodology. Existing implementations have relied on complex families of learning algorithms, such as neural networks and gradient boosting, leaving many of the advantages of simpler model classes, including generalized linear models, unexplored. In this work, we develop `rieszlm`, an R package implementing linear parametric Riesz learning models. For linear Riesz models, minimizing the quadratic Riesz loss yields a closed-form solution, analogous to ordinary least squares. These regression models can be fitted quickly, helping to increase the pace of methodological development and serving as computationally efficient base learners for machine learning ensembles. The `rieszlm` package supports user specification of target estimands, alongside several built-in, widely used estimands, including the average treatment effect and the causal effects of modified treatment policies, and provides diagnostics to assess the quality of fitted Riesz models. We conduct simulation experiments to evaluate the performance of `rieszlm` in terms of bias, variance, mean squared error, and confidence interval coverage. By implementing simple, computationally efficient Riesz learners, `rieszlm` broadens the practical use of Riesz learning in fields ranging from epidemiology to economics and public policy.

Neural Decoding of Transversal Logical Gates on the Surface Code

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Quantum error correction is central to fault tolerance due to its role in bridging the gap between the high physical error rates of existing hardware and the low logical error rates (LER) required to accurately implement deep quantum circuits. Neural decoders have been shown to achieve decoding times comparable to stabilizer-measurement cycle times on certain platforms, with accuracies surpassing those of existing real-time decoders and approaching maximum-likelihood decoding (MLD) at small code distances. This combination of high accuracy and real-time capability makes them a candidate for near-term deployment. However, much of the existing literature has focused on the memory task, leaving neural decoding through logical gates underexplored. In this project, we develop a neural decoder for noisy transversal CNOT circuits on the surface code, decoding logical observables jointly by exploiting the correlated errors in transversal gates. We use an architecture where a 3D convolutional neural network extracts spatiotemporal features from each patch's syndrome volume, and a graph neural network couples patches during the gate through transversal-symmetry-aware edges. The model is trained on circuit-level noise and evaluated by tuple-exact LER. Our decoder achieves a lower LER than correlated-decoding minimum-weight perfect matching (MWPM), a real-time decoder for logical gates, while approaching the accuracy of MLD at small code distances and shallow circuit depths. We aim to extend these results to larger code distances and greater circuit depths. By applying neural decoding to logical gates, this work moves towards algorithmic decoding and, thus, the practical realization of fault-tolerant quantum computing.

Pilot-Informed Survey Design Under Budget Constraints

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Survey design is typically limited by cost. With many potential questions to choose from, selecting a subset of columns can become necessary under budget constraints. Surveys can act as the cheaper proxy of some true state which would be costly to observe directly. For example, self-reported diagnostics and symptoms could be used as proxies for an individual having a specific medical condition. The goal of using the survey would be to minimize the variance of the estimate of a treatment effect in an experiment where we do not observe the true state for most individuals, instead observing only their treatment status and the survey. This project provides a principled approach to survey question selection in this setting, where we leverage a pilot survey dataset to choose the optimal questions to ask. We show that relatively precise estimates can be obtained with a much smaller fraction of survey columns that can be observed relatively cheaply. We fit a ridge regression model and apply an analytic correction term to the pilot's in-sample estimated variance to account for finite-sample learning. Then, we introduce another set of corrections to correct the bias which is induced from the selection process. Finally, we validate our method in the context of a medical trial of Varenicline, a smoking cessation aid. This approach therefore sheds light on how to leverage cheaper forms of data to improve experimental precision.

Analyzing Mid-Decade Congressional Redistricting Ahead of the 2026 Midterms Using Sequential Monte Carlo Simulations

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Mid-decade redistricting is of heightened interest ahead of the 2026 midterm elections in the United States, where the boundaries of congressional districts determine the political composition of the House of Representatives. Computational sampling of redistricting plans is an increasingly popular tool for gerrymander detection, creating a partisan-neutral ensemble of viable plans against which enacted maps can be compared. We analyze enacted congressional district plans from ten states whose maps changed or were reaffirmed through both ordinary legislative action and processes shaped by litigation: Alabama, California, Florida, Louisiana, Missouri, North Carolina, Ohio, Tennessee, Texas, and Utah. Assembling enacted-plan shapefiles from state legislatures, government sources, and the U.S. Census Bureau, we join these to 2020 census voting tabulation district (VTD) demographic and population data alongside 2020 and 2024 precinct-level election results. Using the sequential Monte Carlo method developed by McCartan and Imai (2023) and implemented through the redist package, we generate ensembles of redistricting plans according to federal law and each state's respective redistricting statutes, in order to discern underlying political geography and shifts from gerrymandering effects. Election outcomes under each plan are predicted using partisan vote baselines derived from prior elections, and proportionality of seats is analyzed using a stochastic uniform partisan swing model (Gelman and King 1994), following the approach of Kenny et al. (2023). We assess whether these enacted plans deviate from a neutral baseline, and to what extent proportionality and responsiveness, alongside the competitiveness of these enacted districts, are affected across states shaped by differing redistricting processes and priorities. Results assessing partisan fairness and proportionality across the ten states are forthcoming ahead of the November 2026 elections.

Characterizing the Baryon Cycle of Two Strong Strongly-Lensed Galaxies at Redshift $\sim$1.68

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Most elements were born from stars. Stars live within galaxies, and their element production is part of the "baryon cycle" that changes their host galaxy over time. The baryon cycle begins with hydrogen and helium falling into the galaxy and collapsing into stars. Through nuclear fusion, stars turn gas into heavier elements like oxygen. Finally, the stars' winds and explosive deaths fling the elements out to be recycled into new objects. Star formation peaked around "cosmic noon," roughly 10 billion years ago (redshift $\sim$2). Since elements absorb and re-emit light at unique wavelengths, a galaxy's light reveals its history. However, older galaxies have been understudied because their light is fainter, limiting our understanding of how galaxies evolve. Strong gravitational lensing can help fill this gap: heavy foreground objects bend light that passes by, becoming natural telescopes to magnify background galaxies. We use this rare phenomenon to analyze two galaxies at redshifts 1.679 and 1.677 (Galaxies A and B, respectively). We captured their spectra using the X-Shooter spectrograph and the Multi Unit Spectroscopic Explorer on the Very Large Telescope in Chile. We are studying the shape and strength of their chemical emission and absorption features to probe the underlying physical processes. We find both galaxies are heavily star-forming but contain less dust than previously-examined galaxies at similar redshifts. Galaxy A contains slightly more dust and heavy elements. It is forming stars more quickly than Galaxy B, which is expelling large amounts of gas. The completed project will present a rare comprehensive look into the baryon cycle at cosmic noon. It could explain which properties correlate within each galaxy, and why two galaxies at similar redshifts differ. Altogether, we contribute to a growing effort using high-redshift observations to refine current models of galaxy evolution inferred from the local universe.

