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2020 BECKMAN SYMPOSIUM

BY THE NUMBERS

8 LIVE SESSIONS

22 ON-DEMAND PRESENTATIONS

115 RESEARCH POSTERS

7 BYI FINAL PRESENTATIONS

12 BIO-CHEM TALKS

8 POSTDOC BRIEFINGS

64 COLLEGES & UNIVERSITIES REPRESENTED IN THE POSTER HALL

16 INVITED SPEAKERS

52% MALE SPEAKERS

48% FEMALE SPEAKERS

WELCOME

The Beckman Symposium is a three-day event where Arnold and Mabel Beckman Foundation program awardees present their newest research findings as poster or oral presentations. Attendees are given opportunities to network, learn about a broad range of research topics from their peers, and discuss career tips with invited experts from academia, industry, and medicine.

Due to COVID-19 concerns, this year's event is being presented in a virtual space. The agenda for our first-ever virtual Symposium has been carefully composed to feature a combination of live webinars and pre-recorded content that showcases our Beckman Young Investigators, Arnold O. Beckman Postdoctoral Fellows, and Beckman Scholars, along with a research poster hall, program booths, Q+A chats and networking lounge. Be sure to explore every aspect of the event to accumulate points for a chance to win prizes.

The newest additions to our Beckman Symposium guest list represent local high school science students from the CubeSat program and the inaugural year awardees and mentors of our Orange County Beckman Legacy Award Program. To all attendees: This space was developed to promote sharing of scientific knowledge and to foster collaboration. As a friendly reminder: The Arnold and Mabel Beckman Foundation is committed to providing a safe, productive and welcoming environment for Symposium guests. All participants are expected to abide by the Code of Conduct when spending time online with other Foundation awardees, colleagues in your field, distinguished scientists from across the United States, and other invited guests of the Foundation. The guidelines are intended to ensure that all participants have a pleasant and productive virtual event, free from disruptions.

We hope you enjoy the 2020 Beckman Symposium! Be sure to follow us on social media using these handles and event hashtag:

Twitter: @beckmanfnd
Facebook and Instagram: @beckmanfoundation
LinkedIn: @arnold-and-mabel-beckman-foundation

#BeckmanSymposium

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Need assistance? https://www.labroots.com/support

Zoom Room Schedule

Find Links to These Activities In the Meeting Hall

Need a Zoom background? We've created Symposium Zoom backgrounds and added them to the "Literature" tab in each of our five booths. Head to the Exhibit Hall, choose any booth, and click on "Literature" to find your favorite Zoom background!

1

8/6 at 2pm PT
Beckman Briefings (Invite Only)
Bri McWhorter, MFA gives feedback to 2017 AOB Postdoc Speakers.

2

8/6 at 2:30pm PT
Lab Policy (Open to All)
Chat about this earlier workshop with Jennifer M. Heemstra, PhD.

3

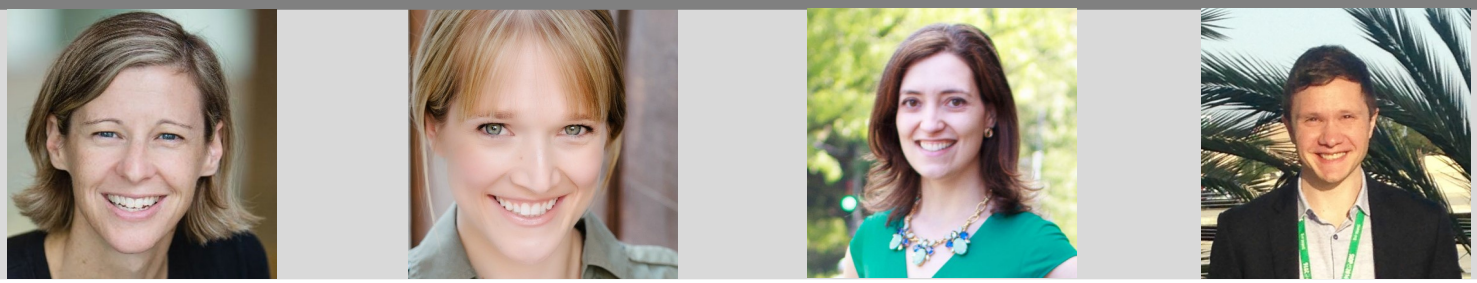
8/6 at 3pm PT
Communicating Science (Open to All)
Chat about this earlier workshop with Carmen Drahl, PhD and Mike Morrison.

4

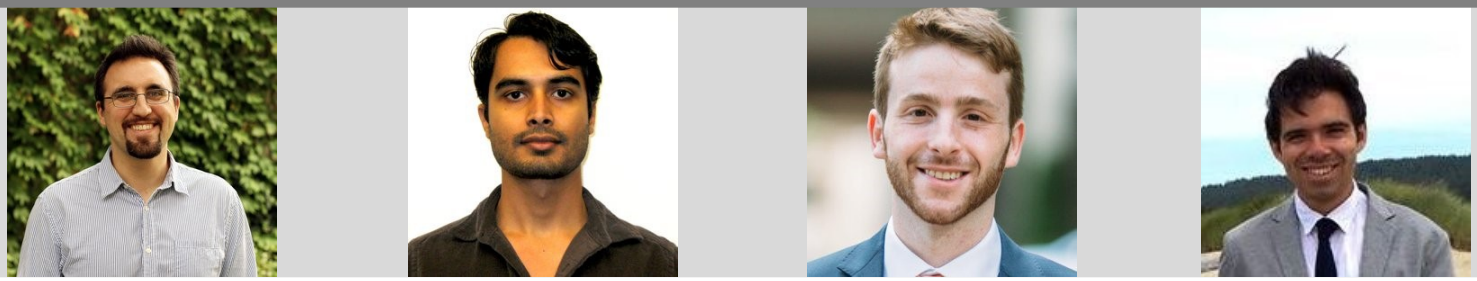
8/7 at 3:30pm PT
Beckman Trivia – LIVE! (Open to All)
Test your trivia knowledge with Brian Goess, PhD and Andrea Tartaro, PhD.

LIVE SPEAKERS - DAY 1

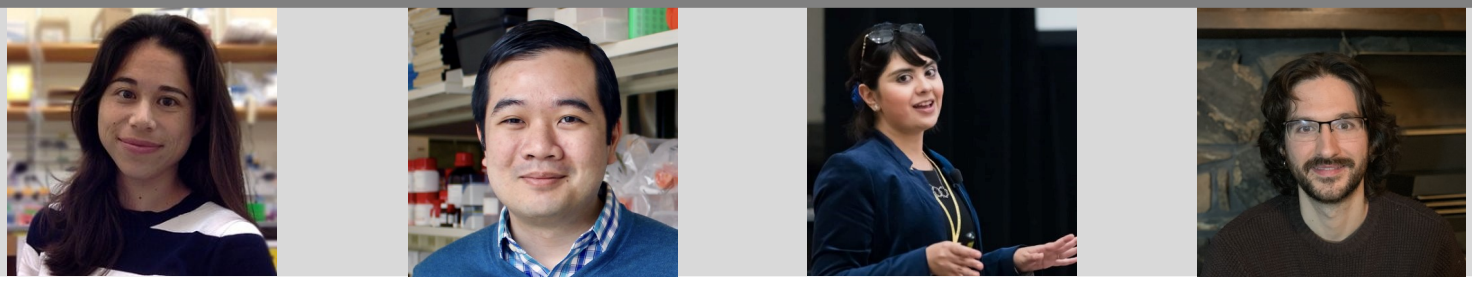
Watch All Presentations in the Auditorium



Program Workshop Speakers (l to r): Jennifer M. Heemstra, PhD; Bri McWhorter, MFA; Carmen Drahl, PhD; Mike Morrison.



Beckman Briefings Speakers (l to r): Marco Allodi, PhD; Kumar Ashtekar, PhD; Jesse Isaacman-Beck, PhD; Francisco Luongo, PhD.



Beckman Briefings Speakers (l to r): Kira Mosher, PhD; Freddy Nguyen, MD/PhD; Massa Shoura, PhD; Eric Strobel, PhD.

Scan the QR code on the **LEFT** to see bios for all of our 2020 Beckman Symposium Speakers.

Scan the QR code on the **RIGHT** to see the Day 1 Agenda as it is displayed on our microsite.

8.6.20 AGENDA

DAY 1 Live Content: PROGRAM WORKSHOPS

8:30-10am Pacific Time – Lab Policy Workshop

Be 'System'atic: Creating Lab Culture and Training Environment Through Lab Policies

Jennifer M. Heemstra, PhD

When I started my faculty job, I thought that just knowing the type of mentor I wanted to be and the lab culture that I wanted to create would be enough to make these things happen. I couldn't have been more wrong. Establishing and maintaining lab culture and mentoring practices doesn't have to be overly complicated, but it takes intentionality and communication. This workshop will explore approaches to designing and implementing systems and policies to support the lab environment that you want to cultivate. ***Open to all attendees, focused toward Beckman Young Investigators***

10:00-11:30am Pacific Time – Beckman Briefings Workshop

Scientific Storytelling

Bri McWhorter, MFA

This workshop will cover how to craft, organize, and deliver an engaging scientific talk. It will show you how to use various techniques to turn your research presentation into an engaging and repeatable story. Following the presentation, Bri will take notes as each **2017 Arnold O. Beckman Postdoctoral Fellow** presents their own Beckman Briefing (lightning talk) to the group. After the workshop, Bri will offer helpful feedback, then meet with each fellow individually to give personalized feedback on how to improve their presentation. ***Open to all attendees, focused toward Arnold O. Beckman Postdoctoral Fellows***

2017 Arnold O. Beckman Postdoctoral Fellows presenting during this session include:

Extracting Photochemical Design Principles from Biological Systems in vivo

Marco Allodi, PhD

Natural light-harvesting systems, such as photosynthetic pigment-protein complexes, efficiently transfer energy through space with high efficiency. Ultimately, we would like to understand the design principles nature evolved to improve optoelectronic devices that rely on light harvesting and energy transfer, such as solar cells. We perform ultrafast 2D electronic spectroscopy measurements on a variety of systems ranging from the Fenna-Matthews-Olson antenna complex isolated from green sulfur bacteria to in vivo cyanobacteria. We observe larger amplitude coherences under reductive conditions that mimic the chemistry of the complex in vivo. We can use spectroscopic tools that allow us to follow the energy in both space and time. In particular we can correlate the existence of quantum coherences, particularly those involving excited electronic states, with faster, more efficient energy transfer, and assessing the role of the ground and excited states in the transfer process. Future work will look at the how changing light conditions influences the complex chemistry in the photosynthetic membranes, ultimately affecting the energy transfer processes.

Exploring the inhibition of Alk2 kinase and dimerization of EGFR kinase

Kumar Ashtekar, PhD

One of the most common pathologically relevant mutated variants of ALK-2 (activin receptor-like kinase-2) has a point mutation (R206H) in its Ser/Thr kinase domain that promotes uncontrolled signaling in rare diseases, namely Fibrodysplasia Ossificans Progressiva (FOP) and Diffuse Intrinsic Pontine Glioma (DIPG). Currently, there are no FDA approved drugs available for ALK-2 inhibition in these diseases. A computational platform has been developed for de novo design of similar dual inhibitors that can simultaneously engage other key targets – similarly augmented by protein -protein interactions. Employing this strategy and iterative modifications, a mutant-selective inhibitor for ALK-2 (R206H) has recently been identified that may have promise for the treatment of FOP and DIPG. Eukaryotic protein kinases are induced to drive phosphorylation-initiated signal transduction via allosteric self-assembly. They explore a continuum of conformations that includes ensembles of 'active state' and 'inactive state' conformers. In the absence of a signaling stimulus, inactive state conformers dominate the continuum. When a signaling event is triggered by ligand binding (initiating self-assembly by homo- or hetero-oligomerization of kinase domains) or by recruitment of adapter proteins, the shift in the monomer/dimer equilibrium favors the active state conformers. We investigate the quantitative effects of patient-derived activating mutations on kinase domain dimerization strength (driving EGFR activation 'from the inside'), activity of the kinase domain monomer and dimer, as well as structural dynamics of EGFR kinase domain activation and possible novel modes of disrupting this self assembly. Understanding the dynamics of constitutive allosteric activation in EGFR mutants seen in lung cancer patients, and how the mutations shift the equilibrium towards the active form of enzyme, are key steps in appreciating and combatting the origins of inhibitor resistance.

8.6.20 AGENDA

DAY 1 Live Content: PROGRAM WORKSHOPS

SPARC - A method to genetically manipulate precise proportions of cells

Jesse Isaacman-Beck, PhD

Many experimental approaches rely on controlling gene expression in select subsets of cells within an individual animal. However, reproducibly targeting transgene expression to specific fractions of a genetically defined cell type is challenging. We developed Sparse Predictive Activity through Recombinase Competition (SPARC), a generalizable toolkit that can express any effector in precise proportions of post-mitotic cells in Drosophila. Using this approach, we demonstrate targeted expression of many effectors in several cell types and apply these tools to calcium imaging of individual neurons, optogenetic manipulation of sparse cell populations in vivo, and genomic profiling of mutant and control neuronal subtypes harvested from the same animals.

Mechanisms for perceptual organization in the rodent visual cortex

Francisco Luongo, PhD

The rodent visual system has attracted great interest in recent years, owing to its experimental tractability, but the fundamental mechanisms used by the mouse to represent the visual world remain unclear. One key step in representing the world in our visual system is that of perceptual organization, whereby individual objects are identified and segmented. An outstanding question is the extent to which perceptual organization is a common computational principle across mammalian visual systems. To answer this we looked for neural and behavioral evidence of such a process in the rodent. We find that mice can segment objects using contrast cues but fail to utilize motion cues. This is in contrast to primates who can use either cue. Lastly, we model the representations in the rodent visual cortex and find they are consistent with a feedforward cascade of computations. This work highlights both the strength and limits of the rodent as a model system for mid level vision.

Dissecting Cell Signaling Networks That Regulate Adult Neural Stem Cell Functions

Kira Mosher, PhD

In the adult mammalian hippocampus, neurogenesis (in which new neurons are generated and integrated into the CNS) is believed to underlie learning and memory. Within the hippocampus, numerous cell types communicate via diverse signals. Some of these signals control neural stem and progenitor cells (NSPCs), which can divide or terminally differentiate into neurons, astrocytes, or oligodendrocytes, and then migrate and integrate into the existing brain circuitry. I have identified novel functions for a ligand-receptor pair, ephrin-A4 and EphA4, in this process. NSPCs express the receptor EphA4, while ephrin-A4 is predominately expressed by mature neurons. In cell culture studies, treating adult NSPCs with ephrin-A4 activated EphA4 and induced neuronal differentiation, and blocking EphA4 ligand-binding with an antagonist reversed these effects. Ephrin-A4/EphA4 signaling also regulated the migration of NSPCs. Finally, using AAV to deliver CRISPR/Cas9 into the brains of adult mice, I found that knocking out EphA4 or ephrin-A4 in select cell types alters neuronal differentiation and migration in vivo. These data thus support a significant role for ephrin-A4/EphA4 signaling in regulating adult neurogenesis.

From biochemical nanosensors to imaging to informatics to COVID-19 convalescent plasma - developing diagnostics and therapies for clinical medicine

Freddy Nguyen, MD/PhD

Current cancer management follows a multipronged approach that include surgery, radiation, and chemotherapy. There is a pressing need for a platform technology to provide precision chemotherapy screening, drug delivery detection, and real-time therapy efficacy monitoring. We have developed single walled carbon nanotube (SWNT) sensors for the detection of chemotherapeutics, more recently for temozolomide (TMZ) and its byproduct 5-Amino-4-imidazolecarboxamide (AIC) with sensitivity at 5-500 μM and in vitro viability up to 7 days in TMZ treated glioblastoma cells. Sensors for irinotecan, cisplatin, and lomustine were developed with sensitivities at 50 μM. H2O2 sensors were used to measure the therapy efficacy of gemcitabine and irinotecan in pancreatic ductal adenocarcinoma in vitro and in vivo. Multiplexing these sensors could yield insights into delivery, diffusion, metabolism, and efficacy of chemotherapeutics in hours or days. Other strategies are being developed such as ratiometric approaches and wavelength-induced frequency filtering to improve performance and sensitivity. A fiber optic platform was developed as a minimally invasive form factor to integrate the sensor hydrogel, optical waveguide, and detection system. As a physician-scientist in NYC, my research rapidly shifted to the role of convalescent plasma (CP) in COVID-19. CP can be used to passively transfer antibodies from recently recovered patients to actively infected treatment-resistant patients. Initial studies revealed antibody neutralizing activity peaked at 31-35 days post symptom onset. Initial outcomes in severe and life-threatening COVID-19 hospitalized patients show CP as a potentially efficacious treatment for non-intubated patients. Retrospective study of 427 CP transfusion events yielded 12.9% of transfusion reaction rate with vast majority due to COVID-19 disease not CP.

8.6.20 AGENDA

DAY 1 Live Content: PROGRAM WORKSHOPS

The "Real" Nuclear Physics: Tracking Genome Dynamics in Time and Space

Massa Shoura, PhD

Extrachromosomal circular DNA (eccDNA) comprises products of genomic recombination that cause somatic changes in gene length and sequence. These circular molecules are derived from canonical linear chromosomal loci, expanding the diversity in coding and regulatory capacity within eukaryotic genomes and transcriptomes. Using a brand-new multidisciplinary approach to investigate eccDNA-mediated allelic diversity, I have identified various coding regions of eccDNA biogenesis, such as Titin and Mucin loci. In order to systematically investigate the biological implications and mechanisms of eccDNA formation, this project will focus on Titin eccDNAs as a prototype for eccDNA-mediated chromosomal rearrangements. Titin (TTN) is an extremely large protein that is responsible for the passive elasticity of muscle, functioning as a molecular spring. This single gene (TTN) is expressed in various isoforms, each with its own associated “spring constant.” It has been assumed that Titin protein diversity results from complex mechanisms dependent on alternative RNA splicing. However, there is thus far no comprehensive alternative-RNA-splicing framework that accounts for the full spectrum of TTN diversity. Preliminary data obtained in the past years of support suggest a novel mechanism of TTN diversity involving circular-DNA excision that generates recombinant TTN loci at the genomic level. Here, I report TTN-eccDNA formation as a potential mechanism for modulating overall myofibrillar passive tension. Results from investigating this novel mechanism for the modulation of cardiovascular stiffness will revolutionize basic, clinical, and therapeutic approaches to cardiovascular diseases. The AOB Award has been instrumental in advancing the field of eccDNA, in general, and in providing a missing key element in DCM biology, consideration of which may drive a reevaluation of current therapies.

Unraveling the interplay between transcription and RNA folding

Eric Strobel, PhD

RNA mediates essential biological processes in all organisms. These functions include catalysis of crucial biochemical reactions such as peptidyl transfer during translation and transesterification during RNA splicing, regulation of gene expression, and defense against foreign nucleic acids. A unifying characteristic of RNA-mediated cellular activities is that their function and specificity frequently depend on RNA secondary and tertiary structures which begin to fold during transcription. RNA sequence can therefore be constrained by its coding potential, by the architecture of its biochemically active folds, and by the requirements of co-transcriptional structure formation. Consequently, understanding the interdependence of these constraints is fundamental to predicting how changes in an RNA sequence affect its structure and biological function. As an Arnold O. Beckman Postdoctoral Fellow, my research has focused on addressing this fundamental challenge through the development and application of systematic in vitro methods for assessing cotranscriptional RNA structure and function. These studies have begun to expose the molecular details of cotranscriptional gene regulation in bacteria and have established a foundation for the continued development of quantitative experimental tools to understand how transcription and RNA folding are coordinated in biological systems.

11:30am-1pm Pacific Time – Communicating Science Workshop

Part I: *How To Promote Your Science And Talk To Reporters Like A Pro*

Carmen Drahl, PhD

Most researchers are curious about how to communicate their science to the media, yet they may also be worried that they'll be misquoted or misrepresented in an article. In an age where science and reason matter more than ever, researchers should empower themselves with techniques that will build collaborative relationships with reporters. While media coverage is never a guarantee, this talk aims to boost researchers' chances of getting noticed by explaining where reporters look for story ideas, and which of those places are most within researchers' control. Strategies to put a project's real-world impact front and center will be discussed. And finally, the talk will offer tips for preparing for an interview with a member of the press.

Part II: *How to Create the Ultimate Scientific Poster with User Experience Design*

Mike Morrison, MA

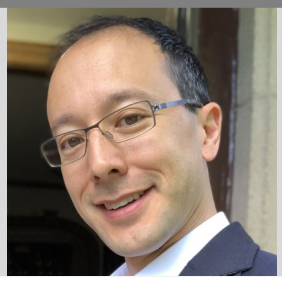
Scientific posters haven't changed in 30 years, which should be alarming to you (nothing in science should be stagnant). And evidence suggests they are incredibly ineffective. In this talk, you will learn the evidence-based design principles that science has discovered in the last 30 years (since the birth of the Internet) and how you can apply them to create fully-modern scientific posters that transmit your knowledge much more effectively to other scientists, and help you and them have more fun at poster sessions too. As a bonus, these same principles apply to presentations, reports --- anything you design for people to use. ***Both parts open to all attendees, focused toward Beckman Scholars***

LIVE SPEAKERS - DAY 2

Watch All Presentations in the Auditorium


Career Trajectory (Academia) Speakers (l to r): Jeffrey Moore, PhD; Ming Chen Hammond, PhD.


Career Trajectory (Industry) Speakers (l to r): Christopher am Ende, PhD; Carmen Drahl, PhD.




Career Trajectory (Medicine) Speakers (l to r): Terrance Kummer, MD/PhD; Shameema Sikder, MD; Kirk Wangensteen, MD/PhD; Lois Smith, MD/PhD.

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8.7.20 AGENDA

DAY 2 Live Content: CAREER TRAJECTORY PANELS

9-10:15am Pacific Time – Profiles in Science: Academia Careers

Part I: *The Team, the Generalist, and Seeing Through Blind Spots*

Jeffrey Moore, PhD

I will tell brief stories of experiences that have shaped my career, generalize the lessons learned, and translate them to three actionable items: (1) be careful with your pronouns, (2) embrace diversity of thinking, and (3) don't be duped. I'll conclude by suggesting a question that will help you know if you are on a successful career path: "Are you listening, learning and getting a little better every day?"

Part II: *Adventures in Molecular Recognition*

Ming Chen Hammond, PhD

In the movie "Moana" the lead character sings the refrain, "There's no telling how far I'll go" before she heads off on the adventure of a lifetime. In this short talk, I will give a personal reflection of my own adventures in science, which started with telling my freshman advisor that I aspired to have a work-study position in a research lab. I was subsequently selected as part of the inaugural class of Beckman Scholars, and most recently, things have come full circle as I became co-Director of the Beckman Scholar Program at the University of Utah, where I am an associate professor of chemistry. My research has spanned the fields of chemical biology, synthetic biology, and microbiology, involved collaborations across the globe, and last year I led an experiment conducted on the International Space Station. In other words, I want to convey to current Beckman Scholars that an academic career is a "Choose Your Own Adventure" type of career, and there is no telling how far they will go! ***Both parts open to all attendees***

10:30-11:45am Pacific Time – Profiles in Science: Industry Careers

Part I: *Adventures in Chemical Biology and Drug Discovery*

Christopher am Ende, PhD

In this presentation, I will discuss my experiences leading to my current position as a scientist and team leader, focused on chemical biology and drug discovery in the pharmaceutical industry. This includes my undergraduate research as a Beckman Scholar at the University of Delaware and graduate work at Stony Brook University. Additionally, I will highlight the innovative chemistry, chemical biology and medicinal chemistry we are doing to support drug discovery at Pfizer Inc.

Part II: *From the Ivory Tower to the Newsroom: Careers in Science Communication*

Carmen Drahl, PhD

A career in science journalism may not be what you think. This talk is more than a rehash of one writer's career path (though there is a little of that). It explains where the majority of science writers work (hint: it's not at publications you can purchase at the newsstand). It also contains statistics about employment prospects and median salaries, and explains the skills and qualities that all science communicators share. This presentation is not only for researchers interested in exploring a career in science writing. It is for any scientist who'd like to be able to recognize a potential journalist among the people they mentor. ***Both parts open to all attendees***

More...

8.7.20 AGENDA

DAY 2 Live Content: CAREER TRAJECTORY PANELS...continued

12-2:30pm Pacific Time – Profiles in Science: Medicine Careers

Part I: *Dual Degrees and Dual Careers -- The Interface between Neurology and Neuroscience*

Terrance Kummer, MD, PhD

During this seminar I will present details of my path from Beckman Scholar to MD-PhD, advanced training as a neurologist, then a neurointensivist, and the interleaving of additional research experience into this clinical training, eventually leading to my establishment of a wet bench laboratory and a paired human physiology laboratory in the intensive care unit. I will describe my group's philosophy of bench-to-bedside translation, present one example of our work in this arena, and briefly highlight our current efforts to understand the mechanisms of traumatic brain injury and its links to Alzheimer's disease.

Part II: *From Oil Refineries to Cataract Surgeries: My Life through Process Flow Diagrams*

Shameema Sikder, MD

In this presentation Shameema Sikder will discuss her career trajectory starting as an undergraduate studying chemical engineering and biochemistry to an Associate Professor of Ophthalmology at Johns Hopkins leading initiatives to change cataract surgery training. She will highlight the impact of being a Beckman Scholar on her career path.

Part III: *The Physician Scientist Track: Long Trajectory and Worth It*

Kirk Wangensteen, MD, PhD

I will present how I came to choose the physician-scientist career pathway. I was inspired from an early age by stories about my great-grandfather, an academic surgeon who innovated gastric suction and is credited for saving thousands of lives. I became involved in research in high school and college, and continued my training in a combined MD/PhD program. As an MD/PhD student I was further inspired by the emerging data from the human genome project to develop tools to improve our understanding of gene functions. I found that the liver is amenable to genetic manipulation, and I came focus my career around using genetic tools and methods to improve our understanding and treatment of human liver disease. My advice for budding scientists is to pursue whatever topic they find inspiring. This way, a long and sometimes toilsome career path will be interesting, fulfilling, and totally worth it.

Part IV: *How to be a Sane Clinician Scientist - A Timeline*

Lois Smith, MD, PhD

This talk will touch on several key points: PhD (MD) important grounding in science; how to develop friendships, gather mentors and collaborators; keep up with the literature; look at evidence basis for medical practice; ask big questions, stay focused, and drill down; build your resume so that it holds together; and publish the highest level science (journals) you can. You need support at home: You will have kids during the training and there will be some down time; marriages can suffer so put effort into your relationship as well. Learning objectives include: 1. How to do it all as a clinician scientist without burning out, and 2. How to have a wonderful time juggling a lot.

LIVE SPEAKERS - DAY 3

Watch All Presentations in the Auditorium

Keynote Speaker: Jennifer M. Heemstra, PhD.

Appreciation Award Presentation and Closing Remarks Speakers (l to r): Anne Hultgren, PhD; William H. May.

Scan the QR code on the **LEFT** to see bios for all of our 2020 Beckman Symposium Speakers.

Scan the QR code on the **RIGHT** to see the Day 3 Agenda as it is displayed on our microsite.

8.8.20 AGENDA

DAY 3 Live Content: Keynote Presentation and Closing Remarks

9:30am Pacific Time: Mental Health in the Sciences

Self-care is Not the Enemy of Performance
Jennifer M. Heemstra, PhD

The highly competitive nature of academic environments might seem to suggest that success can only be obtained at the cost of taking good care of oneself. However, sacrificing self-care can be extremely harmful. This seminar will discuss ways that high performance and self-care can be mutually reinforcing and produce long-term success. A key goal is for each person to take away a set of practical strategies and habits they can employ to support their mental and physical health while also supporting their future success in research. ***Open to all attendees***

11am Pacific Time: Appreciation Award Presentation and Closing Remarks

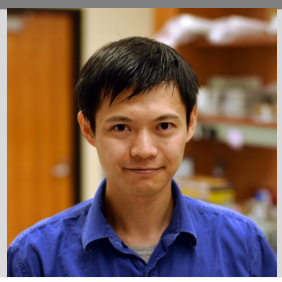
William H. May
Chairman of the Board of Directors

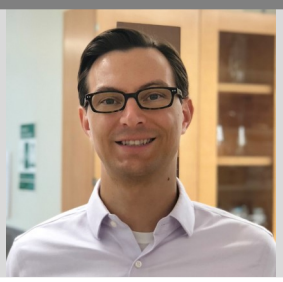
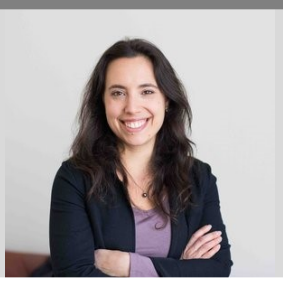
Anne Hultgren, PhD
Executive Director

Join us for Symposium closing remarks, with a presentation by William May, Chairman of the Board, and appreciation award to Craig Gatto, PhD for his years of service on the Beckman Scholars Program Executive Committee. Additional remarks and acknowledgement of trivia and points winners will be delivered by Anne Hultgren, PhD, Executive Director of the Arnold and Mabel Beckman Foundation. ***Open to all attendees***

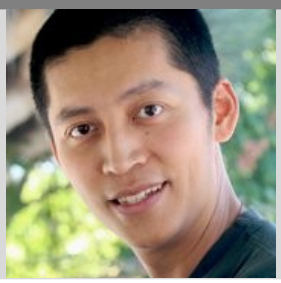
Scan the QR code on the **LEFT** to learn more about Arnold and Mabel Beckman. Scan the QR code on the **RIGHT** to see an overview of the Arnold and Mabel Beckman Foundation.

SPEAKERS WITH PRE-RECORDED ON-DEMAND CONTENT (AVAILABLE ALL DAYS)



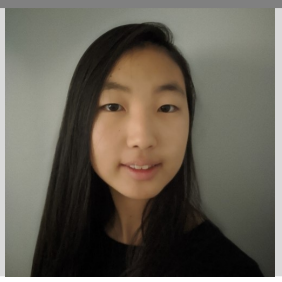



BYI Final Presentation Speakers (l to r): Yiyang Gong, PhD; Markita Landry, PhD; Zachary Pincus, PhD; Gabriela Schlau-Cohen, PhD.


BYI Final Presentation Speakers (l to r): Sabrina Spencer, PhD; Jing-Ke Weng, PhD; Ke Xu, PhD.

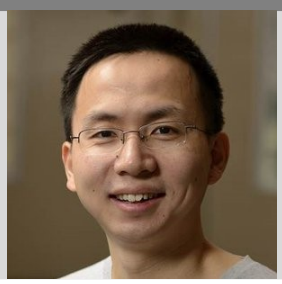


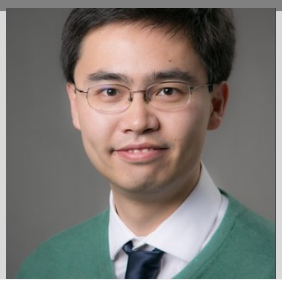



CubeSat Speakers (l to r): Jonathon Bower, Sarina Doshi, Eric Ho, Kaylee Kim.

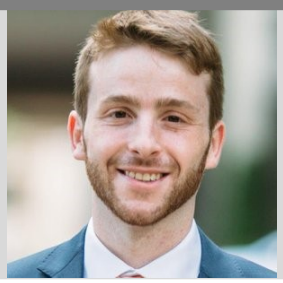
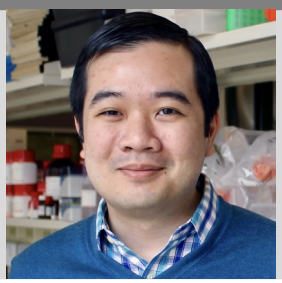
Scan the QR code to see bios for all of our 2020 Beckman Symposium Speakers.

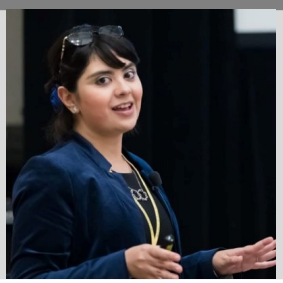
SPEAKERS WITH PRE-RECORDED ON-DEMAND CONTENT (AVAILABLE ALL DAYS)



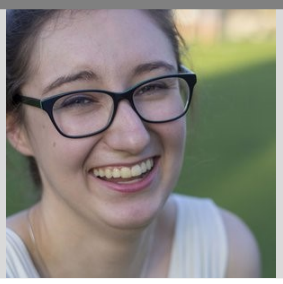
BYI Bio-Chem Speakers (l to r): Chen Li, PhD; Michaela TerAvest, PhD; WeiWei Xie, PhD; Xiaoji Xu, PhD.



AOB Postdoc Bio-Chem Speakers (l to r): Jesse Isaacman-Beck, PhD; Freddy Nguyen, MD/PhD; Liela Romero, PhD; Massa Shoura, PhD.






BSP Bio-Chem Speakers (l to r): Vennela Mannava, Silas Miller, Catherine Weibel, Shoshana Williams.

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BYI Final Presentations

An optical brain-machine interface through the development of protein, microscope, and deep learning tools

Yiyang Gong, PhD

Our work focuses on developing an optical brain-machine interface capable of interacting with neural activity in real-time. In this talk, I will describe our progress toward building the components that form such an interface. These components include protein sensors and actuators that interact with light to read and write neural activity, optical microscopes that can record neural activity from large volumes of brain tissue, and deep learning data processing algorithms that can calculate neural activity in real time. Together, these technology pieces will enable the next generation of neuroscientific experiments that control and investigate the cellular resolution response of the brain.

Nanomaterials Engineering to Probe and Control Living Systems

Markita Landry, PhD

Unique physical, chemical, and optical phenomena arise when materials are confined to the nanoscale. We are accustomed to making observations for the behavior of living systems on a macroscopic scale that is intuitive for the time and size scales of our day-to-day lives. However, the building blocks of life: proteins, nucleic acids, and cells, occupy different spatiotemporal scales. Our lab focuses on understanding and exploiting tunable optical and mechanical properties of nanomaterials to access information about biological systems stored at the nano-scale. In the context of leveraging nanomaterial optical properties, we present recent work on developing and implementing neuromodulator nanosensors to image serotonin or dopamine volume transmission in the extracellular space of the brain. We validate our dopamine nanosensor in acute striatal slices with electrical and optogenetic stimulation of dopamine release, and show disrupted dopamine release or reuptake kinetics when brain tissue is exposed to dopamine agonist or antagonist drugs. In the context of leveraging nanomaterial chemical properties, we also discuss how high aspect ratio nanomaterials can be synthesized to carry biomolecular cargo to living systems. In particular, genetic engineering of plants is at the core of environmental sustainability efforts, but the physical barrier presented by the cell wall has limited the ease and throughput with which exogenous biomolecules can be delivered to plants. We will describe how nanomaterials engineering principles can be leveraged to genetically manipulate living plants, without transgene integration, in efforts to reconcile the benefits of crop genetic engineering with the demand for non-GMO foods. Our work in the agricultural space provides a promising tool for species-independent, targeted, and passive delivery of genetic material, without transgene integration, into plant cells for rapid and parallelizable testing of plant genotype-phenotype relationships.

Systematic, organism-wide gene regulation drives individual lifespan in C. elegans

Zachary Pincus, PhD

Why do some individuals live longer than others? Even identical twins have different lifespans, as do genetically identical model organisms raised in controlled laboratory environments. What then accounts for these differences? Random accumulation of damage, sudden exogenous insults, or internal biological processes that somehow diverge? We find strong evidence for the latter. Using the nematode C. elegans, we find that prospectively long- vs. short-lived individuals are highly divergent in terms of gene regulation. Fully half of a library of promoter::GFP gene-expression reporters can effectively predict future lifespan. Moreover, these reporters represent diverse spatial and temporal expression patterns, suggesting that the regulatory states underlying long and short life are not specific to a particular tissue or a single regulatory process. Long- vs. short-lived individuals exhibit widespread, systematic, and organism-wide differences in gene regulation, well in advance of mortality.

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Heterogeneous ultrafast relaxation in photosynthetic light-harvesting proteins

Gabriela Schlau-Cohen, PhD

In photosynthesis, solar energy capture to conversion occurs with a remarkable near-unity quantum efficiency through energy transport across a network of chromophore-containing proteins. Thermal fluctuations of these proteins lead to changes in the intermolecular interactions that drive energy transport. Despite this variation, high efficiency of transport is maintained. Both the extent to which the dynamics of energy transport vary and how the efficiency is robust to variation remain unclear. Previous measurements either lacked the temporal resolution required or the sensitivity to measure individual proteins, and thus averaged over the fluctuations. Here, we describe a new experiment, single-molecule pump-probe (SM2P) spectroscopy, that measures excited-state dynamics with femtosecond time resolution in single proteins. We demonstrate the power of this technique on cyanobacterial light-harvesting subunits. Our experiments reveal heterogeneous timescales of vibrational relaxation, yet a narrow distribution of energy transfer timescales. These results suggest the protein design serves to tightly regulate energy transfer despite fluctuations of its structure.

Causes and consequences of rapid cancer cell adaptation to therapeutic drugs

Sabrina Spencer, PhD

Despite the increasing number of effective anti-cancer therapies, successful treatment is limited by the development of drug resistance. While the contribution of genetic factors to drug resistance is undeniable, little is known about how drug -sensitive cells first evade drug action to proliferate in drug. Using our new cell-tracking pipeline called EllipTrack, we tracked the response of thousands of single melanoma cells to BRAF inhibitors and show that a subset of cells escapes drug within the first 3 days of treatment. These escapees cycle periodically in drug and out-proliferate non-escapees over extended treatment. Cell-cycle re-entry occurs via a nongenetic mechanism involving activation of ATF4, validated in ex vivo cultures of patient biopsies. Furthermore, escapees experience incomplete licensing of replication origins, leading to heightened DNA replication stress and DNA damage. Our work reveals a mutagenesis-prone, expanding subpopulation of early drug escapees that may represent a reservoir for the development of permanent drug resistance.

Mechanistic basis for the evolution of eukaryotic specialized metabolism

Jing-Ke Weng, PhD

Primary metabolism supports essential chemical processes of living organisms, and is highly conserved among all life forms. In contrast, specialized metabolism contributes to the fitness of its host in specific abiotic and biotic environments, and distributes taxonomically along the evolving tree of life. We seek to understand how complex specialized metabolites are biosynthesized through an assembly line of specialized enzymes, why these specialized metabolic traits are relevant to their hosts under ecological niches, and how these complex pathways could have evolved in a Darwinian fashion. Exploration of the largely untapped eukaryotic specialized metabolic systems not only will advance our understanding of the chemistry of life processes, but also will empower synthetic biologists to engineer microbial production of those high-value natural products of eukaryotic origin in the near future.