European Overseas Settlements, Climate-Matched Migration, and Long-Run Development

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European overseas settlement varied widely across colonial territories, with some destinations developing large, persistent settler populations while others remained sites of sparse or extractive colonial presence. We examine whether climate similarity between European origins and overseas destinations influenced migration, demographic survival, and economic outcomes. Building on Alfred Crosby's Ecological Imperialism hypothesis, we combine genealogical records of more than 300,000 Europeans born between 1500 and 1850 who died outside Europe with high-resolution climate data. Origins and destinations are mapped to $0.5^\circ \times 0.5^\circ$ grid cells, allowing us to measure temperature and precipitation differences between each migrant's birthplace and destination. Using gravity models estimated with Poisson pseudo-maximum likelihood, we find that Europeans were significantly less likely to migrate to destinations with climates unlike those of their origins, especially when destinations were hotter. We then examine individual-level demographic outcomes and find that migrants to less climatically similar environments lived shorter lives and had fewer children. Finally, we connect historical settlement patterns to contemporary outcomes using present-day European ancestry shares and satellite-based nighttime luminosity. Locations settled by more climate-matched Europeans exhibit larger European ancestry shares today and higher levels of economic activity, even within subnational regions. These findings demonstrate that climate compatibility shaped both where Europeans settled and how colonial settlement persisted and affected long-run development. By integrating large-scale genealogical records, gridded climate data, spatial matching, and statistical modeling, our project sheds light on the historical determinants of migration and their long-run implications for economic development.

Encoding Model Analysis of Single-Neuron Function in the 5xFAD Mouse Hippocampus

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Alzheimer's disease (AD) disrupts hippocampal circuits critical for spatial navigation and memory, yet the specific neural computations affected at the single-neuron level remain poorly understood. Prior work in transgenic AD mouse models has demonstrated reduced place cell counts and degraded spatial tuning in hippocampal area CA1, but these analyses rely on classical tuning curve metrics that characterize neurons along a single behavioral dimension. A neuron with no discernible place field, for instance, may nevertheless reliably encode speed or landmark distance, contributions that single-variable tuning curves would classify as noise. This study aims to characterize how AD alters single-neuron encoding of behavioral features in hippocampal regions CA1 and the dentate gyrus (DG) using the 5xFAD transgenic mouse model. Ten mice (eight 5xFAD and two age-matched wild-type littermate controls) were implanted with 80-channel silicon probes and recorded during virtual reality navigation tasks, including forced alternation, novel object recognition, and gradual environmental shifts. Neurons tracked across sessions using cross-day waveform matching will be fitted with encoding models that predict each neuron's firing rate from multiple behavioral variables simultaneously, including spatial, sensory, and reward-related features. Feature importance analysis will then quantify which variables each neuron encodes and how these functional roles differ between 5xFAD and wild-type mice. Longitudinal recordings at six and nine months of age will test whether encoding deficits progress with disease advancement. Thus far, spike sorting and cross-session neuron tracking have been completed for three mice from the first cohort. If AD selectively disrupts encoding of specific behavioral features rather than broadly degrading spatial representations, such feature-specific deficits could serve as earlier, more sensitive biomarkers of cognitive decline than traditional place cell metrics alone.

Pancreatic Cancer Risk Stratification among Carriers of Major Susceptibility Genes

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Pancreatic ductal adenocarcinoma (PDAC) is one of the most lethal cancers, yet diagnosis at an early stage substantially improves survival. PDAC is among the cancers without a U.S.- guideline-recommended screening method for the general population. Carriers of the germline pathogenic gene variants (PGVs) ATM, BRCA1, BRCA2, CDKN2A, and PALB2 are at high risk of PDAC, and their individual risk remains inadequately characterized. There is growing evidence that polygenic risk scores (PRSs), which combine the effects of many disease-associated single nucleotide polymorphisms (SNPs), substantially refine disease risk. Our analysis uses two cohorts, carriers of at least one of the aforementioned PGVs (n = 10,044) and non-carriers (n = 108,109), investigated at both the SNP-level and the PRS-level. At the SNP-level, we compare the effect sizes across the two populations and with published literature estimates to quantify genetic differences between risk groups, and at the PRS-level, we apply and interpret various classification algorithms and transfer learning methods to better predict PDAC. Our work aims to advance early detection of PDAC by giving patients and their providers a quantitative, clinically actionable basis to prioritize and tailor the existing screening modalities to those most likely to benefit, while sparing those at the low end of the risk distribution.

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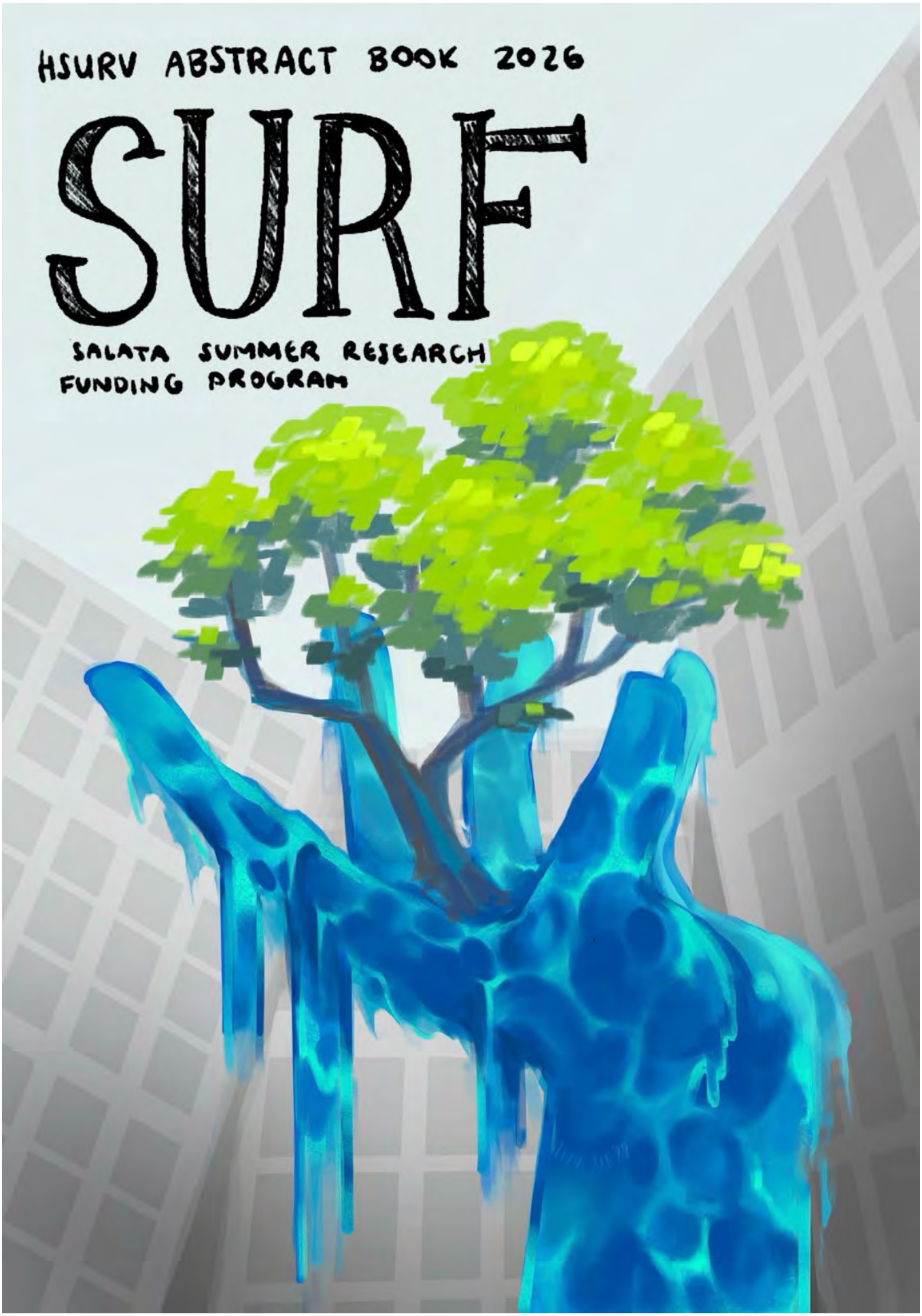

Designing and Printing 3D Electrodes at Different Angles Relative to the Flow

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Harvard College | Pforzheimer House | Chemistry | 2029

The continued reliance on fossil fuels has motivated the development of large-scale energy storage technologies to support the transition to renewable energy. Redox flow batteries offer a promising approach to grid-scale energy storage compared with lithium-ion batteries, whose expense and resource availability limit their implementation in many parts of the world. However, flow cell electrodes are typically composed of porous carbon materials, such as papers, felts, and cloths, whose random architecture makes it difficult to understand how electrode structure affects performance. By contrast, architected electrodes composed of periodic lattices provide known, reproducible structures for investigating these relationships. This project investigated how the angle of electrode features affects electrolyte flow and mass transport through architected electrodes. We fabricated electrodes with systematically varied filament angles to alter the flow path and corresponding flow field while maintaining comparable electrode characteristics. Thus far, these architected electrodes have enabled direct comparison of how electrode angle affects electrolyte flow through a known structure. This work suggests that controlling electrode angle could redistribute electrolyte throughout the electrode and prevent local and global mass-transport limitations. Future work will quantify electrochemical conversion within these architectures to identify electrode designs that promote more uniform mass transport and improve electrochemical performance under flow.

Environmental and Occupational Toxic Exposures at the Intersection of Climate Change, Conflict, and Health: A Scoping Review

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Climate change and armed conflict can independently expose populations to harmful environmental and occupational hazards. When these crises occur together, they can increase the type, intensity, and duration of toxic exposures. Conflict can damage industrial facilities, water systems, buildings, and agricultural land, releasing heavy metals, combustion products, pesticides, and other hazardous substances. At the same time, climate-related stressors such as extreme heat, flooding, drought, and wildfires can spread existing contaminants or create new pathways of exposure. Interestingly, the health effects of these overlapping conditions are often studied separately, making it difficult to understand their combined impact. This scoping review aims to characterize the existing literature on environmental and occupational toxic exposures at the intersection of climate change, conflict or war, and human health. To investigate this topic, we are developing a search strategy with a research librarian and screening studies using predefined inclusion and exclusion criteria. Included sources must address climate-related stressors, conflict or war, and toxic exposure with relevance to human health. We will extract information on the type of toxicant, exposure pathway, affected population, geographic setting, and reported health outcomes, including neurological, developmental, chronic, and intergenerational effects. Once the literature is reviewed, we aim to identify common exposure pathways and areas where evidence remains limited. More broadly, this research may help clarify how climate change and conflict interact to shape toxic exposures and inform future research and public health responses for populations facing multiple environmental threats.

Emerging Environmental Issues in Food Waste Law and Policy

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This research assistantship with the Food and Law Policy Clinic focused on advancing strategies that reduce food waste at the state, federal, and international levels. This work involved analyzing state, federal and international laws, reviewing scientific literature on environmental contaminants, examining policy approaches that improve food waste management, and striving to protect public and environmental health. The primary project consisted of a literature review on compost contamination, examining contaminants such as per- and polyfluoroalkyl substances (PFAS), microplastics, foodware, and heavy metals. This project also examined their sources, environmental and human health impacts, current policy responses, and recommendations for further research. Related work on the Organic Waste Permitting Project and the Mexico City-Level Food Waste Deterrence Project provided important context for evaluating and understanding U.S. food waste policies. The Organic Waste Permitting Project, in collaboration with the Natural Resources Defense Council, included reviewing and conducting original research on different U.S. states and their organic waste management laws and permits. The Mexico City-Level Food Waste Deterrence Project focused on researching municipal food waste reduction policies and food donation requirements and engaging with representatives from the World Wildlife Fund Mexico. Additional responsibilities included collaborating with clinical instructors and interns through workshops and professional development events, attending a Sustainable Agriculture Research and Education (SARE) workshop, and assisting with preparation for the Zero Food Waste Coalition Conference. Together, these projects contributed to identifying science-based policy solutions that strengthen food waste-management systems, improve compost quality, reduce environmental contamination, and support more sustainable and resilient food systems.