Probing (intracellular) physicochemical environments at the nanometer scale, one molecule at a time

Ke Xu, PhD

Recent advances in super-resolution fluorescence microscopy based on single-molecule imaging have led to ~10 nm spatial resolution and exciting science. We are developing new approaches to advance beyond the structural (shape) information offered by existing super-resolution methods, and reveal multidimensional information of intracellular functional parameters, including chemical polarity, diffusivity, and reactivity, with nanoscale resolution and single-molecule sensitivity. To this end, we have been developing new strategies to perform high-throughput, multidimensional single-molecule spectroscopy in the wide-field. In particular, with spectrally resolved SMLM, we encoded functional parameters into the emission spectra of single probe molecules, and so unveiled rich, nanoscale functional and compositional heterogeneities in the membranes of live mammalian cells and in phase-separated surface processes. With single-molecule displacement/diffusivity mapping (SMdM), we mapped out intracellular diffusivity with unprecedented spatial resolution and fidelity, and hence discovered that diffusion in the mammalian cytoplasm and nucleus are both spatially heterogeneous at the nanoscale, and identified the net charge of the diffuser as a previously overlooked, key determinant of diffusion rate. By adding remarkably rich functional dimensions to the already powerful super-resolution microscopy, we thus open up new ways to reveal fascinating local heterogeneities in both live cells and chemical systems.

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CubeSat Presentation

Irvine CubeSat STEM Program

Jonathon Bower, Sarina Doshi, Eric Ho, Kaylee Kim

The Irvine CubeSat STEM Program (ICSP) is a collaboration between Irvine Public Schools Foundation, and Irvine and Tustin Unified school districts that provides teams of students from all six high schools in the City of Irvine the opportunity to assemble, test, and launch a nano-satellite (CubeSat) into low Earth orbit. The program aims to change the way students experience STEM education and inspire the next generation of innovative thinkers, makers, programmers, and explorers. Teams work on different components of the satellite to gain advanced hands-on STEM experience, with mentorship from experts from JPL, NASA, and other industry leaders, before coming together to assemble the final project for launch. Last year, ICSP had two successful launches, making history as the first program to launch two all high school student-built CubeSat's into orbit in less than a year. The program aims to make STEM careers more accessible, especially to underrepresented groups including females and minorities. ICSP offers students the incredible opportunity to gain hands-on, real-world experience that will prepare them for success in college and beyond.

Bio-Chem Presentations—Beckman Young Investigators

Neuromechanics of Locomotor Transitions on Energy Landscapes of Complex Terrain

Chen Li, PhD

Effective locomotion in nature happens by transitioning between multiple modes (e.g., walk, run, climb, slither). Despite this, far more mechanistic understanding of terrestrial locomotion has been on how to generate and stabilize around near-steady-state movement in a single mode. Unlike flight and swimming with aero- and hydrodynamics, a major challenge in understanding terrestrial locomotor transitions is the lack of methods to measure and model how animals actively make use of physical interaction with complex terrain. As a result, robots cannot robustly traverse complex terrain, an ability required for critical applications like search and rescue in earthquake rubble and extraterrestrial exploration over Martian rocks. Our BYI work focuses on using an energy landscape approach to elucidate principles of terrestrial locomotor transitions via integration of biomechanics, sensorimotor control, and terrain physics. Recently, we discovered that an energy landscape approach helps understand probabilistic locomotor transitions. In complex terrain, animals' and robots' locomotor modes are attracted to basins of a potential energy landscape. We have been developing new methods to enable experiments and modeling of how animals and robots actively cross potential energy barriers and hop between basins to make locomotor transitions. These include: (1) terrain platforms and tracking techniques to quantify animal locomotor transitions and terrain interaction, (2) robots with animal-like motion as physical models, and (3) force sensors to measure physical interaction and understand provide feedback control. I will highlight two recent discoveries enabled by these tools: to make locomotor transitions and traverse complex terrain, (1) legged insects actively adjust head, body, and appendages to lower potential energy barriers; (2) besides vision, limbless snakes must use mechanical sensing to adjust body form and control terrain contact to maintain propulsion and stability.

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Bio-Chem Presentations—Beckman Young Investigators

Engineering electroautotrophy

Michaela TerAvest, PhD

My lab is developing a bacterial strain that will catalyze the conversion of carbon dioxide to fuels and products using electrons from an electrode as the sole source of reducing power. This process would represent a new form of metabolism – electroautotrophy. Our platform for developing an electroautotrophic strain is Shewanella oneidensis, a metal-reducing bacterium that already possesses the capacity to exchange electrons with extracellular electrodes. The first key challenge in this project is to create an efficient pathway for electron flow from the electrode to intracellular electron carriers. This requires reversing the direction of electron flow through the native extracellular electron transfer pathway in S. oneidensis. We have demonstrated proof-of-concept for the inward electron transfer pathway by engineering S. oneidensis to catalyze the intracellular reduction of acetoin to 2,3-butanediol using an electrode as the electron source. We are currently working to improve flux through the inward electron transfer pathway by over-expressing the essential components. The second key challenge is to transplant a carbon fixation pathway into S. oneidensis, which is a heterotroph. We have expressed the missing components of the Calvin-Benson-Bassham cycle for carbon fixation in S. oneidensis and are currently working to functionalize the pathway through adaptive laboratory evolution. Moving forward, we will combine the modifications required for inward electron transfer and for carbon fixation to create the electroautotrophic strain.

A novel superconducting family by design: how can we make superconductivity and magnetism coexist in one material?

WeiWei Xie, PhD

In the battle between magnetism and superconductivity, magnetism wins so often that only a handful of magnetic superconductors are known. In this context, here we report our characterization of YbxPt5P, - providing experimental evidence for the possible coexistence of both magnetism and superconductivity in this material. Comparison of samples with different Yb stoichiometry shows that the relative strengths of magnetism and superconductivity can be tuned. The likely coexistence and tunability of such strongly competing electronic states, along with the presence of strong spin orbit coupling due to the large amount of Pt present, makes YbxPt5P a remarkable material and opens the door to a new family of magnetic superconductors.

Liquid phase Peak Force Infrared Microscopy: Super-resolution Infrared Microscopy in the Aqueous Phase

Xiaoji Xu, PhD

Infrared spectroscopy and microscopy directly couples to molecular functional groups, providing chemical information without extrinsic labels. However, conventional infrared spectroscopy and microscopy have two main limitations: lack of spatial resolution due to Abbe's diffraction limit, and restriction of applications in the aqueous conditions due to strong infrared attenuation. On the other hand, many meaningful biological processes and chemical transformation happen in the liquid phase. The understanding of them requires insights from the nanoscale. With the support from Beckman Foundation, we have developed the liquid-phase peak force infrared (LiPFIR) microscopy to deliver both label-free super spatial resolution at 10 nm and compatibility with liquid-phase measurement. We have demonstrated the method on a range of samples, from tracking the surface re-organization of polymers in organic solvent, hydrogen-deuterium isotope exchange and ethanol-induced denaturation of proteins, to imaging of cellular structures in aqueous phases. The LiPFIR microscopy bypasses the two limitations of infrared spectroscopy and microscopy. It will enable label-free spectroscopic investigations of chemical reactions and biomolecular transformations from the tens of nanometer scale.

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Bio-Chem Presentations—Arnold O. Beckman Postdoctoral Fellows

SPARC - A method to genetically manipulate precise proportions of cells

Jesse Isaacman-Beck, PhD

Many experimental approaches rely on controlling gene expression in select subsets of cells within an individual animal. However, reproducibly targeting transgene expression to specific fractions of a genetically defined cell type is challenging. We developed Sparse Predictive Activity through Recombinase Competition (SPARC), a generalizable toolkit that can express any effector in precise proportions of post-mitotic cells in Drosophila. Using this approach, we demonstrate targeted expression of many effectors in several cell types and apply these tools to calcium imaging of individual neurons, optogenetic manipulation of sparse cell populations in vivo, and genomic profiling of mutant and control neuronal subtypes harvested from the same animals.

From biochemical nanosensors to imaging to informatics to COVID-19 convalescent plasma – developing diagnostics and therapies for clinical medicine

Freddy Nguyen, MD/PhD

Current cancer management follows a multipronged approach that include surgery, radiation, and chemotherapy. There is a pressing need for a platform technology to provide precision chemotherapy screening, drug delivery detection, and real-time therapy efficacy monitoring. We have developed single walled carbon nanotube (SWNT) sensors for the detection of chemotherapeutics, more recently for temozolomide (TMZ) and its byproduct 5-Amino-4-imidazolecarboxamide (AIC) with sensitivity at 5-500 μM and in vitro viability up to 7 days in TMZ treated glioblastoma cells. Sensors for irinotecan, cisplatin, and lomustine were developed with sensitivities at 50 μM. H2O2 sensors were used to measure the therapy efficacy of gemcitabine and irinotecan in pancreatic ductal adenocarcinoma in vitro and in vivo. Multiplexing these sensors could yield insights into delivery, diffusion, metabolism, and efficacy of chemotherapeutics in hours or days. Other strategies are being developed such as ratiometric approaches and wavelength-induced frequency filtering to improve performance and sensitivity. A fiber optic platform was developed as a minimally invasive form factor to integrate the sensor hydrogel, optical waveguide, and detection system.

Copper Hydride Catalysis for the Synthesis of Axially Chiral Allenes

Liela Romero, PhD

Allenes, compounds containing two double bonds across three contiguous carbons, are versatile synthetic intermediates due to their substituent loading capacity and ability to generate one or more new stereogenic centers through axial-to-central chirality transfer. This structural motif is also present in over 150 natural products and a variety of bioactive molecules. Despite their prevalence and distinct reactivity, catalytic methods to access chiral 1,3-disubstituted allenes with high levels of selectivity from achiral starting materials remains a goal in chemical synthesis. We have developed a mild and general strategy for the highly selective semi-reduction of prochiral 1,3-enynes. A diverse array of enantioenriched 1,3-disubstituted allenes are furnished in up to 98% yield and 99% enantioenrichment. This reaction is enabled by chiral copper hydride catalysts in the presence of water as a benign and abundant proton source. Additional applications of this method further illustrate the advantage of this simple protocol for the selective synthesis of mono-deuterated allenes and chiral 2,5-dihydropyrroles.

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Bio-Chem Presentations—Arnold O. Beckman Postdoctoral Fellows

Tracking Genome Dynamics in Time and Space

Massa Shoura, PhD

Extrachromosomal circular DNA (eccDNA) comprises products of genomic recombination that cause somatic changes in gene length and sequence. These circular molecules are derived from canonical linear chromosomal loci, expanding the diversity in coding and regulatory capacity within eukaryotic genomes and transcriptomes. Using a brand-new multidisciplinary approach to investigate eccDNA-mediated allelic diversity, I have identified various coding regions of eccDNA biogenesis, such as Titin and Mucin loci. In order to systematically investigate the biological implications and mechanisms of eccDNA formation, this project will focus on Titin eccDNAs as a prototype for eccDNA-mediated chromosomal rearrangements. Titin (TTN) is an extremely large protein that is responsible for the passive elasticity of muscle, functioning as a molecular spring. This single gene (TTN) is expressed in various isoforms, each with its own associated "spring constant." It has been assumed that Titin protein diversity results from complex mechanisms dependent on alternative RNA splicing. However, there is thus far no comprehensive alternative-RNA-splicing framework that accounts for the full spectrum of TTN diversity. Preliminary data obtained in the past years of support suggest a novel mechanism of TTN diversity involving circular-DNA excision that generates recombinant TTN loci at the genomic level. Here, I report TTN-eccDNA formation as a potential mechanism for modulating overall myofibrillar passive tension. Results from investigating this novel mechanism for the modulation of cardiovascular stiffness will revolutionize basic, clinical, and therapeutic approaches to cardiovascular diseases. The AOB Award has been instrumental in advancing the field of eccDNA, in general, and in providing a missing key element in DCM biology, consideration of which may drive a reevaluation of current therapies.

Bio-Chem Presentations—Beckman Scholars Program

Carbon dioxide utilization in plastic production: Development of a nickel catalyst

Vennela Mannava

Carbon dioxide emissions, known to exacerbate climate change, have been increasing rapidly over the past century. One strategy to alleviate this issue is carbon capture and utilization (CCU), in which some of the abundant atmospheric CO_2 is used as a carbon source for the production of valuable compounds. An attractive target is sodium acrylate, the building block of superabsorbent sodium polyacrylate found in hygiene products and many other common goods. Currently, sodium acrylate is synthesized by sequential oxidations of propylene over heterogeneous catalysts at high temperatures. Researchers have instead sought a one-step process coupling CO_2 and ethylene, which is more sustainable and uses much less expensive starting materials. This method could consume a large quantity of atmospheric CO_2. However, coupling with ethylene is not spontaneous. Homogeneous nickel catalysts have shown great promise for enabling this reaction, but the reported systems suffer from low efficiency. The main obstacle is a very stable nickelalactone intermediate, which contains a rigid Ni–pre-acrylate ring that resists the release of free sodium acrylate from the catalyst. My project aims to develop nickel complexes which include an N-heterocyclic carbene (NHC) in a supporting bidentate ligand. The characteristic strong electron donation and steric imposition of NHCs are expected to destabilize nickelalactones and to promote ring-opening, thereby enabling efficient catalytic production of sodium acrylate. Initial results support the instability of a simple bis(NHC) nickelalactone, and experiments testing sodium acrylate production are underway. Computational investigation of NHC-containing ligands with varying electronic and steric effects also helps to elucidate their capability to support the target reaction. This family of ligands could be the key to efficient nickel catalysts coupling CO_2 and ethylene for sodium acrylate production, thus contributing to global CCU efforts.

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Bio-Chem Presentations—Beckman Scholars Program

ShadowAuxin: Optimization of Quenching FRET Pairs for a Fluorescent Auxin Biosensor

Silas Miller

Auxin is a hormone crucial in nearly every aspect of plant growth and development. Advancing our understanding of auxin signaling in maize and other crop plants may provide needed tools for agricultural scientists to help feed a growing population in the face of global climate change. However, existing tools for detecting and measuring auxin level and location have significant shortcomings that can limit their utility in plants. We are working to build and test a novel auxin biosensor, ShadowAuxin, capable of accurate quantification and tracking of auxin in live plants. Our biosensor design relies on the dimerization of two fluorescent proteins (a donor and an acceptor) capable of Förster Resonance Energy Transfer (FRET) when in close proximity. Our biosensor utilizes a quenching fluorescent protein acceptor in the FRET pair; when this pair are held in close proximity by fused dimerization domains, the donor fluorescent signal should dim. Pilot experiments in yeast cells have shown that quenching FRET can be measured via fluorescence flow cytometry, and have revealed the importance of dimer-domain choice and carefully controlled protein expression level. A new pair of human-hormone inducible promoters has enabled us to precisely control the expression level of donor and acceptor proteins in order to maximize FRET quenching. This system allowed observation of quenching FRET without significant cellular toxicity; however we observed a maximum of only 12.9% decrease in fluorescent signal. This is likely due to off-target dimerization and imperfect intracellular stoichiometry of the fluorescent proteins. Therefore, current and future experiments focus on increasing FRET efficiency by adjusting promoter strength and testing new sets of heterodimerization domains. Ultimately, this quenching FRET system will be coupled to an auxin-sensing domain to generate a biosensor that relies on single-color fluorescence measurements and provides rapid response and wide dynamic range.

More Exquisitely Adapted Species Have Higher Structural Disorder in Vertebrate Protein Domains

Catherine Weibel

Protein structural disorder helps avoid misfolding and aggregation, but in impeding protein folding might also impede function. The balance between these two selective pressures on protein biophysics might vary among species as a function of the effectiveness of weak selection. We predicted the Intrinsic Structural Disorder (ISD) of Pfam domains across 118 fully-sequenced vertebrate species and estimated the effect of species identity on to control for differences in Pfam composition across species. We compared this to each species' Codon Adaptation Index of Species (CAIS), a metric we developed to quantify for effectiveness of selection from synonymous codon usage, corrected for total genomic GC content and amino acid composition, to be comparable across species. Simple correlations between ISD and CAIS indicate that well-adapted species tend to have high ISD (Spearman's $R = 0.67$, $p < 2e\text{-}16$). To correct for phylogenetic confounding and resulting pseudoreplication, we transformed CAIS and ISD species effect data using Phylogenetic Independent Contrasts (PIC). Phylogenetically controlled linear models confirmed that better-adapted species have higher ISD (Spearman's $R = 0.43$, $p = 1.2e\text{-}7$). This relationship is conserved across protein domains dated older than 2.1 Gya and protein domains dated younger than 1.5 Gya, though the relationship is stronger in recent domains than in ancient. This indicates selection for higher disorder, with the greater benefit to more recently emerged vertebrate protein domains.

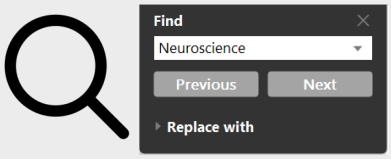
Prevalence and reactivity of fused-rubredoxin AlkBs

Shoshana Williams

Over 100 distinct alkane monooxygenase (AlkB) enzymes containing a covalently bound, or fused, rubredoxin domain were identified and analyzed using bioinformatic techniques. One such protein was cloned as a full-length protein and truncated with its rubredoxin domain deleted. Its catalytic activity was evaluated, and its interaction with exogenous electron transfer partners was examined. These experiments shed light on the diversity of AlkB structure and reactivity, and the interaction of AlkBs with electron transfer partners.

POSTERS

Following are poster abstracts from our 115 poster authors at the virtual 2020 Beckman Symposium. **All posters can be found in the Poster Hall.** This year, we invited our poster authors to present a landscape pdf of their poster and also gave them the option of including a mp4 audio summary.



Want to look at a specific group of posters, like those on Neuroscience, Synthetic Chemistry, Atmospheric Science, or other? Click the magnifying glass icon at the top of your pdf. When the FIND screen appears, type in your search criteria and click next to find and view them quickly.

In the Poster Hall you can view all of the posters as a group or you can search by category. The three categories are:

Posters Authored by Beckman Young Investigators

Posters Authored by Arnold O. Beckman Postdoctoral Fellows

Posters Authored by Beckman Scholars

BY THE NUMBERS

37 BYI POSTERS

22 POSTDOC POSTERS

BIOLOGY POSTERS **50.4%**

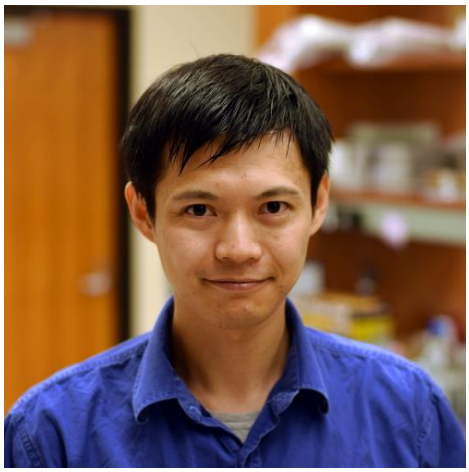
CHEMISTRY POSTERS **49.6%**

56 BSP POSTERS

53% MALE POSTER AUTHORS

47% FEMALE POSTER AUTHORS

Yiyang Gong, PhD
2016 Beckman Young Investigator
Biology (Neuroscience)
Duke University



Microscopy and data processing components of an optical brain machine interface

Genetically encoded fluorescent indicators and microscopy help understand brain function by generating large-scale in vivo recordings in multiple animal models. Further development of the optical and data processing tools will improve the ability of neuroscientists to quickly and accurately record and understand the imaging results. For optical microscopy, we demonstrate two novel imaging modalities for fast volumetric recording of neural activity. First, we demonstrate a hybrid light-sheet light-field microscope that improves the contrast of volumetric light-field imaging. Second, we demonstrate a new oblique light-sheet microscope configuration that increases the capture efficiency of fluorescence emission. For data processing, we developed and characterized a novel deep learning method to quickly and accurately segment active neurons from two-photon fluorescence imaging videos. These methods are more accurate and an order-of-magnitude faster than existing methods when operating on a single desktop computer.

Markita Landry, PhD
2016 Beckman Young Investigator
Biology (Neuroscience)
University of California, Berkeley

Imaging Striatal Dopamine Release Using a Non-Genetically Encoded Near-Infrared Catecholamine Nanosensor

Neurotransmission – chemical communication of neurons in the brain – plays a critical role in brain function. Neuromodulators such as dopamine are thought to signal across broader spatial regions than classical neurotransmitters, and aberrations in their signaling are implicated in psychiatric and neurodegenerative disorders including depression, addiction, and Parkinson's disease. Until recently, measuring the dynamics of dopamine and other neuromodulators could not be achieved at spatiotemporal resolutions necessary to understand how neuromodulators regulate the function of neural circuits, and how dysfunctions in this regulation lead to disease. We have developed probes that can image neuromodulators in the brain with high spatiotemporal resolution. We first describe the synthesis and implementation of a nanoscale dopamine probe constructed from single wall carbon nanotubes (SWNT) non-covalently functionalized with (GT)6 oligonucleotides. We demonstrate this probe enables imaging of dopamine dynamics in striatal brain tissue and has uncovered endogenous variability in neurochemical responses to dopamine agonist or antagonist drugs. We anticipate this probe and others of its class will enable synaptic-scale inquiries of the role of neuromodulators in brain health and disease.

Zachary Pincus, PhD
2016 Beckman Young Investigator
Biology (Evolution & Population Biology)
Washington University, St. Louis

Systematic, organism-wide gene regulation drives individual lifespan in C. elegans

Why do some individuals live longer than others? Even identical twins have different lifespans, as do genetically identical model organisms raised in controlled laboratory environments. What then accounts for these differences? Random accumulation of damage, sudden exogenous insults, or internal biological processes that somehow diverge? We find strong evidence for the latter.

Using the nematode C. elegans, we find that prospectively long- vs. short-lived individuals are highly divergent in terms of gene regulation. Fully half of a library of promoter::GFP gene-expression reporters can effectively predict future lifespan. Moreover, these reporters represent diverse spatial and temporal expression patterns, suggesting that the regulatory states underlying long and short life are not specific to a particular tissue or a single regulatory process. Long- vs. short-lived individuals exhibit widespread, systematic, and organism-wide differences in gene regulation, well in advance of mortality.

Gabriela Schlau-Cohen, PhD
2016 Beckman Young Investigator
Chemistry (Biochemistry)
Massachusetts Institute of Technology

Heterogeneous ultrafast dynamics in photosynthetic proteins

In photosynthesis, solar energy capture to conversion occurs with a remarkable near-unity quantum efficiency through energy transport across a network of chromophore containing proteins. Thermal fluctuations of these proteins lead to changes in the intermolecular interactions that drive energy transport. Despite this variation, high efficiency of transport is maintained. Both the extent to which the dynamics of energy transport vary and how the efficiency is robust to variation remain unclear. Previous measurements either lacked the temporal resolution required or the sensitivity to measure individual proteins, and thus averaged over the fluctuations. Here, we describe a new experiment, single-molecule pump-probe (SM2P), that measures excited-state dynamics with femtosecond time resolution in single proteins. We demonstrate the power of this technique on cyanobacterial light-harvesting subunits. Our experiments reveal heterogeneous timescales of vibrational relaxation, yet a narrow distribution of energy transfer timescales. These results suggest the protein design serves to tightly regulate energy transfer despite fluctuations of its structure.

Sabrina Spencer, PhD
2016 Beckman Young Investigator
Chemistry (Biochemistry)
University of Colorado, Boulder

Melanoma subpopulations that rapidly escape MAPK pathway inhibition rely on stress signalling and incur DNA damage

Despite the increasing number of effective anti-cancer therapies, successful treatment is limited by the development of drug resistance. While the contribution of genetic factors to drug resistance is undeniable, little is known about how drug-sensitive cells first evade drug action to proliferate in drug. Here we track the response of thousands of single melanoma cells to BRAF inhibitors and show that a subset of cells escapes drug within the first 3 days of treatment. These escapees cycle periodically in drug and out-proliferate non-escapees over extended treatment. Cell-cycle re-entry occurs via a nongenetic mechanism involving activation of mTORC1 and ATF4, validated in ex vivo cultures of patient biopsies. Furthermore, escapees experience incomplete licensing of replication origins, leading to heightened DNA replication stress and DNA damage. Our work reveals a mutagenesis-prone, expanding subpopulation of early drug escapees that may represent a reservoir for the development of permanent drug resistance.

Jing-Ke Weng, PhD
2016 Beckman Young Investigator
Biology (Genetics)
Whitehead Institute for Biomedical Research

The chloroalkaloid (-)-acutumine is biosynthesized via a Fe(II)- and 2-oxoglutarate-dependent halogenase in Menispermaceae plants

Colin Y Kim, Andrew J Mitchell, Christopher M Glinkerman, Fu-Shuang Li, Tomáš Pluskal, Jing-Ke Weng

Plant halogenated natural products are rare and harbor various interesting bioactivities, yet the biochemical basis for the involved halogenation chemistry is unknown. While a handful of Fe(II)- and 2-oxoglutarate-dependent halogenases (2ODHs) have been found to catalyze regioselective halogenation of unactivated C-H bonds in bacteria, they remain uncharacterized in the plant kingdom. Here, we report the discovery of dechloroacutumine halogenase (DAH) from Menispermaceae plants known to produce the tetracyclic chloroalkaloid (-)-acutumine. DAH is a 2ODH of plant origin and catalyzes the terminal chlorination step in the biosynthesis of (-)-acutumine. Phylogenetic analyses reveal that DAH evolved independently in Menispermaceae plants and in bacteria, illustrating an exemplary case of parallel evolution in specialized metabolism across domains of life. We show that at the presence of azide anion, DAH also exhibits promiscuous azidation activity against dechloroacutumine. This study opens avenues for expanding plant chemodiversity through halogenation and azidation biochemistry.

Ke Xu, PhD
2016 Beckman Young Investigator
Chemistry (Instrumentation Development)
University of California, Berkeley

Probing intracellular physiochemical environments at the nanometer scale, one molecule at a time

We are developing new optical microscopy approaches to reveal multidimensional information of intracellular physicochemical parameters, including chemical polarity, diffusivity, and reactivity, with nanoscale resolution and single-molecule sensitivity. To this end, we have been developing new strategies to perform multidimensional single-molecule spectroscopy with ultrahigh throughput. In particular, with spectrally resolved single-molecule localization microscopy, we encoded functional parameters into the emission spectra of single probe molecules, and so unveiled rich, nanoscale functional and compositional heterogeneities in the membranes of live mammalian cells and in phase-separated surface processes. With single-molecule displacement/diffusivity mapping (SM*d*M), we mapped out intracellular diffusivity with unprecedented spatial resolution and fidelity, and hence discovered that diffusion in the mammalian cytoplasm and nucleus are both spatially heterogeneous at the nanoscale, and identified the net charge of the diffuser as a previously overlooked, key determinant of diffusion rate. By adding remarkably rich *functional* dimensions to the already powerful super-resolution microscopy, we thus open up new ways to reveal fascinating local heterogeneities in both live cells and chemical systems.

Jeremy Baskin, PhD
2017 Beckman Young Investigator
Chemistry (Biochemistry)
Cornell University

Synthetic Lipid Biology: Membrane Engineering via Controlled Phospholipid Synthesis in Vivo

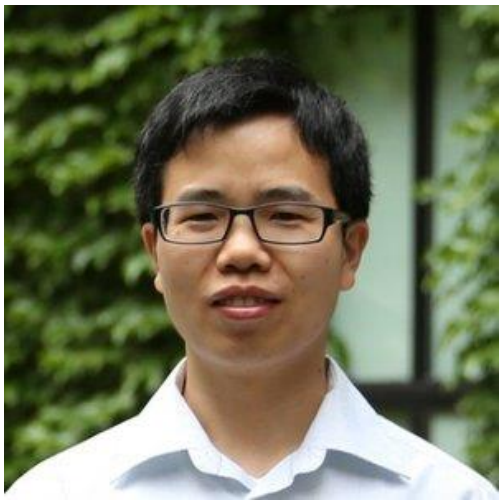
Phosphatidic acid (PA) is both a central phospholipid biosynthetic intermediate and a multifunctional lipid second messenger produced at several discrete subcellular locations. The modes of action of PA can differ based on stimulus, biosynthetic source, and site of production. How cells regulate local production of PA to direct diverse signaling outcomes remains elusive. To unravel these questions, we have focused our efforts on improving and expanding the toolkit for both visualizing and perturbing cellular PA production, with spatiotemporal precision. Toward the first goal, we have harnessed the exquisite selectivity of chemoenzymatic labeling and click chemistry tagging to develop a method for directly visualizing PA production by phospholipase D (PLD) enzymes. This method, termed IMPACT, has revealed sites of PLD-mediated PA signaling elicited by diverse physiological stimuli and features subcellular, organelle-level resolution. To complement these visualization tools, we have also generated a suite of light-controllable, optogenetic PLDs to generate tunable amounts of PA on specific organelles. Collectively, these approaches represent powerful approaches for revealing spatiotemporally defined functions of PA in response to physiological and pathological stimuli.

Pamela Chang, PhD
2017 Beckman Young Investigator
Biology (Immunology, Virology & Infectious Disease)
Cornell University

Chemical Technologies for Elucidating and Controlling Inflammation

Inflammation is a vital physiological process in infection and tissue repair after injury, but uncontrolled, chronic inflammation caused by overactivation of immune cells occurs in many diseases. Current anti-inflammatory drugs are delivered systemically and cause off-target effects in otherwise healthy tissues, and thus, there is a great demand for next-generation technologies to locally inhibit activation of the immune system to limit these side effects. We aim to develop precision chemical tools to inhibit local inflammation by modulating the functions of select target populations of immune cells and apply these tools to both study fundamental biological mechanisms of inflammatory pathways and control the immune response in therapeutic settings.

Dan Fu, PhD
2017 Beckman Young Investigator
Chemistry (Biochemistry)
University of Washington



Cell Phenotyping and microenvironmental imaging with a multimodal microscope

Biological systems are highly complex due to the intricate spatial organizations of different types of cells, the intrinsic heterogeneity of living cells, and the intimate interaction of cells with their microenvironment. Characterizing the phenotypic behavior of single cells within their native microenvironment is critically important in revealing the underlying pathophysiologic processes of various complex diseases such as cancer and neurodegenerative diseases. We aim to develop a new quantitative imaging platform that integrated multiple nonlinear optical imaging modalities for simultaneous, multiparametric imaging of cellular and microenvironmental features from living cells and animals. Specifically, we use intrinsic molecular contrasts from biomolecules to measure fundamental single cell properties such as size, density, metabolic activity, and growth. When augmented with deep learning, we can further improve feature extraction to generate organelle specific information. Together with cell specific labeling, we further demonstrate that we can image a multitude of cell and microenvironmental features within live mouse brain. These new imaging capabilities will help us tackle unknown questions in tissue development, cancer growth, and drug resistance.

Erik Grumstrup, PhD
2017 Beckman Young Investigator
Chemistry (Imaging & Spectroscopy)
Montana State University

Establishing Nanoscale Structure-Function Relations through Correlative Microscopy

Casey L. Hickey, Geoffrey Piland, Erik M. Grumstrup

Department of Chemistry and Biochemistry,
Montana State University, Bozeman MT

Although solution processing methods provide an attractive route toward development of low-cost functional materials, these accessible fabrication approaches can engender high concentrations of microscopic structural defects that are detrimental to performance. In lead halide perovskites, structural disorder derived from solution processing has been implicated as an important determiner of photophysical properties. However, a direct correlation between the functional properties of these materials and the local crystal structure in which non-equilibrium states evolve has remained elusive, in part because structural heterogeneities occur on length scales that defy conventional characterization techniques. To address this knowledge gap, we have combined ultrafast pump-probe microscopy and electron backscattering diffraction to directly correlate charge carrier transport with the local diffraction pattern contrast, an indicator of crystal quality. Spatial correlation of these measurements strongly suggests that even on individual single crystal $CsPbBr_3$ domains, microscopic variability in the crystal quality profoundly impacts the efficiency of charge carrier transport.

Jose Rodriguez, PhD
2017 Beckman Young Investigator
Chemistry (Imaging & Spectroscopy)
University of California, Los Angeles

Towards ab initio fragment-based determination of protein structures from MicroED data

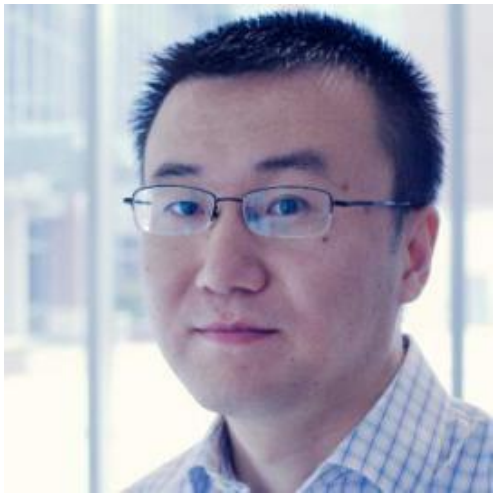
Structure determination of novel biological macromolecules by X-ray crystallography can be facilitated by the use of small structural fragments, some only a few residues long, as effective search models for molecular replacement to overcome the phase problem. We investigate the use of fragment-based methods to overcome the phase problem with the electron cryomicroscopy (cryoEM) method known as microcrystal electron diffraction (MicroED). Our approach provides phasing solutions for a structure of Proteinase K from 1.6Å data using model fragments derived from structures of proteins sharing sequence identity as low as 20%. The combined set of fragments was sufficient to arrive at a solution that resembled that determined by conventional molecular replacement using the known target structure as a search model. This approach obviates the need for a single, complete and highly accurate search model when phasing MicroED data and permits the evaluation of large fragment libraries for this purpose.

A. Fatih Sarioglu, PhD
2017 Beckman Young Investigator
Biology (Biosensor Development)
Georgia Institute of Technology

All-Electronic Lab-on-a-Chip Platforms for High-Throughput Multi-Modal Cell Phenotyping

Our goal is to develop lab-on-a-chip platforms with integrated electronic readout for high-throughput multi-modal cellular analysis. To achieve this goal, we pursue a highly multidisciplinary approach that combines traditionally distant technical disciplines such as biosensor and microfluidic system design/microfabrication, multiplexing schemes used in telecommunications, and advanced signal processing used in autonomous robotic systems.

Bo Wang, PhD
2017 Beckman Young Investigator
Biology (Evolution & Population Biology)
Stanford University

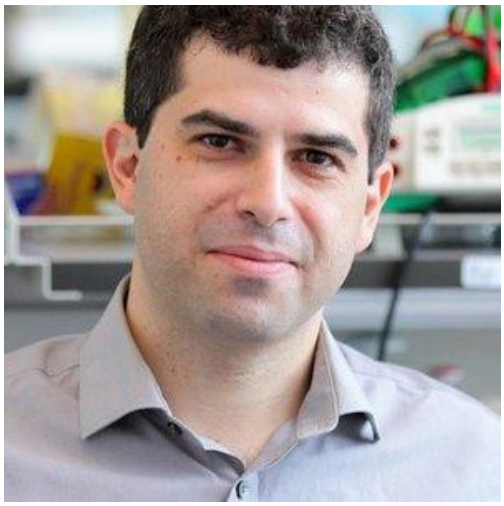


Response to non-self tissues in chimeric planarians causes regeneration defects

Department of Bioengineering, Stanford University

Many animals reproduce asexually through fragmentation followed by regeneration, often using multipotent stem cells that are capable of continually dividing and differentiating to rebuild any missing body parts. This process is susceptible to accumulation of somatic mutations and emergence of cheating cells, which may over-proliferate and propagate across generations, neglecting their duties in making somatic tissues. Despite this obvious risk, it is unknown whether these animals have mechanisms to sense the presence of genetically altered cells, and if so, whether the regeneration process is affected by this response. Planarian flatworms provide a powerful model as they are capable of unparalleled regeneration as well as forming chimeric fusions when tissue fragments are surgically stitched together. We created chimeras comprising distinct *Schmidtea mediterranea* genotypes, and the fused tissue fragments integrated anatomically. However, we amputated the chimeras along the anterior-posterior axis, the tail piece failed to regenerate a new head. This regeneration defect can be rescued by knocking down activin or beta-catenin. Our work reveals the link between allogeneic response and regeneration program and pinpoints the underlying molecular regulators.

Dmitriy Aronov, PhD
2018 Beckman Young Investigator
Biology (Neuroscience)
Columbia University



Memory-related activity in the hippocampus of food-caching birds

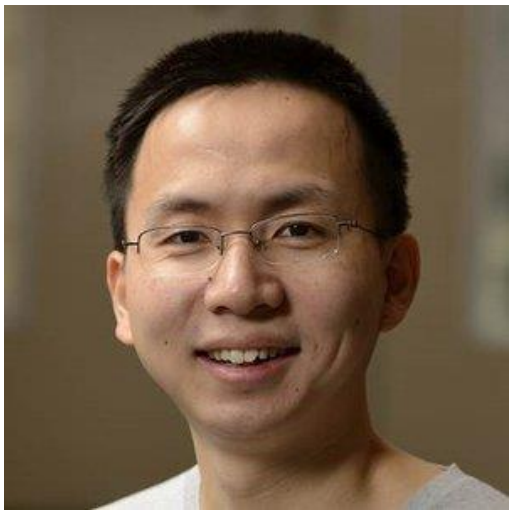
The brain captures snapshots of distinct events, forming “episodic memories” that can last a lifetime. The hippocampus is a brain region critical for this function, yet it is unknown how patterns of hippocampal activity are related to specific memories. We study memory using specialized model organisms – food-caching birds from the chickadee family. Chickadees cache many food items at scattered, hidden locations and use memory to retrieve these caches later in time. We have developed behavioral arenas where birds cache and retrieve food in laboratory settings. We have also adapted miniaturized recording technologies to record from the hippocampus in these birds. I will present the first recordings of hippocampal activity when birds cache and retrieve seeds. We find that hippocampal activity is enhanced during caching. Different subsets of neurons are active during different caching episodes, creating a unique “barcode”-like code for each episode. The same subset is reactivated before the bird retrieves that same seed later. These patterns are consistent with neural representations of unique episodes and may provide a link between hippocampal activity and memory.