Flowable Luminescent Solar Concentrating Windows

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Across the globe, buildings account for around 30% of final energy demand, much of which is used to maintain comfortable indoor environments through heating, cooling, and lighting. As hotter summers increase cooling demand and the building sector moves toward net-zero energy design, facades and windows offer an important but underutilized opportunity. Rather than serving only as static barriers, building envelopes could help actively regulate sunlight, manage heat, and generate electricity. Luminescent solar concentrators (LSCs) provide one route toward this goal. They absorb sunlight with luminescent materials, re-emit it at longer wavelengths, and guide part of that emission toward photovoltaic cells. Because they are semitransparent and collect both direct and diffuse sunlight without active solar tracking, LSCs have been studied as solar-harvesting components for building-integrated photovoltaics. Most LSC research has focused on static devices, including solid-state concentrators and liquid systems in which the liquid serves as a host for luminophores. This work instead investigates flow-enabled liquid luminescent solar concentrators as adaptive building-envelope devices. In these systems, the active liquid medium becomes a mobile control element, where electrically or thermally driven fluid filling, draining, and circulation can tune optical transmission, photovoltaic output, and heat transport on demand. Beyond these tunable operational modes, the liquid platform introduces design knobs, including emitter type, emitter concentration, solvent properties, cavity thickness, and flow rate, enabling precise design of spectral, thermal, and electrical behavior within one device architecture. Ongoing experiments will attempt to validate how previously challenging functionalities can be enabled by flowable liquid LSCs. These functions include active cooling of photovoltaic cells to improve electrical output, emitter switching to improve device longevity and sustainability, temperature-actuated switching between transparent and electricity-harvesting states, and active adjustment of spectral emission and filtering. Overall, liquid LSCs may offer a path toward adaptive window technologies for agricultural, residential, and commercial buildings.

Socio-economic Impact Assessment of Waste Wool Building Cladding Technology

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Over the past decades, the global textile industry has seen a significant shift from natural fibers to synthetic fibers. As a result, the American sheep and wool industry, which encompasses a network of producers, industrial workers, and business owners, has struggled to adjust to this changing economic landscape. Likewise, producers and processors of wool are burdened with excessive waste streams given rigid standards in the textile industry for fiber length and grade. Finding ways to upcycle this valuable material is therefore an imperative environmental and socio-economic intervention that numerous products have attempted to address. Notably, waste wool was used to create a panel suitable for exterior building cladding. What remains to be explored is the potential of this project to impact the broader network of suppliers when scaled to an industrial level. This research explores the implications of this innovation through (a) interviews with producers and business owners connected to the industry, (b) detailed documentation of the materials and processes embedded at each step of manufacturing, and (c) quantitative and qualitative analysis of the health and sustainability impacts. The input gathered will be compiled into a narrative video that follows the waste wool's journey from sheep to consumer, while more broadly creating a roadmap for design methods that align with the environmental, social, and economic pillars of sustainability. The results of this exploration will be displayed at the Oslo Architecture Triennale in Norway.

Climate Change and Indoor Transmission Risks of Airborne Infectious Diseases

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Faculty Advisor(s): Joseph Allen
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The COVID-19 pandemic highlighted how building characteristics influence the spread of infectious diseases while exposing a shortage of tools for predicting transmission risk during emerging outbreaks. Although the Wells-Riley model was later adapted to estimate airborne infection risk of COVID-19, it does not account for diseases transmitted through droplets, fomites, or multiple transmission pathways. Therefore, this study aims to develop a universal infectious disease risk model extending the Wells-Riley framework by integrating multiple transmission routes across diverse indoor environments. As an initial proof of concept, upper respiratory tract (URT) and lower respiratory tract (LRT) infectivity parameters were back-calculated from a well-characterized SARS-CoV-2 restaurant outbreak in Guangzhou, China, in 2020. These values were used to predict an infection risk of 0.133 for an independent restaurant outbreak in Jeonju, Korea, in 2020, compared to an observed infection risk of 0.182, demonstrating agreement between predicted and observed transmission. To expand this into a universal model, this study will conduct a literature review of approximately 40 outbreak case studies spanning different infectious diseases and indoor environments. Epidemiological data reported in the literature will define plausible bounds for URT and LRT infectivity parameters, and nonlinear optimization will identify parameter values that best reproduce reported transmission across collected outbreaks rather than individual outbreak back-calculations. We will incorporate these calibrated parameters into a Markov chain model coupled with a dose-response model to predict infection probabilities for each disease-environment scenario. We will then evaluate performance by comparing predicted infection risks with reported transmission rates across the analyzed outbreaks. By integrating multiple transmission pathways into a single data-calibrated model, this work aims to provide a flexible tool for estimating indoor disease risk using user-specific inputs. Such a model could support earlier risk assessment during emerging outbreaks, enabling decision-makers to evaluate potential transmission before epidemiological data become available.

Climate Shocks and Urban Mobility in Developing Countries

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Harvard College | Leverett House | Economics & Philosophy | 2027

Climate change is intensifying extreme heat, heavy rainfall, storms, and flooding in cities around the world. Yet researchers still have limited evidence on how these shocks affect daily movement within cities, especially in developing countries where climate exposure is high and traditional mobility data are scarce. This project examines whether large-scale smartphone location data can help fill that gap by measuring how urban mobility changes during and after climate shocks. The project uses a high-resolution smartphone location dataset to study mobility patterns in large cities in developing countries. We have developed a pipeline that transforms raw smartphone location traces into more usable mobility data, as well as evaluating memory use, compression, read times, and data coverage to determine how the pipeline should scale across countries. We are also working on applying this pipeline across more countries and time periods, refine mobility metrics such as likely home locations based on where devices generate most of their pings, and connect mobility changes to climate shocks. By making global smartphone mobility data more comparable across cities, this research will help reveal how extreme weather impacts movement, access, and urban resilience.