Alistair Boettiger, PhD
2018 Beckman Young Investigator
Biology (Developmental Biology)
Stanford University

Beyond enhancer-promoter contact: leveraging deep learning to connect super-resolution DNA traces to transcription

Chromatin architecture plays an important role in gene regulation. Recent advances in super-resolution microscopy have made it possible to measure chromatin 3D structure and transcription in thousands of single cells. However, leveraging these complex datasets with a computationally unbiased method has previously not been achieved. Here, we present a deep learning-based approach to better understand to what degree chromatin structure relates to transcriptional state of individual cells. Furthermore, we explore methods to “unpack the black box” to determine in an unbiased manner which structural features of chromatin regulation are most important. We apply this approach to the Optical Reconstruction of Chromatin Architecture dataset of the bithorax gene cluster in Drosophila melanogaster and show it significantly outperforms previous contact-focused methods. We find the structural information is distributed across the domain, overlapping and extending beyond domains identified by prior genetic analyses. Individual enhancer-promoter interactions are a minor contributor to predictions of activity.

Chen Li, PhD
2018 Beckman Young Investigator
Biology (Engineering)
Johns Hopkins University



Neuromechanics of Locomotor Transitions on Energy Landscapes of Complex Terrain

Effective locomotion in nature happens by transitioning between modes (e.g., walk, run, climb). However, mechanistic understanding of terrestrial locomotion has mainly been on how to generate and stabilize around near-steady-state movement in a single mode. Consequently, robots cannot robustly traverse complex terrain for critical applications like search and rescue. Our research focuses on using an energy landscape approach to elucidate how animals and how robot should make active adjustments to make locomotor transitions. Recently, we discovered that locomotor transitions can be modeled as barrier-crossing transitions on potential energy landscapes. We are developing tools to enable experiments and modeling of locomotor transitions: (1) experimental platforms and techniques to quantify locomotor transitions and active adjustments, (2) robots with animal-like motion as physical models, and (3) force sensors to measure physical interaction during adjustments. We highlight two discoveries enabled by these tools: (1) legged insects actively adjust head, body, and appendages to lower potential energy barriers; (2) besides vision, limbless snakes must use mechanical sensing to adjust body form and control terrain contact to maintain propulsion and stability.

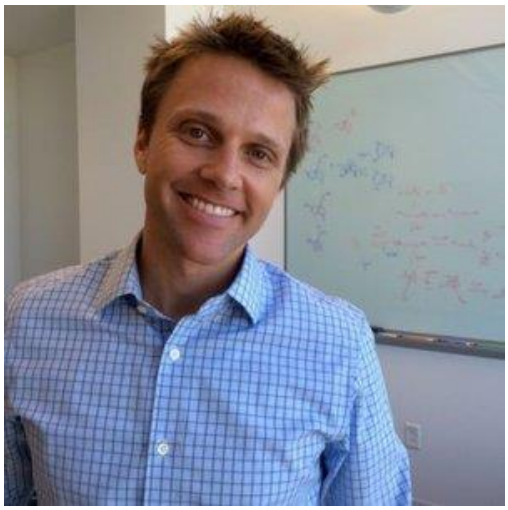
Jean-Hubert Olivier, PhD
2018 Beckman Young Investigator
Chemistry (Organic Chemistry)
University of Miami

Molecular Strategies to Engineer 2D Nanoscale Objects: Toward Organic Piezoelectric Materials

Chuan Liu, Arindam Mukhopadhyay, Brianna Bernard, Jean-Hubert Olivier

The molecular engineering of 2-dimensional nanoscale objects is at the forefront of developing new classes of hybrid semiconducting materials. While the rules and principles to assemble monomeric porphyrin-derived building blocks are well established, the aggregation of larger π- conjugated cores that feature electronically coupled porphyrin arrays has been vastly underexplored. We report the synthesis, spectroscopy, assembly, and solid-state properties of a new class of butadiyne-bridged (porphinato)zinc(II) dimer chromophores. Spectroscopic investigation unravels the formation of aggregates in an aqueous medium, leading to the formation of 2-dimensional objects that expand across microscale dimensions. Analysis of the height profile exploiting atomic force microscopy indicates that one porphyrin dimer comprises the thickness of the solid-state hierarchical superstructure and underscores the promise of this approach to engineer solid-state platforms for (opto)electronic devices. Furthermore, initiation of non-covalent interactions between building blocks by means of a chemical stimulus (pH) reveals that a nucleation-growth process governs the aggregation of the π-conjugated chromophores in an aqueous medium. This work provides new tools to modulate the structure-function relationships of supramolecular architectures equipped with enticing optical properties.

Ian Seiple, PhD
2018 Beckman Young Investigator
Chemistry (Pharmaceutical Chemistry)
University of California, San Francisco



Platforms for the generation of new classes of antibiotics

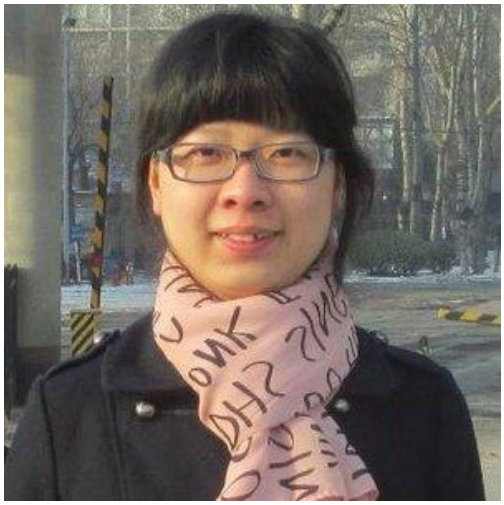
The bacterial ribosome is one of the most prolific targets for antibiotics. Our Beckman work focuses on antibiotics that bind to the bacterial ribosome but have not yet reached their therapeutic potential due to lack of chemistry to modify their structures. It comprises three aims: 1) modular synthesis, 2) synthesis of chimeric antibiotics, and 3) binding-induced hybridization. Each of these three aims centers around a structurally rich and unique class of antibiotics: the pleuromutilin antibiotics. We have initiated a new route to the pleuromutilin core that will enable rapid functionalization of all three rings. We have conducted a screen for synergy among protein synthesis inhibitors, and found that, pleuromutilins exhibit synergistic antibacterial effects with streptogramin antibiotics, and have characterized their binding with CryoEM. Finally, we have synthesized an unprecedented chimeric molecule of an oxazolidinone and macrolide antibiotic.

Michaela TerAvest, PhD
2018 Beckman Young Investigator
Biology (Molecular & Cell Biology)
Michigan State University

A bacterial chassis to convert electricity and carbon dioxide into fuels

My lab is developing a bacterial strain that will catalyze the conversion of carbon dioxide to fuels and products using electrons from an electrode as the sole source of reducing power. This process would represent a new form of metabolism – electroautotrophy. Our platform for developing an electroautotrophic strain is *Shewanella oneidensis*, a metal-reducing bacterium that already possesses the capacity to exchange electrons with extracellular electrodes. A key challenge in this project is to transplant a carbon fixation pathway into *S. oneidensis,* which is a heterotroph. We have expressed the missing components of the Calvin-Benson-Bassham cycle for carbon fixation in *S. oneidensis* and are currently working to functionalize the pathway through adaptive laboratory evolution. Moving forward, we will combine the modifications required for inward electron transfer and for carbon fixation to create the electroautotrophic strain.

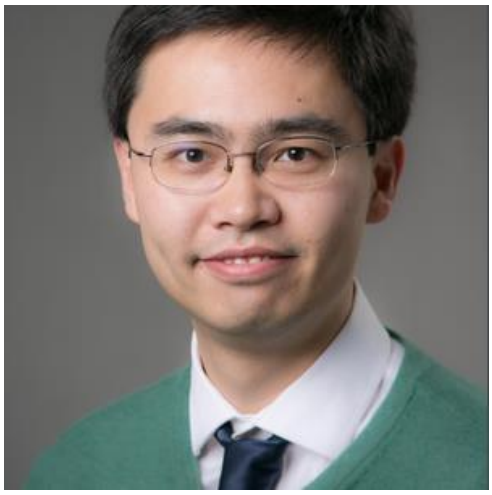
Weiwei Xie, PhD
2018 Beckman Young Investigator
Chemistry (Materials Science & Development)
Louisiana State University



Chemistry Perspectives to New High T_c Superconductors

The interplay between superconductivity and magnetism, only occurring under very restricted conditions, has the potential to lead to exotic new condensed matter physics and quantum devices. The coexistence of superconductivity and magnetism in a single material system is very rare. Recently, we discovered a new material Yb_xPt_5P in tetragonal structure with the space group *P*4/*mmm*. The structure can be considered as the anti-format of heavy-fermion superconductor, $CeCoIn_5$. In $Yb_{0.20(1)}Pt_5P$, we observe a superconducting transition around 0.6 K and a magnetic state near 0.3 K. As increasing the occupancy of Yb, the superconductivity was suppressed in $Yb_{0.96(1)}Pt_5P$. Our new quantum material appears to be a distinct platform for studying the interactions between superconductivity and magnetism, in a material where strong spin-orbit coupling is present.

Xiaoji Xu, PhD
2018 Beckman Young Investigator
Chemistry (Imaging & Spectroscopy)
Lehigh University



Development of Pulsed Force Kelvin Probe Force Microscopy and Integration with Peak Force Infrared Microscopy

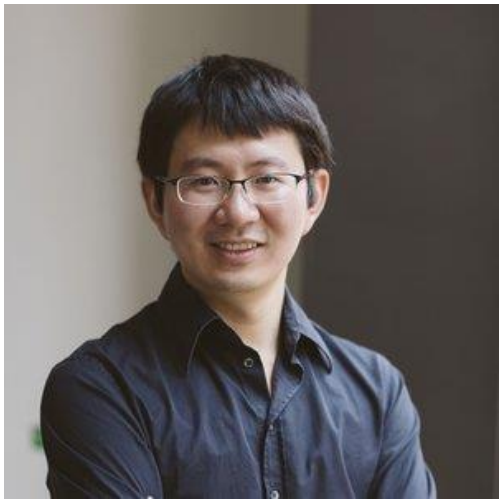
Correlative scanning probe microscopy (SPM) with chemical identity, surface potential, and mechanical properties provides insight into structure-functional relationships of nanomaterials and structures. However, simultaneous measurement with a comparable and high spatial resolution for these modalities remains challenging. In this poster, we first develop the pulsed force Kelvin probe force microscopy (PF-KPFM) for imaging surface potential at 10 nm spatial resolution. Then, we seamlessly integrate nanoscale photothermal infrared imaging with Coulomb force detection of PF-KPFM to form a multimodal SPM mode, the Peak Force Infrared – Kelvin Probe Force Microscopy (PFIR-KPFM). PFIR-KPFM enables simultaneous nano-mapping of infrared absorption, surface potential, and mechanical properties with ~10 nm spatial resolution in one single-pass scan. With its high spatial resolution, the new method allows identification of the ohmic versus Schottky contact between materials. PFIR-KPFM reveals correlations between residual charges and secondary conformation in amyloid fibrils of FapC. PFIR-KPFM is generally applicable to other types of heterogeneous materials at the nanoscale for correlative multimodal characterization at the nanoscale.

Keriann Backus, PhD
2019 Beckman Young Investigator
Biology (Biochemistry)
University of California, Los Angeles

Expanding the Druggable Proteome

Chemical probes are powerful tools for characterizing protein function, which offer the advantages of producing graded effects (both agonism and antagonism) and acute application, features that are well suited to the study of essential genes and post translational processes. Despite their proven utility, most human proteins (>90%) lack selective chemical probes, and entire classes of proteins remain 'undruggable.' Prior chemoproteomics studies have demonstrated that the human proteome contains hundreds and quite possibly even thousands of small molecule-targetable, termed ligandable, cysteine residues. However, what remains unclear is whether and how the attached probes alter protein function. Combining proteomics, genomics, and covalent probes, our research aims to decipher the functions of these numerous ligandable cysteines, and by doing so we will generate a roadmap for the use of covalent probes to study and manipulate protein function. Here we report progress towards a proteogenomic platform to identify functional and druggable acquired cysteine residues as a new approach to develop precision therapies.

Chenfeng Ke, PhD
2019 Beckman Young Investigator
Chemistry (Materials Science & Development)
Dartmouth College



Guided Supramolecular Butterfly Effect Enabled 3D-Printing

We demonstrated a synthetic approach to stabilize a chaotic set of kinetic states of polypseudorotaxanes via a supramolecular butterfly effect, and selectively harness a crop of them through guided crystallization. The high energy molecular structures of these polypseudorotaxanes were amplified to mesoscale as topologically varied crystalline polymer networks, enabling their use as viscoelastic hydrogels for 3D-printing. We showed simultaneous access of two meta-stable states diverged from the same polypseudorotaxanes ink at different printing temperatures, realizing spatial programming of a heterogeneous 3D-printed moisture-responsive actuator. Our approach of introducing chemical entities to tune kinetic and thermodynamic factors in supramolecular architectures will not only enable rapid access of multiple meta-stable materials but also pave a path for the development of polymer materials that operate out-of-equilibrium.

Wesley Legant, PhD
2019 Beckman Young Investigator
Biology (Imaging & Spectroscopy)
University of North Carolina, Chapel Hill

Intelligent Microscopes to Observe and Interact with Dynamic Specimens

Modern microscopes can produce terabytes of highly complex data. However, these instruments are still operated in the same point-and-shoot manner as their counterparts from over 100 years ago. Real-time image analysis and artificial intelligence could fundamentally change how we use these instruments in our work, and allow us to capture rare cellular events, at statistically significant numbers, and at high spatiotemporal resolution. These tools could be combined with targeted photomanipulation to dynamically interact with biological specimens as they change over time. We aim to benckmark these tools by imaging chromosome motion during cell division with the ultimate goal to quantify and control chromosome segregation errors in living cells. Errors in the mitotic process impact nearly all living organisms, ranging from fungi to humans, with immense implications for human health. However, because they require capturing the same cell at multiple stages of the division process, many longstanding and fundamental questions about normal and abnormal cell division can only be answered via high resolution live-cell imaging.

Frank Leibfarth, PhD
2019 Beckman Young Investigator
Chemistry (Materials Science & Development)
University of North Carolina, Chapel Hill

Stereoselective Ionic Polymerizations

The stereochemistry of vinyl polymers, known as polymer tacticity, is intimately linked to their resultant material properties. We have recently designed chiral counterions that systematically bias the reactivity and chain-end stereochemical environment during cationic polymerization. In this Beckman Project, we aim to translate this unique concept to create new classes of stereo-defined plastics that are derived from naturally occurring resources and have a drastically reduced environmental footprint. This presentation will describe three efforts in pursuit of this goal: *i)* Developing an automated synthetic platform for the high throughput screening of reaction conditions; *ii*) Evaluating the use of chiral counterions for the ring-opening polymerization of bioderived lactones; and *iii)* Pursuing initial work toward stereoselective radical polymerization. Each of these pursuits represent important “pieces of the puzzle” toward building the intellectual and experimental capacity to accomplish our goals. The fundamental contributions in the interdisciplinary areas of reaction automation, asymmetric catalysis, and polymer science is anticipated to make a lasting contribution in the field of sustainable polymer chemistry.

Jarad Mason, PhD
2019 Beckman Young Investigator
Chemistry (Inorganic Chemistry)
Harvard University

Increasing the Intrinsic Porosity of Liquids Through Coordination Chemistry

Although coordination chemistry and reticular design principles are routinely applied to control the structure—and porosity—of solids, the application of similar principles to liquids is in its infancy. Conventional liquids contain tiny, transient voids whose fleeting existence is due to thermally induced fluctuations in local density. This transient free volume affects many bulk macroscopic properties—including viscosity, conductivity, and gas solubility—but is difficult to control in a predictable fashion. Directional interactions mediated by coordination bonds between metals and organic bridging organic ligands offer exciting new possibilities for controlling the local structure and transient porosity of liquids. However, even though tens of thousands of metal–organic frameworks have been reported in the literature, there are surprisingly few examples of such compounds with accessible liquid states. The existence of matter in the liquid state requires attractive interactions between constituent species to be sufficiently counteracted by repulsive interactions—imparting fluidity while still maintaining local order. Here, I highlight initial efforts by my laboratory to design, synthesize, and characterize coordination network-forming liquids, emphasizing thermodynamic strategies to lower the melting temperature of three-dimensional metal–organic frameworks and new approaches to probe relationships between transient porosity and gas solubility.

Jia Niu, PhD
2019 Beckman Young Investigator
Chemistry (Synthetic Chemistry)
Boston College

Mechanistic Insight into Visible Light-Mediated Radical Cascade-Triggered Ring-Opening Polymerization

In this presentation, a novel photocatalytic approach to control radical cascade-triggered ring-opening polymerization (RCT-ROP) under visible light irradiation is discussed. Correlation between rate of the polymerization and the reduction potential of the photocatalysts suggested a photoinduced electron transfer mechanism. The ability of the visible light-mediated polymerization to be conducted at room temperature allowed for a mechanistic understanding of the deviation of the first-order kinetics exhibited in the late stage of the polymerization. Experimental and computational studies showed that the sulfur dioxide generated in situ by the cascade process reversibly inhibited radical propagation. The sulfur dioxide inhibition could be effectively eliminated by argon sparging at the elevated temperatures. The visible light-mediated polymerization not only facilitated the mechanistic studies of RCT-ROP, but also provided new strategies to chemically and spatiotemporally control the polymerization.

Kimberly See, PhD
2019 Beckman Young Investigator
Chemistry (Materials Science & Development)
California Institute of Technology

Divalent Ion Conductivity in the Solid-State

Next generation energy storage technology based on divalent working ions will provide safe, more sustainable, and higher capacity batteries. A significant roadblock to their development is a lack of understanding surrounding divalent ion conductivity in the solid-state, a process crucial to the operation of electrodes and solid-state electrolytes. To develop a fundamental understanding of divalent ion conduction, we first target solid-state divalent ion conduction in electronic insulators. We report the first electronically insulating Zn^{2+} conductor, $ZnPS_3$, and discuss the ionic conductivity pathways. Through metal substitution in $ZnPS_3$, we can tune the crystal chemistry and develop structure-property relationships. We report a diverse family of isostructural materials with either isovalent or aliovalent substituents on the Zn site. Additionally, we show that redox activity can be introduced into $ZnPS_3$ via V^{3+} substitution. In parallel, we have devised material and device optimizations to increase the accuracy of measurements and decrease cell-to-cell variability. These results begin to provide fundamental understanding of divalent ion conduction in solids and facilitate the realization of a latticed matched solid state divalent ion battery.

Leslie Schoop, PhD
2019 Beckman Young Investigator
Chemistry (Materials Science & Development)
Princeton University

The Influence of Chemical Bonds on the Electronic Properties of Solids

In the discipline of chemistry, it is common to have guidelines and heuristics that help to predict how chemical reactions will proceed. We are interested to expand these heuristics to understand electronic properties of inorganic solids. In this poster, I will show how delocalized chemical bonds in certain structural networks allow us to define chemical descriptors that predict so-called topological materials, which is a new form of quantum matter, of interest for their exotic electronic and optical properties. I will also show how structural instabilities benefit the electronic structure. By taking advantage of chemical doping and induced electronic instabilities we were able to introduce one of the first “clean” magnetic topological semimetal.

Kirk Wangensteen, PhD
2019 Beckman Young Investigator
Biology (Molecular & Cell Biology)
University of Pennsylvania

Innovative genetic approaches to target MYC-driven cancer

MYC is one of the most prominent oncogenes driving cancer. It becomes active in Hepatocellular carcinoma (HCC), a devastating type of cancer. Unfortunately, no effective drugs can block MYC. Here, we have designed two strategies to target MYC in HCC. **AIM 1 is to discover MYC binding partners that are required for tumorigenesis.** We designed an *in vivo* CRISPR inhibition (CRISPRi) screening system to systematically target MYC partner genes in a model of MYC-driven HCC. We have screened hundreds of genes that physically interact with MYC to identify which ones are necessary for MYC-driven tumorigenesis. We are finding excellent potential drug targets. **AIM 2 is to directly inhibit MYC with peptides.** We have designed a peptide screening approach to disrupt MYC activity, with the potential to translate to a functional activity in live cells. By combing pooled cyclic peptide expression libraries, a barcoded MYC reporter, and high throughput sequencing, we have designed a new pooled functional screening system to identify active peptide inhibitors of MYC. We present our early results with these innovative systems.

Brad Zuchero, PhD
2019 Beckman Young Investigator
Biology (Neuroscience)
Stanford University

IMAGeNs: genetically encoded tools for determining the role of myelin in brain circuits

Human perception, thought, and memory are all made possible by the activity and connections between the 100 billion neurons in the brain. These complex functions arise from a combination of (1) the strength of synapses that connect neurons together, (2) the ability of neurons to fire electrically, (3) and the speed at which electrical signals propagate through neuronal axons. Neuroscientists have long focused on understanding how synapses and electrical excitability contribute to higher-order brain functions. However, far less is known about whether the speed of electrical signals through axons is also dynamically tuned to regulate brain function. We aim to determine how myelin—the electrical insulator around axons that speeds nerve signaling—contributes to the plasticity of neuronal circuits. We are building novel tools for perturbing myelin in the brain, called **IMAGeNs (Inhibitors of Myelination Around Genetically-defined Neurons)**. IMAGeNs will enable us to dissect how myelin contributes to specific brain circuits and types of neurons, bringing us closer to a holistic understanding of how cells in the brain collaborate to build a functional nervous system.

Jennifer Bridwell-Rabb, PhD
2020 Beckman Young Investigator
Chemistry (Biochemistry)
University of Michigan

O_2-dependent and O_2-independent strategies for C-H bond functionalization in chlorophyll biosynthesis

The ability of photosynthetic organisms to harness solar energy and transform carbon dioxide into fuel, biomass, commodity chemicals, and/or produce hydrogen makes them attractive for integration into industrial processes. However, several obstacles remain in using photosynthetic organisms for these applications, including sensitivity of enzymes that produce hydrogen to molecular oxygen and an uneven distribution of light in bioreactors. Towards optimizing the use of photosynthetic organisms in these endeavors, previous studies have focused on understanding the photosynthetic and hydrogen-producing machinery of photosynthetic organisms to build artificial systems, engineering photosynthetic microorganisms to have improved metabolic yields, or redesigning bioreactors to improve light harvesting. Our laboratory instead, as outlined in this proposal, focuses on understanding the already existing mechanisms that photosynthetic organisms use to live in nearly every habitat on Earth. By studying the existing ways that organisms adapt to the light and oxygen available in different environments, we want to uncover ways to overcome inefficiencies in employing photosynthetic organisms for various applications.

Laura Duvall, PhD
2020 Beckman Young Investigator
Biology (Neuroscience)
Columbia University

Peptide signals that enforce paternity in mosquitos

Ae. aegypti mosquitoes are the primary vectors for the pathogens that cause Zika, dengue fever, and chikungunya. A single mating event provides a female with sperm to fertilize all of the offspring she will produce for the rest of her life. During mating, male mosquitoes transfer peptide signals that act on receptors expressed in the female that block her from mating with other males. This enforces his paternity and ensures that he is the father of all of her offspring. These signals can also be used in a form of competition between two species termed “satyrization” when males of one species inappropriately “mate” with females of another species and block females from mating with males of their own species. This prevents the females from successfully reproducing, effectively sterilizing them. We aim to identify peptides transferred from the male to the female, determine which receptors they activate in the female, and ask how interspecies competition may affect these receptors. The molecules that we discover could be used to develop new ways to control mosquito populations.

Sarah King, PhD
2020 Beckman Young Investigator
Chemistry (Imaging & Spectroscopy)
University of Chicago

A new spectroscopic method to probe the "unreachable": uncovering how buried interfaces control function in photoelectrochemical cells

Ultrafast charge transfer across the interface between two different materials underpins performance and energy storage in solar cells and batteries, catalysis, and medical devices. The mechanism of this interfacial charge transfer step, and whether it's efficient, fast, and free of deleterious side reactions, is dictated by the electronic states and ultrafast processes at the buried interface. However, the electronic structure and dynamics at buried interfaces have proven notoriously difficult to selectively probe with the current spectroscopic methods. I will describe our new research project aimed at solving this problem – eliminating the current restrictions in time-resolution, stability, experimental interpretation, and the use of unsuitable model systems via the innovation of a new all-optical, actively-stabilized, time-resolved heterodyned sum-frequency-generation spectrometer. Using the new capabilities of this spectrometer to probe iron oxides, we will uncover the gatekeeping role of electronic states at the buried iron oxide/water interface and the role of passivating layers in improving the water splitting capabilities of iron oxides in order to identify strategies for improving iron oxide-based applications such as solar energy storage.

Maxwell Robb, PhD
2020 Beckman Young Investigator
Chemistry (Organic Chemistry)
California Institute of Technology

A Universal Molecular Design Platform for Mechanically Triggered Release

Stimuli-responsive polymers are materials that respond to external or environmental stimuli by changing their chemistry. Polymer mechanochemistry is a nascent field of research at the intersection of polymer chemistry, organic chemistry, and materials science that leverages mechanical force as a specific stimulus to activate chemical reactions of unique stress-responsive molecules called mechanophores. Our research aims to develop a modular and general mechanophore design platform that will enable the mechanically triggered release of functional molecules from stimuli-responsive polymers. Polymers that release functional cargo molecules in response to mechanical force are exciting targets for a diverse range of applications including drug delivery, sensing, self-healing materials, and catalysis.

Yue Wang, PhD
2020 Beckman Young Investigator
Chemistry (Materials Science & Development)
University of California, Merced

Mechanically Adaptive Conducting Polymers

Conducting polymers are attractive candidates for next-generation applications such as wearable electronics and soft robots. However, similarly to virtually all other thermoplastic materials, conducting polymers deform through a viscoelastic mechanism, meaning they break more easily when the material is deformed quickly. As a result, wearable electronics made using these materials would be prone to damage when used under conditions involving sudden movements, such as during sports. This property is highly detrimental, as constant biometric monitoring is especially important during high-intensity physical activities. Here, we report the development of mechanically adaptive conducting polymers—a new class of polymers with toughness that scales with the rate of stretching, meaning they become tougher with increasing deformation rate. For instance, as the rate of stretching increased from 2.5 to 10000 %/min, the toughness of this material increased by over two orders of magnitude. Such mechanically adaptive behavior can potentially increase the life cycle and durability of the organic electronics, and reduce polymer and electronic waste.

Marco Allodi, PhD
2017 Arnold O. Beckman Postdoctoral Fellow
Chemistry (Biochemistry)
University of Chicago

Extracting Photochemical Design Principles from Biological Systems *in vivo*

Natural light-harvesting systems, such as photosynthetic pigment-protein complexes, efficiently transfer energy through space with high efficiency. Ultimately, we would like to understand the design principles nature evolved to improve optoelectronic devices that rely on light harvesting and energy transfer, such as solar cells. We perform ultrafast 2D electronic spectroscopy measurements on a variety of systems ranging from the Fenna-Matthews-Olson antenna complex isolated from green sulfur bacteria to *in vivo* cyanobacteria. We observe larger amplitude coherences under reductive conditions that mimic the chemistry of the complex *in vivo*. We can use spectroscopic tools that allow us to follow the energy in both space and time. In particular we can correlate the existence of quantum coherences, particularly those involving excited electronic states, with faster, more efficient energy transfer, and assessing the role of the ground and excited states in the transfer process. Future work will look at the how changing light conditions influences the complex chemistry in the photosynthetic membranes, ultimately affecting the energy transfer processes.

Kumar Ashtekar, PhD
2017 Arnold O. Beckman Postdoctoral Fellow
Chemistry (Chemical Engineering)
Yale University

Exploring the dimerization and inhibition of EGFR kinase domain

Eukaryotic protein kinases are induced to drive phosphorylation-initiated signal transduction via allosteric self-assembly. They explore a continuum of conformations that includes ensembles of 'active state' and 'inactive state' conformers. In the absence of a signaling stimulus, inactive state conformers dominate the continuum. When a signaling event is triggered by ligand binding (initiating self-assembly by homo- or hetero-oligomerization of kinase domains) or by recruitment of adapter proteins, the shift in the monomer/dimer equilibrium favors the active state conformers. We investigate the quantitative effects of patient-derived activating mutations on kinase domain dimerization strength (driving EGFR activation 'from the inside'), activity of the kinase domain monomer and dimer, as well as structural dynamics of EGFR kinase domain activation and possible novel modes of disrupting this self assembly. Understanding the dynamics of constitutive allosteric activation in EGFR mutants seen in lung cancer patients, and how the mutations shift the equilibrium towards the active form of enzyme, are key steps in appreciating and combatting the origins of inhibitor resistance.

Liela Bayeh-Romero, PhD
2017 Arnold O. Beckman Postdoctoral Fellow
Chemistry (Synthetic Chemistry)
Baylor University

Copper Hydride Catalysis for the Synthesis of Axially Chiral Allenes

Allenes, compounds containing two double bonds across three contiguous carbons, are versatile synthetic intermediates due to their substituent loading capacity and ability to generate one or more new stereogenic centers through axial-to-central chirality transfer. This structural motif is also present in over 150 natural products and a variety of bioactive molecules. Despite their prevalence and distinct reactivity, catalytic methods to access chiral 1,3-disubstituted allenes with high levels of selectivity from achiral starting materials remains a goal in chemical synthesis.

We have developed a mild and general strategy for the highly selective semi-reduction of prochiral 1,3-enynes. A diverse array of enantioenriched 1,3-disubstituted allenes are furnished in up to 98% yield and 99% enantioenrichment. This reaction is enabled by chiral copper hydride catalysts in the presence of water as a benign and abundant proton source.

Jesse Isaacman-Beck, PhD
2017 Arnold O. Beckman Postdoctoral Fellow
Biology (Neuroscience)
Stanford University

Molecular Mechanisms of Neural Circuit Stability

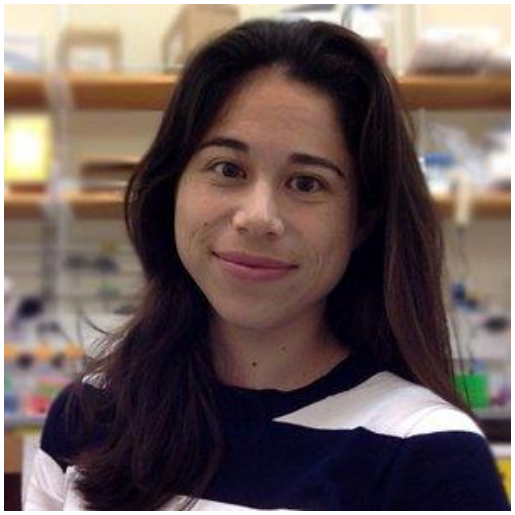
Animals develop neural circuits to adapt and behave. Amazingly, circuits function stably as an animal grows, learns and ages. How do neurons compensate for fluctuating expression of the molecules they use to signal? Do individual neurons use the same mechanisms? While molecular mechanisms of neural circuit plasticity have been interrogated, how they ensure robust output remains poorly characterized. I generated genetic tools to address these questions in the *Drosophila* visual system. Here, I present Sparse Predictive Activity through Recombinase Competition (SPARC) an all- genetic method to express effectors in precise proportions of cell populations. I combined this approach with a novel gene silencing method to delete a voltage-gated calcium channel (VGCC) from ~50% of cell populations. I compared changes in mutant and wild type gene expression using single-cell RNAseq and defined ~150-200 genes that might compensate for VGCC deletion (ion transporters, calcium-responsive enzymes, transcription factors). I will determine how neurons and circuits alter expression of these genes to stabilize stimulus-evoked responses in different cell types to define cell-type specific molecular mechanisms that drive neural circuit robustness.

Francisco Luongo, PhD
2017 Arnold O. Beckman Postdoctoral Fellow
Biology (Neuroscience)
California Institute of Technology

Investigating neural signals for perceptual organization in the mouse

The rodent visual system has attracted great interest in recent years, owing to its experimental tractability, but the fundamental mechanisms used by the mouse to represent the visual world remain unclear. In the primate, researchers have argued that a key step in visual representation is perceptual organization, the delineation of figures as distinct from backgrounds. To determine if mice display evidence of such a representation, we carried out a study using 2-photon imaging and electrophysiological recording across rodent visual cortex. We found no evidence of such signals. We train mice on an object segmentation task and found that they were severely limited in their ability to segment figure from ground using motion cues. Primates, in contrast, could readily segment figures independent of pattern and utilize motion cues. Modeling revealed that the texture dependence of both the mouse's behavior and neural responses could be explained by a feedforward neural network model lacking explicit segmentation capabilities. Overall, these findings reveal a fundamental limitation in the ability of mice to segment visual objects compared to primates.

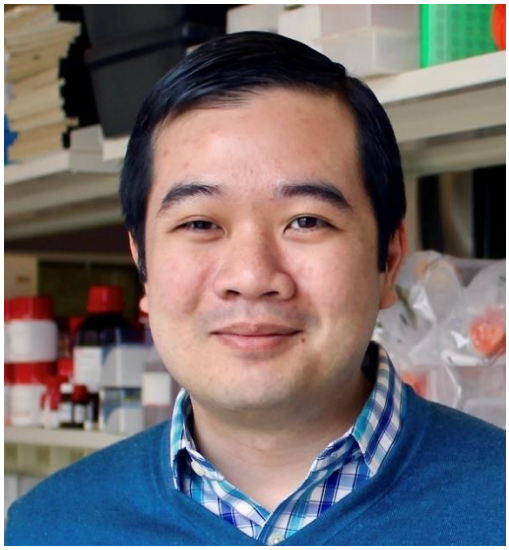
Kira Mosher, PhD
2017 Arnold O. Beckman Postdoctoral Fellow
Biology (Neuroscience)
University of California, Berkeley



Dissecting cell signaling networks that regulate adult neural stem cell functions

In the adult mammalian hippocampus, neurogenesis (in which new neurons are generated and integrated into the CNS) is believed to underlie learning and memory. Within the hippocampus, numerous cell types communicate via diverse signals. Some of these signals control neural stem and progenitor cells (NSPCs), which can divide or terminally differentiate into neurons, astrocytes, or oligodendrocytes, and then migrate and integrate into the existing brain circuitry. I have identified novel functions for a ligand-receptor pair, ephrin-A4 and EphA4, in this process. NSPCs express the receptor EphA4, while ephrin-A4 is predominately expressed by mature neurons. In cell culture studies, treating adult NSPCs with ephrin-A4 activated EphA4 and induced neuronal differentiation, and blocking EphA4 ligand-binding with an antagonist reversed these effects. Ephrin-A4/EphA4 signaling also regulated the migration of NSPCs. Finally, using AAV to deliver CRISPR/Cas9 into the brains of adult mice, I found that knocking out EphA4 or ephrin-A4 in select cell types alters neuronal differentiation and migration *in vivo*. These data thus support a significant role for ephrin-A4/EphA4 signaling in regulating adult neurogenesis.

Freddy Nguyen, PhD
2017 Arnold O. Beckman Postdoctoral Fellow
Chemistry (Materials Science & Development)
Massachusetts Institute of Technology



From biochemical nanosensors to imaging to informatics to COVID-19 convalescent plasma – developing diagnostics and therapies for clinical medicine

Current cancer management follows a multipronged approach that include surgery, radiation, and chemotherapy. There is a need for a platform to provide precision chemotherapy screening, drug delivery detection, and therapy efficacy monitoring. We developed single walled carbon nanotube sensors for detecting chemotherapeutics, more recently for temozolomide (TMZ) and its byproduct 5-Amino-4-imidazolecarboxamide with sensitivity at 5-500 µM and in vitro viability up to 7 days in TMZ treated glioblastoma cells, and for irinotecan, cisplatin, and lomustine with sensitivities at 50 µM. H2O2 sensors were used to measure therapy efficacy of gemcitabine and irinotecan in pancreatic ductal adenocarcinoma in vitro and in vivo. Multiplexing these sensors could yield insights into delivery, diffusion, metabolism, and efficacy of chemotherapeutics. Other strategies are being developed such as ratiometric approaches and wavelength-induced frequency filtering to improve performance and sensitivity. A fiber optic platform was developed as a minimally invasive form factor to integrate the sensor hydrogel, optical waveguide, and detection system. As a physician-scientist in NYC, my research rapidly shifted to the role of convalescent plasma and antibody development in COVID-19.

Massa Shoura, PhD
2017 Arnold O. Beckman Postdoctoral Fellow
Biology (Molecular & Cell Biology)
Stanford University

Tracking Genome Dynamics in Time and Space

Extrachromosomal circular DNA (eccDNA) comprises products of genomic recombination that cause somatic changes in gene length and sequence. These circular molecules are derived from canonical linear chromosomal loci, expanding the diversity in coding and regulatory capacity within eukaryotic genomes and transcriptomes. Using a brand-new multidisciplinary approach to investigate eccDNA-mediated allelic diversity, I have identified various coding regions of eccDNA biogenesis, such as Titin (*TTN*). Preliminary data obtained in the past years of support suggest a novel mechanism of *TTN* diversity involving circular-DNA excision that generates recombinant *TTN* loci at the genomic level. Here, I report *TTN*-eccDNA formation as a potential mechanism for modulating overall myofibrillar passive tension. Results from investigating this novel mechanism for the modulation of cardiovascular stiffness will revolutionize basic, clinical, and therapeutic approaches to cardiovascular diseases. The AOB Award has been instrumental in advancing the field of eccDNA, in general, and in providing a missing key element in DCM biology, consideration of which may drive a reevaluation of current therapies.