"I [Don't] Love that Dirty Water": An Investigation of Harmful Algae Blooms and Water Quality Monitoring in the Charles River

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Mentor(s):
Faculty Advisor(s): Fiamma Straneo
Harvard College | Mather House | Environmental Science & Engineering | 2027

The Charles River watershed is home to around one million people in the Boston Metropolitan area. The river's lower basin is used by 20,000 people a day, making it among the busiest recreational river segments in the world. Yet, the Charles River struggles with harmful algae and cyanobacteria bloom (HAB) events. HABs, excessive growths of cyanobacteria in eutrophic aquatic environments, destroy water quality, and when they decompose, they absorb excessive amounts of oxygen, causing hypoxia and dead zones in aquatic environments. They also release dangerous toxins such as microcystins, which can make water unsafe for consumption and recreational purposes. There are limited methods to treat, prevent, and manage HABs, making effective HAB monitoring vital to public health and ecosystem protection. Thus, there is a need to better understand the factors driving HABs on the Charles River to improve HAB monitoring for public safety and water quality. This study investigates the environmental conditions associated with HAB occurrence in the Charles River and evaluates current HAB monitoring approaches. The project utilizes five years (2021–2025) of water quality data from the U.S. Environmental Protection Agency's continuous monitoring buoy in the lower Charles River basin, together with weekly grab sample data collected by the Charles River Watershed Association. Environmental variables, including physical, chemical, and biological water quality measurements, are analyzed using Python to identify relationships between water quality conditions and HAB indicators. Additional field observations and water sampling may supplement these datasets as resources permit. This ongoing research aims to identify the environmental conditions that favour HAB development and assess the strengths and limitations of current monitoring efforts. The findings are expected to improve understanding of HAB dynamics in the Charles River and inform future monitoring and management strategies to better protect water quality, ecosystem health, and public safety.

Air Pollution, Climate Change and Health Impacts: Solutions- Oriented Exposure Science

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Faculty Advisor(s): Mary Rice
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Outdoor air pollution is a major driver of climate change and represents substantial factors in cardiopulmonary illness. Chronic obstructive pulmonary disease (COPD), a permanent ailment impacting approximately 15% of the American adult population over age 40, usually caused by smoking, is exacerbated by such exposures. However, the exact correlation between actual pollutant concentrations and the worsening of COPD, requires further clarification. This multicenter clinical trial, created by Johns Hopkins University but conducted under the guidance of Dr. Mary Rice at Beth Israel Hospital, pursues dual objectives. One being the quantification of dose-response dynamics between real pollution levels and their medical consequences. The other being the assessment of climate stabilization tactics to produce practical healthcare data in the wake of climate change. Furthermore, this trial includes a randomized clinical study determining if high-efficiency particulate air (HEPA) filtration systems enhance respiratory outcomes and pulmonary performance for individuals diagnosed with eosinophilic COPD. This trial builds on the earlier APECS study, a six-year investigation conducted by Dr. Rice at Harvard University, that examined similar research questions on a smaller scale. The current study now aims to replicate and extend those findings across multiple research sites.

Spectral Reconstruction of Functional Trait Gradients in Herbarium Oaks

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Faculty Advisor(s): Jeannine Cavender-Bares
Harvard College | Leverett House | Integrative Biology & Environmental Science & Engineering | 2028

Understanding how plant functional traits can vary systematically across environmental gradients correlated with temperature, precipitation, and latitude is central to predicting ecosystem responses to climate change. However, traditional approaches for measuring these characteristics are labor-intensive, spatially-limited, and often destructive, leaving gaps in understanding of global trait distributions. Herbarium collections, which house hundreds of millions of preserved plant specimens accompanied by georeferenced locality data spanning centuries, represent a largely untapped resource for addressing this challenge. This project intends to evaluate whether reflectance spectra from dried oak foliar specimens can predict traits central to the leaf economics spectrum (LES) and ultimately recover known trait-environment relationships. Quercus was selected as the study system because oaks are among the most speciose genera in North America and display well-documented intraspecific and interspecific trait variation among climatic continua. We will collect spectral, leaf mass per area (LMA), lignin, cellulose, hemicellulose, carbon, and nitrogen measurements to train and validate Partial Least Squares Regression models that can be applied to broader herbarium datasets and compared with climatic variables. So far, more than 750 individual leaves have been scanned using spectrometers, as well as weighed and photographed to calculate LMA. Remaining leaf material will be ground to a fine powder to undergo ANKOM fiber analysis and elemental chemistry methods that will further quantify structural and chemical traits. The SpecTraits pipeline will then be implemented to build a model and assess whether trait estimates for oaks sampled from HERBarium Spectral Hub for Advancing Research and Exploration (HERBSHARE) can successfully reproduce established ecological gradients. By testing whether herbarium spectroscopy preserves biologically meaningful patterns, this study seeks to validate herbarium collections as quantitative resources for macroecology and historical biodiversity research, enabling large-scale trait mapping without additional field collection and raising awareness about ongoing efforts in global herbarium spectral digitization.

Ownership and Incentive Channels Surrounding European Union Carbon Market Design

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Faculty Advisor(s): Robert Stavins
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In carbon markets, the question of ownership is largely a question of incentives, from potential increased political pressure for reforms to soft budget constraints preventing the internalization of risk. We look at the role of ownership in dictating incentives in the European Union's Emissions Trading Scheme (EU ETS), one of the most foundational market systems for carbon emissions allowances in the world. As free allocation slowly phases out in favor of auctions, the specific channels of ownership and government structure in stimulating abatement is not properly understood, especially following recent market liberalization policies that created a split between state-owned and private utilities. We constructed a panel dataset of 4,000+ power sector firms throughout the EU, along with variables of government-market influence and democratic progressiveness, to examine the effect of ownership and ideology on emissions trading behavior, output, and long-term planning. Using a panel regression with fixed effects, event study models, and qualitative documentation on investment, innovation, and abatement decision-making, emerging evidence suggests state ownership is correlated with lower emissions, especially in the third phase of the scheme. Environmental policy stringency, approximated by carbon price among market and nonmarket policies, affect the role of ownership in curbing emissions significantly, with state-owned firms in less stringent countries emitting more. The threshold for state ownership advantage seems to be at the level of strong environmental policy: meaningful carbon prices, renewable quotas, active research and development, implying different incentive mechanisms on both sides of the threshold. In addition, foreign firms are associated with greater emissions, and democracy is highly correlated with fewer emissions and a larger allowance surplus. This work will be continued via more specific investigation into mechanisms and interactions with particular policies including research and development, motivated by and building towards structural modeling via principal-agent or soft budget constraint models.