Eric Strobel, PhD
2017 Arnold O. Beckman Postdoctoral Fellow
Biology (Molecular & Cell Biology)
Northwestern University

Chemical roadblocking of DNA transcription for nascent RNA display

Eric J. Strobel, John T. Lis, Julius B. Lucks

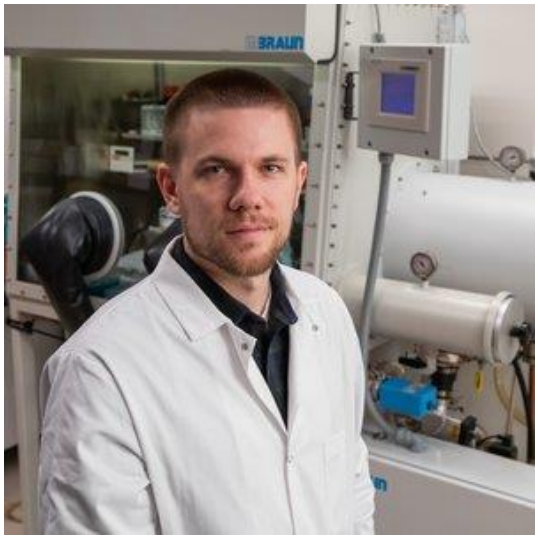
Site-specific arrest of RNA polymerases (RNAPs) is fundamental to several technologies that assess RNA structure and function. Current *in vitro* transcription "roadblocking" approaches inhibit transcription elongation by blocking RNAP with a protein bound to the DNA template. One limitation of protein-mediated transcription roadblocking is that it requires the inclusion of a protein factor that is extrinsic to the minimal *in vitro* transcription reaction. In this work, we developed a chemical approach for halting transcription by *Escherichia coli* RNAP. We first established a sequence-independent method for the site-specific incorporation of chemical lesions into double-stranded DNA templates by sequential PCR and translesion synthesis. We then show that interrupting the transcribed DNA strand with either an internal desthiobiotin-triethylene glycol modification or 1,N^6-etheno-2'-deoxyadenosine base efficiently and stably halts *Escherichia coli* RNAP transcription. By encoding an intrinsic stall site within the template DNA, our chemical transcription roadblocking approach enables the display of nascent RNA molecules from RNAP in a minimal *in vitro* transcription reaction.

James Bour, PhD
2019 Arnold O. Beckman Postdoctoral Fellow
Chemistry (Organic Chemistry)
Massachusetts Institute of Technology

Toward Site-Isolated Organometallics: General and Modular Access to Phosphine-Containing Metal-Organic Frameworks

Owing to their high surface areas, crystallinity, and structural diversity, metal-organic frameworks have emerged as attractive platforms for the heterogenization of traditional molecular catalysts. Immobilization of such species can favorably affect their activity, selectivity, and recyclability. The overwhelming majority of MOF-based transition-metal-catalyst systems to date feature transition-metal-catalyst enters supported by hard donor atoms such as oxygen and nitrogen. The resulting weak ligand fields are not appropriate for many catalyst systems. Soft donor atoms such as P(III) centers can decompose under during material synthesis or preclude material formation all together. The objective of this project is to develop a modular approach to the synthesis of MOFs featuring unprotected P(III) centers that is *general across multiple classes of MOFs.* Such materials are expected to substantially advance the investigation of organometallics in site isolated environments and under nanoconfinement. Herein we report the synthesis of S-tetrazine MOFs and their post-synthetic modification with a variety of dienophile-tagged phosphines. We demonstrate that this approach is general to at least five materials and multiple dienophiles, which enables rapid elaboration of parent frameworks into a variety of P(III) MOFs.

Quinn Burlingame, PhD
2019 Arnold O. Beckman Postdoctoral Fellow
Chemistry (Chemical Engineering)
Princeton University



Designing small-molecule organic absorbers for semi-transparent, UV-absorbing solar cells

Organic solar cells are ideal for semi-transparent applications due to their “peaky” absorption, which allows them to selectively absorb non-visible photons while transmitting visible light. Such devices embody a fundamental tradeoff between transparency and power generation that must be optimized to fit each potential application—for example, powering electrically dimmable smart windows. To inform the design of organic absorbers that target various combinations of power generation and transparency, we employ optical simulations based on a set of computer-generated optical constants that mimic organic materials with varying absorption cutoffs and absorption coefficients. We find a cutoff wavelength of 420 nm produces the most power without degrading aesthetics of the solar cell. Absorption coefficients around $5x10^5$ cm^{-1} result in optimal devices, as they allow for absorption of most light within a ~100 nm absorbing layer, and do not create unwanted reflections due to refractive index contrast in the device stack. A series of novel absorber materials was also synthesized and integrated into organic solar cells with absorption cutoffs traversing the same range as the simulations—though increased absorption strength is needed for improved performance.

Alice Chang, PhD
2019 Arnold O. Beckman Postdoctoral Fellowship
Chemistry
University of Minnesota, Twin Cities

Tough, Sustainable Plastics *via* Graft Block Polymer Design

Alice B. Chang, Aristotelis Zografos, Frank S. Bates
Department of Chemical Engineering and Materials Science
University of Minnesota, Twin Cities

The molecular architecture – that is, the way in which polymer chains are connected – dramatically impacts the properties of plastics. In our work, we aim to develop a modular platform for tough and sustainable plastics based on poly($_{D,L}$-lactide)-*b*-poly(4-methylcaprolactone) graft block polymers. Linking two or more chemically distinct blocks structures plastics at the nanoscale, improving the mechanical properties; introducing grafts amplifies shear thinning and strain hardening behavior, improving the melt processability. Living ring-opening metathesis polymerization enables precise control over the graft block architecture, enabling systematic studies of key structure-property relationships. In this poster, we highlight the connections between molecular design and physical impact in terms of the melt processability. Understanding design rules based on the molecular architecture — *independent* of specific choices of block and backbone functionality — allows the materials to both meet the needs of sustainability and be customized for specific applications.

Kangway Chuang, PhD
2019 Arnold O. Beckman Postdoctoral Fellow
Chemistry
University of California, San Francisco

An End-to-End Approach to Learning on Molecular Ensembles

Institute for Neurodegenerative Diseases, Department of Pharmaceutical Chemistry University of California, San Francisco, 675 Nelson Rising Ln, San Francisco, CA 94143

Modern drug discovery benefits from new machine learning approaches to virtual screening. Despite the known importance of three-dimensional and spatial information for biomolecular recognition, similarity-based virtual screening and quantitative structure-activity relationship approaches have failed to yield substantial improvements by incorporating spatial information. We describe a set-based deep learning approach for directly learning biologically-relevant small-molecule ensembles that contribute to binding specificity. This approach leverages two levels of representation learning: 1) individual conformers are encoded as spatial graphs using a graph neural networks, and 2) molecular ensembles are represented through a set-based attention mechanism that intelligently aggregates conformer information. In contrast to previous approaches, this deep learning framework can be trained to predict complex polypharmacology of small molecule ligands from conformational ensembles and simultaneously discover relevant binding modes *directly from data*.

Julie Fenton, PhD
2019 Arnold O. Beckman Postdoctoral Fellow
Chemistry (Organic Chemistry)
Northwestern University

Progress Towards Application-Relevant Porous Polymer Membranes: Solution-Processed Thin Films and Stability Enhancement by Monomer Exchange

Covalent organic framework (COF) materials are a class of crystalline, permanently porous polymers with a regular reticular architecture. The stable covalent bonds and tunable pore sizes seem to optimally position COFs as functional membranes with intuitive structure-property relationships, potentially relevant for molecular separations and water desalination. However, COFs are most often isolated as insoluble, polycrystalline powders, which significantly limits their utility. More effective material processing methods that produce high-quality COFs in functional morphologies are in demand. Our lab has recently developed a solution processing approach for converting imine-linked COF powders into robust, free-standing films of arbitrary thickness and lateral dimension, providing a general, facile pathway between readily accessible powders and a device-ready form of the same material. We show that these imine-linked films can subsequently be converted to hydrolytically stable β-ketoenamine linkages via a monomer exchange process, which preserves a continuous film morphology and the characteristic material features of a COF. Efforts to optimize these processes to deliver improved film quality, preferentially orient the COF domains, and assess performance as size-sieving membranes are ongoing.

Miguel Gonzalez, PhD
2019 Arnold O. Beckman Postdoctoral Fellow
Chemistry (Organic Chemistry)
Harvard University

Taming the Chlorine Radical: Selective C–H Activation using Photogenerated Chlorine-Atom Complexes

Selective C–H activation remains one of the most intensely studied reactions across many fields of chemistry, due to its applications in both industrial and fine chemicals synthesis. Although chlorine radicals have been established as potent hydrogen-atom abstraction agents in free-radical chlorination reactions and, more recently, in photoredox catalysis, the high reactivity of these intermediates severely limits their selectivity. We demonstrate that the secondary coordination sphere of a metal complex can confine photoeliminated chlorine radicals and enforce steric control over their reactivity. Specifically, a series of pyridinediimine (PDI) iron(iii) chloride complexes exhibit activity for the photochlorination of alkanes with selectivity for primary and secondary C–H bonds, overriding thermodynamic preference for weaker tertiary C–H bonds. Characterization of these iron(iii) complexes by single-crystal X-ray diffraction and time-resolved transient absorption spectroscopy experiments suggest that this site-selective reactivity arises from a relatively long-lived arene–Cl• complex between the photoeliminated chlorine atom and aromatic groups in the secondary coordination sphere. Finally, photocrystallograpic techniques enable the direct observation of chlorine radical elimination and reactivity in the solid state.

Stewart Mallory, PhD
2019 Arnold O. Beckman Postdoctoral Fellow
Chemistry (Materials Science & Development)
California Institute of Technology

Space-time Concentration Scales Reveal Hidden Features in the Mechanical Properties of Active Colloids

By introducing the notion of concentration scales, we identify universal and previously unreported features of the dynamical and mechanical properties of active Brownian particles (ABPs). These subtle yet important features are codified by recognizing that the characteristic length scale of an active particle's trajectory, the run-length, introduces a new concentration scale φ^*. Using large-scale computer simulations, we demonstrate that this new run-length dependent concentration φ^*, which is the trajectory-space analogue of the overlap concentration in polymer solutions, delineates distinct concentration regimes in which interparticle collisions characteristically alter particle trajectories. Using φ^* and concentration scales associated with colloidal jamming, the mechanical equations-of-state for ABPs can be collapsed onto a master curve which contains a number of previously overlooked features. This perspective gives rise to a framework for the construct of highly accurate mechanical equations-of-state which are necessary to quantitatively model the behavior of ABPs. Equations-of-state that fully capture these features qualitatively alter theoretical predictions for a range of phenomena as we explicitly demonstrate by computing the spinodal for a suspension of purely-repulsive ABPs.

Hossein Robatjazi, PhD
2019 Arnold O. Beckman Postdoctoral Fellow
Chemistry (Chemical Engineering)
University of California, Santa Barbara

Dynamic behavior of Al native oxide-supported metal catalysts: exposing uniform atomically dispersed species via strong metal-support interactions

The ability to manipulate adsorbate-surface interactions through controlling the nature of exposed metal sites is critical for tuning the reactivity of supported metal catalysts. Here we demonstrate that dynamic control of active sites through the so-called “strong metal—support interactions” encapsulation goes beyond reducible oxide supports by demonstrating the dynamic behavior of Pt catalysts supported on the 2-4 nm thick native oxide layer of aluminum nanocrystals (AlNCs). Our solid-state NMR studies revealed that, compared to typical *γ*-alumina, the native oxide of AlNC has a distinct Al coordination environment, which could lead to unique metal-support interactions. *In situ* CO probe FTIR measurements suggest that reductive treatment of the catalyst in H_2 (300°C) results in the covering of ~1 nm Pt particles by an apparent AlO_x overlayer, leaving only uniform atomically dispersed Pt species exposed for catalysis with the overlayer retreats off Pt particles following re-oxidation. We investigated the influence of the Al_2O_3—induced SMSI state on dynamic control of the Pt active sites through assessing the reactivity of the pretreated catalysts for low-temperature ethylene hydrogenation reaction.

Alexander Schuppe, PhD
2010 Arnold O. Beckman Postdoctoral Fellow
Chemistry
Massachusetts Institute of Technology

Enantioselective Hydrocyanation of Olefins without Cyanide

Alexander W. Schuppe, Gustavo M. Borrajo-Calleja, Stephen L. Buchwald

Department of Chemistry, Massachusetts Institute of Technology, 77 Massachusetts Avenue, Cambridge, MA 02139

Although hydrocyanation of feedstock olefins is conducted on a million-metric ton scale annually to produce nitrile polymers, these protocols employ gaseous hydrogen cyanide and form achiral products. Enantioenriched nitriles are found in numerous natural products, materials and pharmaceuticals, however, the currently available methods to access this substructure often necessitate the use of extremely hazardous chemical reagents and are limited to minimally functionalized substrates. Though strategies for the asymmetric olefin hydrocyanation have existed for decades, few synthetic advances been achieved. Herein, we report a cyanide-free dual Pd/CuH-catalyzed protocol for the asymmetric Markovnikov hydrocyanation of vinyl arenes and the anti-Markovnikov hydrocyanation of terminal olefins in which oxazoles function as nitrile equivalents. After an initial hydroarylation process, the oxazole substructure was deconstructed using a [4 + 2]/retro-[4 + 2] sequence to afford the enantioenriched nitrile product under mild reaction conditions.

Adam Slavney, PhD
2019 Arnold O. Beckman Postdoctoral Fellow
Chemistry (Organic Chemistry)
Harvard University

Highly-structured Liquids from Melts of Porous Solids

Solid-state framework materials represent a unique class of solids with large internal surface areas in which chemists are able to exercise fine control of the crystalline structure through a carefully tuned combination of strong, directional bonding interactions and rigid organic struts. This level of control has enabled the design of highly effective materials for uses as varied as ion transport and gas capture and storage. However, despite these achievements, normal liquids remain the media of choice for many industrial applications as their fluidity greatly simplifies process design. While fluids in general are disordered states of matter, they can still be highly structured on the molecular level, as exemplified by the extensive hydrogen-bonding network found in water. Exploiting directional interactions and molecular rigidity in a fluid is an underexplored strategy for creating liquids with highly-tunable and exotic properties such as porosity in the liquid state. Here we will present preliminary results towards the goal of realizing porosity and fluidity in the same material via melting of a porous hydrogen-bonded organic salt.

Patrick Smith, PhD
2019 Arnold O. Beckman Postdoctoral Fellow
Chemistry (Organic Chemistry)
Massachusetts Institute of Technology

SQUID Magnetometry of Graphite-Conjugated Porphyrin Complexes

Metal complexes grafted to carbon materials using pyrazine linkers display electrochemical behavior distinct from that of solution or more traditional surface-tethered molecules. Namely, these “graphite-conjugated” complexes do not undergo simple electron transfer reactivity, but rather redox events are only observed when coupled to an interfacial ion transfer, reminiscent of bulk metallic behavior. We have established methodology for the determination of per-site magnetic moment of graphite-conjugated metalloporphyrins grafted on carbon powder at low concentrations (< 1 at. %). Using this method, we are studying the magnetic properties of 3*d* GC-porphyrin complexes, as well as some complexes grafted by more traditional tethering methods. We have so-far been able to observe significantly different behavior between GC-, amide-linked, and extended amide-linked TPP(Co) (TPP = tetraphenylporphyrin) complexes, as well as between TPP(Co) and TPP(Cu) porphyrins, none of which display the $S = ½$ Curie law behavior expected for neutral Co or Cu porphyrins. These data are being interpreted within the framework of the Anderson impurity model.

Benjamin Snyder, PhD
2019 Arnold O. Beckman Postdoctoral Fellow
Chemistry (Organic Chemistry)
University of California, Berkeley

Conversion of Methane to Methanol in Metal-Organic Frameworks

Methane is an abundant source of energy and potent greenhouse gas. Its conversion to methanol under mild conditions remains an economically significant, but fundamentally challenging goal of modern chemistry. The methane-to-methanol conversion currently in use is energy intensive, requiring multiple steps at high temperatures and pressures. A number of synthetic and biological systems have been identified that hydroxylate methane under ambient conditions, however each has practical limitations: instability, high cost, and/or low catalytic performance. We aim to address these issues with an emerging class of microporous materials called metal-organic frameworks (MOFs), which show great potential for supporting high densities of catalytic sites facilitating low temperature methane-to-methanol conversion.

Dayne Swearer, PhD
2019 Arnold O. Beckman Postdoctoral Fellow
Chemistry (Materials Science & Development)
Stanford University

Optically Coupled Electron Microscopy: The Nanophotonics of Lanthanide-doped Alkaline-Earth Rare-Earth Fluorides

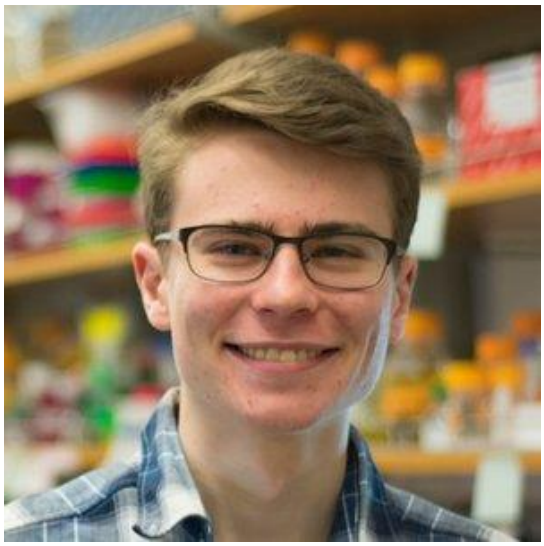
Many fundamental nanophotonic processes occur across diverse scales that vary in space and time. To engineer optimized nanophotonic systems, investigations at spatial and temporal limits are often required. Here, we utilize the high-resolution imaging capabilities of a transmission electron microscope equipped with a commercial holder capable of collecting light from individual nanostructures. This experimental approach is presented in the context of a novel ceramic nanoparticle system: lanthanide-doped alkaline-earth rare-earth fluorides. These nanomaterials are synthesized through a simple solvothermal decomposition of trifluoroacetate salts in coordinating solvents. To date, thirty varieties have been produced. Time-resolved cathodoluminescence (CL) single-particle spectroscopy of ten-variants of lanthanide-doped $BaYF_5$ will be presented. These nanophosphors have unique optical signatures at the ensemble and single-particle level. Multiplexed spectral imaging reveals that parasitic CL absorption complicated the direct interpretation of CL measurements of mixed samples, but EELS and time-resolved CL may present alternatives for future applications in imaging. Particularly, the optical and temporal emission fingerprints of these nanophosphors may offer a replacement for contrast-based immunogold labeling — the current standard in cryo-EM for studying integral proteins.

Christina Beck
2019 Beckman Scholar
Biology (Molecular & Cell Biology)
Pomona College

CRP and Cra have Opposing Roles in the Regulation of *fruB* Expression in *Vibrio cholerae*

Vibrio cholerae is the causative agent of cholera, a diarrheal disease which infects between three and five million individuals annually. In order to survive in both the human small intestine, where pathogenesis occurs, and aquatic reservoirs, *V. cholerae* must adapt to available carbon sources by selectively producing the necessary metabolic machinery. In this project, we focused our attention on fructose, one of the most abundant sugars in freshwater environments, and how *V. cholerae* regulates fructose metabolism at the genetic level. More specifically, we focused on the roles of Cra and CRP, two known global transcriptional regulators, in regulating the expression of *fruB*, the first gene of the fructose operon *fruBKA*. Using transcriptional reporters, we found Cra to be a repressor of *fruB* and CRP to be an activator of *fruB*. We also identified the approximate location of -10 and -35 hexamers within the *fruB* promoter. Here, we present a model for *fruB* expression and regulation in *V. cholerae* and lay the foundation for future mechanistic studies which investigate regulatory activity in the *fruB* promoter.