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SUMMER UNDERGRADUATE RESEARCH IN GLOBAL HEALTH PROGRAM

SELINA ZHANG

Lost In tR(N)Anslation: Navigating Inhibitors of Mycobacterial tRNA Charging and their Resistance Pathways

Student: Mieti Adi
Mentor(s): Kritee Mehdiratta
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Tuberculosis remains one of the world's most urgent public health challenges, warranting continued exploration of novel drug targets and therapeutics. The recent success of ganfeborole, a first-in-class inhibitor of mycobacterial leucyl tRNA synthetase in phase 2a clinical trials, has highlighted the potential of targeting aminoacyl-tRNA synthetases in controlling mycobacterial infection. Aminoacyl-tRNA synthetases (aaRS) are essential enzymes in *Mycobacterium tuberculosis* (Mtb) that catalyse the transfer of a specific amino acid to their cognate tRNA, a process termed tRNA charging. Inhibition of aaRS leads to accumulation of uncharged tRNA within the cells which results in translation inhibition and consequently bacterial death. In addition to ganfeborole, there are multiple Mtb aaRS inhibitors in development. Consequently there is a need to maintain the effectiveness of aaRS inhibitors by predetermining how microbes may build resistance to them. Ongoing work in Rubin lab is studying the effectiveness of compound DDD806905 and investigating potential resistance mechanisms. DDD806905 was previously characterized as methionyl-tRNA synthetase (MetRS) inhibitor in *Leishmania donovani*. Using whole-cell assays, the lab has established DDD806905 to be effective against Mtb. Whole genome sequencing of resistant mutants raised in the model organism *Mycobacterium smegmatis* (Msmeg) against DDD806905 surprisingly identified SNPs in two genes: MSMEG_4760 and MSMEG_3055. In this study, we are investigating the role of these two genes in maintaining tRNA homeostasis within mycobacteria and how these mutations cause resistance against the metRS inhibitor, DDD806905. Overexpression of a wild type copy of MSMEG_3055 in the resistant strain reversed susceptibility and made the resistant strain sensitive against DDD806905. This establishes the role of MSMEG_3055, (S-adenosylmethionine synthetase gene) as a key determinant of DDD806905 resistance. Continuing work is focused on further dissecting the contribution of MSMEG_4760. Together, our findings reveal previously unrecognized genetic determinants that drive resistance to MetRS inhibitors and can provide insights into mycobacterial tRNA biology.

Letters and Lessons: A Qualitative Analysis of Heat Officer Feedback

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Harvard College | Currier House | Social Studies | 2028

Chief Heat Officers (CHOs) are among the emerging government roles dedicated to mitigating the impacts of urban heat. Officials in these positions have the potential to play a crucial role in preventing heat-related deaths and building more heat-resilient communities. This qualitative analysis examines and categorizes the contents of 28 "Letters to a New Heat Officer" from a convening of CHOs and other climate officials from across the United States. The analysis explores the CHO's framing of the urban heat crisis through the key challenges and strategies described. Codes, clusters and themes were developed using grounded theory. An independent AI-generated analysis was used to identify potentially overlooked themes and patterns, and AI results supported the primary analysis. As a collection, the letters place a strong emphasis on a justice-oriented and community-centered approach to solution building in cities affected by urban heat, which involves focusing on vulnerable populations and facilitating resident participation in decision-making. Emerging themes also suggest the importance of effectively communicating the heat crisis to diverse stakeholders, navigating institutional constraints, prioritizing systemic revisions to infrastructure, and sustaining personal commitment. These findings are based on a small, self-selected sample of letters, and may not reflect the full range of CHO perspectives on urban heat challenges or solutions. Future work should elicit further feedback from CHOs on the strengths and weaknesses of heat action implementation in their geographic region. Opportunity for further investigation includes focusing on the role of data in managing urban heat, especially given the lack of evaluation-based content in the letters.

International Quality Improvement Collaborative (IQIC): The Importance of Databases

Student: Lia Galindo
Mentor(s): Allison Boretsky
Faculty Advisor(s): Kathy Jenkins
Harvard College | Winthrop House | Molecular & Cellular Biology | 2027

Low- and middle-income countries (LMICs) face severe barriers to performing cardiovascular surgeries and catheterizations because of limited resources and clinical capacity. In settings with weak healthcare infrastructure, congenital anomalies are the fourth leading global cause of neonatal death, while congenital heart disease (CHD) places severe financial burdens on families navigating high medical costs. The International Quality Improvement Collaboration (IQIC) for CHD collects pediatric patient data to account for critical variables, including clinical characteristics, medical history, preoperative management, and clinical outcomes. Drawing on data from 58 participating sites across 18 countries in 2025, IQIC completed a 10% audit to validate registry data. These metrics are risk-adjusted using the Risk Adjustment for Congenital Heart Surgery (RACHS-1) method, which accounts for patient differences such as surgical risk category, age group, and prematurity when comparing mortality rates. Thus far, this project has focused on auditing site engagement and resolving data gaps caused by database transition, global conflict, and the COVID-19 pandemic. An active site directory was built to track 135 institutions, revealing that only 63 sites remained actively engaged from 2023 to 2025. This directory recovered 32 previously lost sites, updated contacts, and determined registry statuses to build an updated map of global site locations. Moving forward, these datasets will be organized into site-specific annual reports to track individual progress. These reports will educate programs on procedural complications and areas for quality improvement. Ultimately, the directory will track the activity of LMIC sites to inform a systematic approach to maintaining active status or re-engaging inactive sites. By providing direct, targeted clinical results in annual site reports and establishing an international network of knowledge exchange, IQIC aims to translate data into long-term global health equity and reduced surgical mortality in pediatric cardiology.

Comparative Analysis of Anti-PfCSP Monoclonal Antibodies Using a 3D Matrigel Cytotoxicity Assay

Student: Marvel Hanna
Mentor(s):
Faculty Advisor(s): Azza Idris
Harvard College | Lowell House | Biomedical Engineering | 2027

Globally, there are about 282 million new malaria cases. Monoclonal antibodies targeting the *Plasmodium falciparum* circumsporozoite protein (PfCSP) have the potential to prevent malaria infection by neutralizing sporozoites, the infectious stage of the parasite, before they reach the liver. Understanding how differences in anti-malaria efficacy among anti-PfCSP monoclonal antibodies influence parasite survival is essential for improving antibody-based therapies and vaccine development. The objective of this study is to compare the functional activity of the monoclonal antibodies L9, CIS43, and R26C using a three-dimensional (3D) Matrigel cytotoxicity assay. Considering the reported differences in anti-malaria efficacy among these antibodies, we hypothesize that L9 and CIS43 will reduce sporozoite survival more effectively than R26C. GFP-expressing PbPf sporozoites (*Plasmodium berghei* engineered to express the *P. falciparum* circumsporozoite protein) are embedded within a 3D Matrigel matrix, which mimics the physical properties of host tissue. mCherry-expressing *P. berghei* sporozoites serve as an internal control to account for variation in parasite recovery. Parasites are incubated with L9, CIS43, and R26C monocolan antobides. The study will compare the effects of antibody identity and concentration on sporozoite survival and evaluate how differences in anti-malaria efficacy are reflected in this 3D assay. These findings will contribute to a better understanding of anti-PfCSP monoclonal antibody function and may support the development of improved malaria prevention strategies.

Harvard Medical School's Institutional History of Minority Recruitment and Engagement with Black Communities from 1968-1973

Student: John Kim
Mentor(s):
Faculty Advisor(s): Daniel Palazuelos
Harvard College | Dunster House | History & Science | 2028

Martin Luther King Jr.'s assassination in 1968 marked a pivotal moment in the racial history of the United States, exposing underlying racial tensions that made integration seem even more difficult. As the US shifted into the post-civil rights era, discussions on social justice and equality of opportunities intensified across institutions, including at Harvard Medical School. HMS faculty and students advocating for racial equality in medicine, from medical education to community health, launched initiatives and committees to expand minority admissions and engage with Boston's black communities. However, there is a lack of scholarly emphasis on how political, economic, or institutional challenges to these initiatives limited or closed those efforts. Archival collections at the HMS Countway Library of Medicine and interviews with HMS faculty were used to understand the institutional history of HMS from the 1960s to the present, with a focus on 1968-1973. Although this study currently continues to access archival collections, preliminary scans of the documents suggest that a combination of systemic educational inequality resulting in academic competency concerns and unstable federal funding for scholarships hindered efforts to expand admission for minority students. Institutional difficulties in communication among faculty and students may have also blurred the longstanding success of community engagement plans. With more data and analysis, this paper hopes to offer an explanation for why past organized efforts for minority and community healthcare at HMS struggle, which can inform how their current equivalent, the HMS Office for Community Centered Medical Education, can navigate future challenges and establish Harvard Medical School's strong commitment to caring for the most underserved.

Cost-Effectiveness Modeling of Generative AI Therapy Interventions for Depression: a Markov analysis using new RCT evidence.

Student: Merissa Lawrence
Mentor(s):
Faculty Advisor(s): Anushka Patel
Harvard College | Quincy House | Economics | 2027

Earlier rule-based chatbots like Eliza and Woebot were limited by input flexibility; generative AI (genAI) chatbots, however, can be trained on expertly written therapist-patient dialogues. GenAI chatbots show evidence of improving mental health symptoms, though their cost-effectiveness remains unevaluated. We conducted an early-stage cost-effectiveness analysis of three genAI chatbot interventions, Therabot, PATH, and Limbic Care, using their published RCTs. Each intervention was evaluated against a different comparator, and a two-state Markov cohort model of clinically significant depressive symptoms (PHQ-9 10; U.K. NHS perspective) was created for each intervention. Incremental Cost Effectiveness Ratios (ICER) were calculated for the trial period and one-year horizon. Within-trial ICERs were as follows: 6,054 per QALY gained for Therabot (vs waitlist), 3,000 for PATH (vs NHS website), and 29,933 for Limbic Care (vs digital workbook). Therabot and PATH were dominant (cost-saving with health gains), and robust across all sensitivity analyses. Their break-even prices were approximately 609 and 526 at the 20,000/QALY threshold. Limbic's one-year benefit is a reflection of baseline differences between arms, not the treatment effect. Limbic was dominated (equal health outcomes and greater cost) when the model was aligned with trial's finding of equivalent effectiveness. Overall, cost-effectiveness largely varied across the different intervention-comparator pairs, and were driven by comparator choice rather than the intervention. GenAI therapy is found to be extremely cost-effective against low-intensity comparators, though shows no incremental value against matched active digital content. These findings are key for comparator selection, pricing, and future economic evaluations of genAI mental health interventions.

Modeling Analysis for Healthcare Financing: Preventative Treatment of Hypertension and Diabetes in Ethiopia

Student: Jia Michel
Mentor(s):
Faculty Advisor(s): Mohammad S. Jalali
Harvard College | Eliot House | Computer Science | 2029

In Ethiopia, hypertension and diabetes lead to premature deaths more frequently than in high-income countries. This is related to high barriers to care, with systemic inequities formed from political turmoil and financial constraints. In order to reduce these financial burdens, the Ethiopian government has introduced the Community-Based Health Insurance (CBHI) program. However, the efficacy of CBHI on hypertension and diabetes treatment access is still unclear, inhibiting future allocation of resources. Systems Dynamics Models, a computer-aided simulation methodology, aid in navigating variables such as the complexity of intervention points, extended delays, and behavioral feedback, such as treatment-seeking. This study will build upon the established model created by the Mohammad S Jalali Lab in partnership with the Amhara Regional Health Bureau and funded by the World Health Organization. The previous model projected that CBHI coverage would increase from 75% in 2025 to over 90% by 2035, which would allow hypertension and diabetes treatment to increase from 28.0% to 38.5%, and from 11.0% to 14.8%, respectively. The original study focused on late treatment access, and there is limited analysis of CBHI's efficacy on early interventions such as lifestyle changes. The potential success of early interventions for high-risk individuals could influence the overall prevalence of hypertension in Ethiopia. In order to account for early interventions, we are conducting literature reviews to find estimates, and we will build a new intervention into the model, analyze percent changes of prevalence of hypertension and diabetes, and percent changes of people in treatment. Our research will ultimately determine the influence of lifestyle changes on the well-being and quality of life for hypertensive patients in Ethiopia.

Evaluating Prevalence of ESBL-Producing Enteric Bacteria in Pre-Term Infants in the NICU over the Course of the First Four Weeks of Life

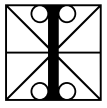
Student: Nafisa Zaman
Mentor(s): Damien Slater
Faculty Advisor(s): Jason Harris
Harvard College | Eliot House | History & Science | 2028

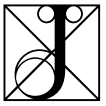
Beta-lactam antibiotics are among the most widely used agents for treating bacterial infections, but their increasing use has contributed to rising rates of resistance, including extended-spectrum beta-lactamase (ESBL)-producing enteric bacteria. These pathogens are of particular concern in the neonatal intensive care unit (NICU), where colonization can increase the risk of invasive infection and limit treatment options. We conducted a longitudinal, retrospective study of preterm infants hospitalized in the Massachusetts General Hospital NICU to determine the prevalence and carriage dynamics of ESBL-producing enteric bacteria. 83 infants with gestational ages ranging from 22–32 weeks were enrolled across two periods (November 2022–November 2023 and November 2024–June 2025). The child's first stool sample was collected as a baseline, and weekly samples were collected over the next four weeks. Stool samples were stored frozen in a glycerol-containing medium to preserve bacterial viability for downstream culture. Screening for ESBL-producing enteric bacteria was performed using an enrichment culture followed by plating on MacConkey agar supplemented with cephalosporins. Presumptive ESBL-producing isolates were confirmed using a clavulanate inhibition disk diffusion test. Species identification was performed using a combination of molecular and biochemical methods. In parallel, antibiotic resistance genes and gut microbiome composition were assessed using metagenomic sequencing. This work is ongoing at the time of abstract submission; however, we anticipate that this study will provide insight into the prevalence of ESBL-producing organisms in the NICU and enable further investigation of clinical and environmental factors associated with colonization.

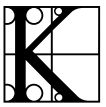
Autographs

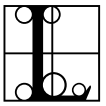
Autographs

Index









Julia Wu LENA XIE Emily Kung SELINA ZHANG!

WHAT YOU NEED FOR RESEARCHING

C. hemisphaerica

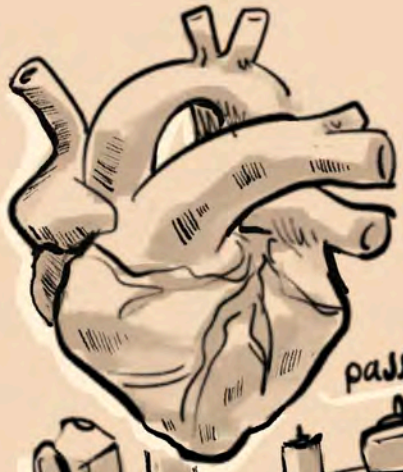
D. rerio

C. elegans

archives

patience

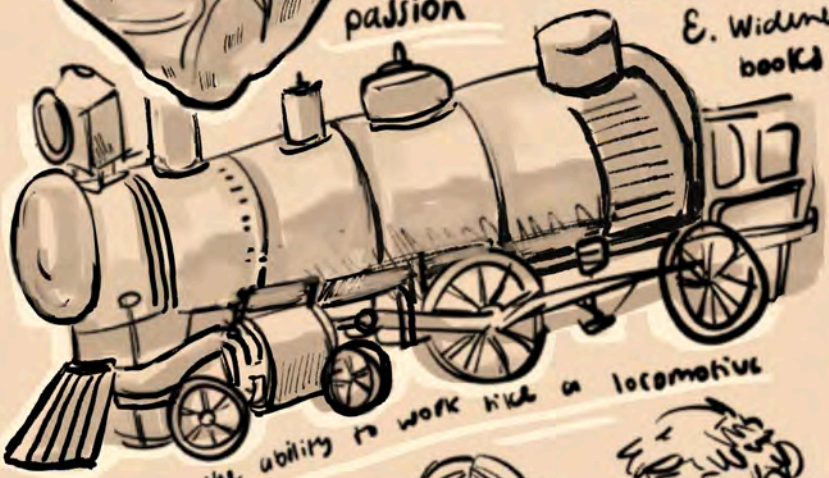
S. cerevisiae



passion

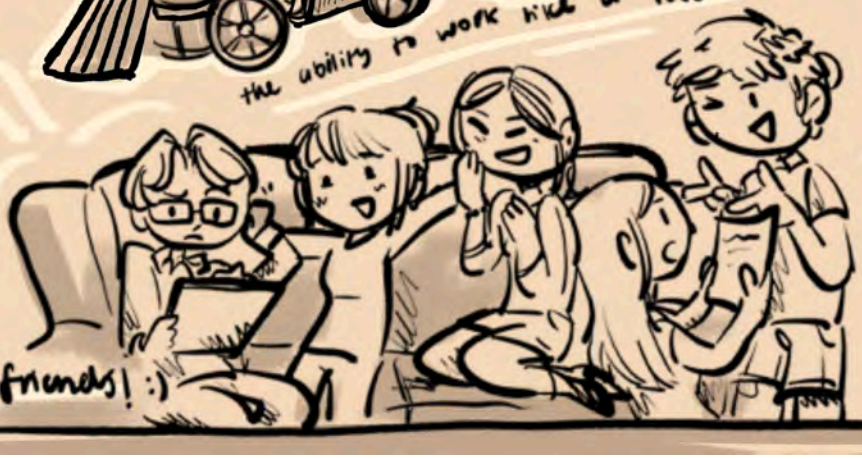
E. Widmer books.

funding



the ability to work like a locomotive

hands (many hands make light work)



friends! :)

M. musculus