Erik Bidstrup
2017 Beckman Scholar
Biology (Synthetic Biology)
Northwestern University



Development of an Improved Orthogonal Ribosome

A core goal of synthetic biology has been the evolution of macromolecular machines for compelling societal and scientific applications, including the use of directed evolution to engineer the ribosome to make new medicines and materials. A notable success of ribosome engineering was the development of the first fully orthogonal tethered ribosome, oRibo-T. Despite their potential, the translation capacity of orthogonal ribosomes is limited, and past directed evolution efforts were hindered by the ribosome's size and interconnectedness. Here we present the development of Ribo-Tv3, a tethered ribosome with an over 50% improvement in orthogonal protein translation. To evolve Ribo-T for improved function, we demonstrate the use of Rosetta-guided design in iterative evolution experiments, and a new technique termed Evo- link (evolution and linkage of distant regions). Evo-link couples flexible molecular biology techniques with next-generation sequencing for the high-throughput evolution of functionally linked regions that are distal in primary sequence. Our work demonstrates the power of computational structural modeling for informing library design, and the Evo-link's potential to optimize functionally linked sequences in macromolecular machines for diverse applications.

Julianna Cresti
2017 Beckman Scholar
Chemistry (Biochemistry)
Villanova University

Investigation of Conformational State of the 26S Proteasome and Protein Unfolding Ability Using FRET

The 26S proteasome is a eukaryotic multiprotein complex that mechanically degrades mutated and misfolded proteins. In doing so, it undergoes a series of conformational changes from s1 states, in which substrate is unbound, to s3 or s3-like states, in which substrate is translocated. The 19S particle of yeast proteasome was mutated with two fluorescent proteins, and the proteasome were transformed and purified to be used for tracking energetic conformational changes associated with the structure's ability to engage, unfold, and degrade proteins. The distance-dependent spectroscopic technique FRET was employed to measure changes in fluorescence intensity at the peak of the energy acceptor. FRET peak intensities were compared for substrates known to induce specific conformational changes. Doubly tagged proteasome exhibited higher FRET signal in the presence of the non-hydrolyzable ATP analog, ATPγS to bias the proteasomal conformation toward s3 or s3-like states. Additionally, a mutant predicted to favor s1-like states exhibited FRET signal comparable to wildtype upon addition of ATP, but significantly lower signal with ATPγS.

Gillen Curren
2017 Beckman Scholar
Chemistry (Atmospheric & Earth Sciences)
Villanova University

Comparing the Heavy Metal Concentrations of Estuarine Organisms from Different Estuaries on the East Coast

Coastal estuaries and saltwater marshes are among the world's most productive ecosystems. They provide many ecosystem services, such as carbon sequestration, storm protection, and pollutant filtration. However, coastal estuaries have been affected by increased heavy metal concentrations due to human activities such as vehicle usage; higher heavy metal concentrations affect the health of the coastal wetland ecosystem. This project seeks to compare soil and organismal concentrations of heavy metals in the Plum Island (MA), Delaware River (NJ), and Kennebec River (E) estuaries. The samples collected from the estuarine systems will be hot acid digested and analyzed with an inductively coupled plasma mass spectrometer. From samples already analyzed, it seems soil samples from near the ocean had lower heavy metal concentrations. Mussel heavy metal concentrations were higher when the mussels were larger. Metal concentrations such as arsenic and lead were above EPA and FDA standards, for both mussel and soil samples. Heavy metal concentrations will be compared between species and estuaries to determine which species and estuary has the highest average heavy metals concentration.

Taylor Fish
2017 Beckman Scholar
Chemistry (Analytical Chemistry)
Brigham Young University

Development of Immunoaffinity Monolith Extraction of Preterm Birth Risk Biomarkers in 3D-Printed Microfluidic Systems

Preterm birth (PTB), the most common complication of pregnancy, results in roughly 15 million early births each year and is the leading cause of infant death and illness. The effects of preterm birth cost the United States alone billions of dollars in annual healthcare costs. If clinicians were able to predict the risk of preterm birth, they would be able to employ preventative measures that could reduce the likelihood of PTB. Unfortunately, no PTB risk clinical diagnostic tool currently exists. Recent discoveries show that specific biomarkers found in maternal blood serum are correlated with a risk of preterm birth. Recent innovations demonstrate that the use of 3D-printed devices shows great promise to effectively analyze PTB biomarkers and diagnose the risk of PTB. Extraction of PTB biomarkers from maternal blood serum is a key step to facilitate PTB risk diagnosis. Extraction of two PTB biomarkers, corticotropin releasing factor and ferritin has been demonstrated. Potentially optimized conditions for extraction of a third PTB biomarker, lactoferrin, are also discussed.

Xiaoyi Sean Hu
2017 Beckman Scholar
Biology (Molecular & Cell Biology)
Northwestern University

Impact of Protein Spherical Nucleic Acid Design Parameters on Immunostimulation

The protein spherical nucleic acid architecture (ProSNA), which consists of a protein-core with a dense shell of radially oriented oligonucleotides, is a promising platform for cancer immunotherapy when synthesized with an antigenic protein-core and immunostimulatory, CpG DNA adjuvants. The ProSNA architecture protects the components from degradation and enhances their co-delivery into dendritic cells. I aimed to characterize the impact of two ProSNA design parameters — protein-DNA conjugation chemistry and DNA shell density — on immune activation. I synthesized ProSNAs with either a traceless linkage that liberates the native protein and DNA upon intracellular reduction or with a non-cleavable linkage. The traceless linker resulted in more robust T-cell proliferation and memory responses than a non-cleavable ProSNA. I also investigated the impact of surface DNA density by comparing ProSNAs with the same number of adjuvant strands but increasing numbers of non-immunostimulatory strands. Increasing the surface DNA density augmented the resulting memory responses. These results demonstrate the importance of the rational design of these parameters to maximize the structure's efficacy, thereby developing the design roadmap for future ProSNA-based cancer immunotherapeutics.

Molly Madden
2017 Beckman Scholar
Biology (Molecular & Cell Biology)
University of Colorado, Boulder

The Functional Impact of an Embryonic Myosin Mutation that Causes Freeman Sheldon Syndrome

Freeman-Sheldon Syndrome (FSS) is a rare skeletal muscle disease characterized by birth defects including a small mouth opening and malformation of the hands and feet. It is caused by point mutations in the embryonic myosin gene, which encodes a muscle motor protein, but the mechanisms by which a mutation disrupts fetal muscle development are not understood. To better understand FSS pathogenesis, the most clinically severe mutation (T178I) was studied at the molecular level to determine its impact on myosin motor function, and at the cellular level to determine the initial cellular response to potential changes in myosin behavior. The molecular effects of T178I on myosin's enzymatic activity and mechanical motor function were measured using *in vitro* ATPase and motility assays, respectively, to help elucidate the disease trigger. The data shows a trend of increased actin affinity for the T178I mutation compared to WT myosin. To study the compensatory response, we designed a gene-editing strategy to express T178I in mouse myoblast cells, which will be studied during muscle differentiation in culture.

Ella Mullikin
2017 Beckman Scholar
Chemistry (Chemical Physics)
Wellesley College

A New Method for Modeling Astrochemical Photoprocesses in Cold Cores

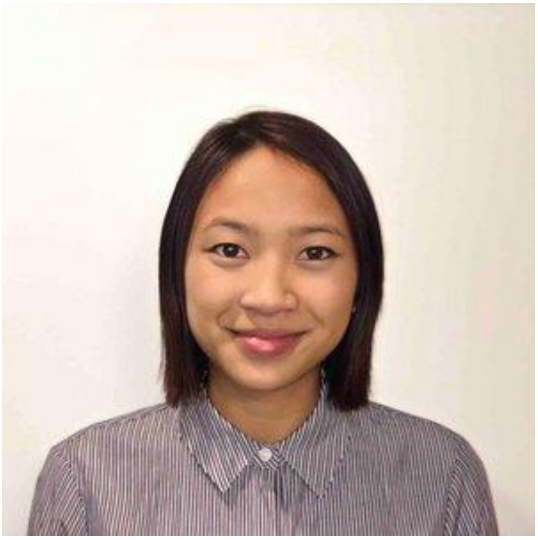
Advances in observational astrochemistry have resulted in the detection of complex organic molecules (COMs) and prebiotic molecules (e.g. glycoaldehyde) in cold prestellar cores in the interstellar medium. Photoprocessing of icy dust grains is a likely formation route for these molecules. A new model is presented which, unlike previous astrochemical models, handles prebiotic molecule-forming reactions at low-temperatures. This model adapted from Shingledecker et al. (2019) is used to calculate ozone production as a function of irradiation time. Based on comparison to experimental results, the model adequately describes interstellar photoprocessing and can be used to update existing large-scale astrochemical models.

Audrey Muscato
2017 Beckman Scholar
Biology (Neuroscience)
Bowdoin College

Mechanisms underlying individual variability in cardiac neuromuscular system responses to modulators in the American lobster, *Homarus americanus*

Central pattern generators produce patterned outputs independent of sensory input. The cardiac neuromuscular system of the American lobster (*Homarus americanus*) is driven by a central pattern generator called the cardiac ganglion (CG), which is composed of nine neurons, making it a model system of study. Modulation of the CG allows for functional flexibility in its typically fixed output. One neuropeptide family that modulates the contraction amplitude and frequency of the lobster heart is C-type allatostatin (AST-C I-III). Previous research has shown great individual variation in the responses of the CG to AST-C I and III. We hypothesized that the mechanism behind this individual variation is differential expression of AST-C receptors and/or their downstream targets. We recorded physiological responses of the cardiac system to AST-C and then sequenced CG RNA from the same lobsters. Differential expression of one of the AST- C receptors and a number of downstream factors—which are associated with G-protein coupled receptor pathways—is correlated with physiological response. These findings inspire further experimentation investigating molt cycle as the underlying cause.

Gwendolyn Pyeatt
2017 Beckman Scholar
Chemistry (Organic Chemistry)
Boston University



Structural characterization of KEAP1 variants to guide the design of KEAP1-Nrf2 peptide inhibitors

KEAP1 is a major regulator of Nrf2-mediated oxidative stress response, and thus the KEAP1-Nrf2 protein-protein interaction (PPI) is widely recognized as a drug target for oxidative stress-related diseases. PPIs often take place between large, flat interfaces, making them difficult to block using small molecules. One alternative to traditional small-molecule drugs that has proven effective in the potent inhibition of PPIs is using macrocycles or cyclic peptides. We previously identified Arg415 as the KEAP1 residue with the most significant contribution to binding energy between KEAP1 and Nrf2. As the mutation of Arg415 to alanine abolished Nrf2 binding entirely, a KEAP1 R415K variant was generated to better understand the binding energetics between this residue and Nrf2. This more conservative mutation caused a 40-fold decrease in binding affinity, which suggests that retaining the charge alone was not sufficient to restore wild-type binding affinity. KEAP1 R415K crystals have also been optimized to obtain unliganded and Nrf2-peptide bound structures and determine which interactions with Nrf2 are lost by introducing this mutation.

Kristen Read
2017 Beckman Scholar
Biology (Structural Biology)
Brigham Young University

Structural and functional analysis of RPE65 folding by the cytosolic chaperonin CCT

A key step in the visual cycle is the trans-to-cis isomerization of retinoid intermediates by RPE65. Mutations in RPE65 disrupt this process and result in retinal dystrophies such as Leber congenital amaurosis (LCA). Little is known, however, about how RPE65 is folded or how folding is disrupted by mutations. We have evidence that RPE65 folding is assisted by the cytosolic chaperonin CCT. Both WT RPE65 and LCA-associated mutants interact with CCT. Notably, interactions between CCT and the mutants are approximately twice as strong as the interaction with the WT despite reduced expression levels. In addition, radiolabel pulse-chase analysis shows that nascent RPE65 associates with CCT and dissociates over time. These results suggested that RPE65 is a substrate of CCT and prompted us to seek a high-resolution cryo-EM structure of the complex to better understand how CCT folds RPE65. We isolated the complex using a tandem-affinity approach and obtained a preliminary 4.2 Å structure. Improving the structure will provide a basis for understanding how CCT handles the folding defects caused by RPE65 mutations.

Sarah Shnayder
2017 Beckman Scholar
Biology (Immunology, Virology & Infectious Disease)
Tufts University

Interplay of the Gut Microbiome, Inflammation, and Lifespan

Inflammation is a natural physiological response that promotes healing and protection from antigenic factors. However, when this process persists in the absence of a pathogen, it becomes harmful to healthy tissues. The chronic, low-grade inflammation that develops specifically during the aging process is a phenomenon termed “inflammaging”. This is associated with a higher incidence of diseases such as cancer, cardiovascular disease, and Alzheimer’s disease. It is proposed that one of the roots of “inflammaging” is the perturbations in the gut microbial composition with age. Characteristic of this aged microbiome is reduced diversity, an abundance of opportunistic bacteria, and a reduction in commensal bacteria, all of which are thought to contribute to the inflammatory milieu. Thus, we propose that the reintroduction of an anti-inflammatory bacteria would prevent the damage caused by a chronic immune response, and thereby extend overall lifespan. This hypothesis was tested in *Drosophila melanogaster*, with results showing a mean lifespan extension and health span improvement with treatment of freeze-dried *Parabacteroides distasonis* (P.dist) anti-inflammatory bacteria.

Isabel Thompson
2017 Beckman Scholar
Biology (Evolution & Population Biology)
Grand Valley State University

The country lizard and the city lizard: Comparing spatial genetic structure of Galápagos lava lizards occurring in natural and human-modified landscapes

Fauna of the Galápagos Islands is under increasing threat due to the growing demands of human activity. The impact of anthropogenic pressures is unknown for lava lizards (genus *Microlophus*), a group of nine species common throughout the Galápagos. *M. bivitattus* genetic samples were collected across a gradient of natural and human-modified habitats on the island of San Cristóbal in 2017/2018. Microsatellite primer optimization occurred Summer/Fall 2019. Our main objective is to fill a knowledge gap on the ecology and spatial genetic structure of Galápagos lava lizards using microsatellite genotypes to 1) estimate dispersal distances, 2) compare levels of gene flow and inbreeding, and 3) examine the distribution of related individuals across the landscape and in relation to landscape factors (e.g., habitat type, elevation). The results of this study will provide novel information on the impacts of human development on endemic lizard ecology and inform conservation efforts on the islands.

Peyton Tierney
2017 Beckman Scholar
Biology (Bioengineering)
Boston University

Exploration of a Nanoparticle-Based Bioremediation Solution for Per and Polyfluoroalkyls Substances (PFAS)

PFAS pose a unique problem to human health due their widespread uses and longevity. The development of a nanoparticle-based bioremediation solution offers a potential method of curbing the negative consequences of PFAS exposure by selectively removing these substances. We are seeking to create a molecularly imprinted polymer functionalized superparamagnetic iron oxide nanoparticle capable of selectively binding a subset of short-chain PFAS as a new and efficient method for the removal of these contaminants from solution. The design of these particles was aided by computational modeling. Future in vitro experimentation to determine the efficacy of the particles will be quantified and validated by mass spectrometry.

Elizabeth Wade
2017 Beckman Scholar
Chemistry (Biochemistry)
University of San Diego

The Use of SPR to Probe HMGB1 Binding Interactions with Cell Clearance Molecules

High Mobility Group Box 1 (HMGB1) is a small protein primarily in the nucleus of eukaryotes. Within the nucleus, HMGB1 enhances transcription by binding to the DNA and attracting transcription factors. Beyond its role in transcription, HMGB1 is also known to relocate to the extracellular matrix (ECM) in damaged cells. Ideally, HMGB1 will bind to immune receptors and help expunge infectious pathogens via proinflammatory responses. However, this is not always the case. Many studies point to HMGB1 prolonging inflammation in patients suffering from cystic fibrosis and lupus--diseases associated with defective cell clearance. What experimentation has failed to show, though, is how HMGB1 may be involved in blocking cell clearance. Therefore, the aim of this experiment is to characterize the role of HMGB1 in cell clearance which leads to prolonged inflammation.

Nicole Carrillo-Vallejo
2018 Beckman Scholar
Chemistry (Organic Chemistry)
College of William and Mary

Diels-Alder Cycloaddition/Cycloreversion Sequences: Synthesis of Substituted Pyridines from Oxazinones

This study reveals an alternative sequence for the synthesis of substituted pyridines beginning from aldehyde and azidoacetate precursors. The sequence utilizes a novel way to create oxazinones, which react with various alkynes in a [4+2] cycloaddition and r[4+2] cycloreversion process to yield 1,2 or 1,3 substituted pyridines. The complete synthesis of an ErbB4 receptor inhibitor, which is a potent inhibitor of neurite outgrowth, is described as an application to this Diels-Alder/retro Diels-Alder reaction.

Ziyan Chen
2018 Beckman Scholar
Biology (Evolution & Population Biology)
College of William and Mary

Investigations of Natural Variation in *FLO11* in the Budding Yeast, *Saccharomyces cerevisiae*

Microbes exhibit social behaviors, such as biofilm formation, in order to survive and reproduce. Biofilms are layers of aggregated microbial cells which adhere to one another and to a surface. These films afford cells a structure through which they share nutrients and communicate with each other. *S. cerevisiae* is known to form biofilms, and to engage in a form of self-recognition. The protein that mediates social behavior and recognition, Flo11p, is a pH-sensitive, membrane-anchored protein involved in cell-cell adhesion. Our study investigated natural variation in yeast biofilm mats via measurements of both pH and glucose levels at three locations on yeast biofilm mats for selected strains. We are additionally investigating the effect of natural *FLO11* alleles and specific mutations on the ability of Flo11p to interact. Interaction strength is quantified via quantitative cell aggregation microscopy, or QCAM. We find significant variation in pH gradients of biofilm mats, and presumably Flo11p functioning. Thus, future work will focus on the specifics of Flo11p-mediated social interactions.

Ariel Gale
2018 Beckman Scholar
Chemistry (Physical Chemistry)
Furman University

Catalytic Activity of Water Molecules in Gas Phase Glycine Dimerization

The dimerization of glycine is the simplest oligomerization of amino acids and plays an important role in biology. Although this reaction is thermodynamically unfavorable in the aqueous phase, it has been shown to be spontaneous in the gas phase. This may have profound implications in prebiotic chemistry, as common atmospheric prenucleation clusters are thought to have participated in gas phase reactions in the early Earth's atmosphere. We hypothesize that particular arrangements of water molecules in these clusters could lead to lowering of the reaction barrier of amino acid dimerization and lead to abiotic catalysis towards polypeptides. We test our hypothesis on a system of the cis transition state of glycine dimerization solvated by one to five water molecules using a combination of a genetic algorithm based configurational sampling, density-functional theory geometries, and domain-based local pair natural orbital coupled-cluster electronic structure. We show that the Gibbs free energy barrier for the concerted cis mechanism can be lowered by the first four water molecules, but with progressively diminishing effects.

Grayson Hamrick
2018 Beckman Scholar
Chemistry (Organic Chemistry)
Haverford College

Bioprospecting for Novel Natural Products in Ancient Non-Actinobacteria

Microbes are incredible little factories of chemicals; harnessing their productive prowess results in many of the therapeutics most commonly used today. We focused on the non-Actinobacterial strain *Gloeocapsa sp.* PCC 7428, a cyanobacterium whose genome was found to contain a putative type II polyketide synthase (PKS) biosynthetic gene cluster in a 2015 bioinformatics study. Type II PKSs produce a variety of useful chemicals, but difficulty expressing the biosynthetically vital KS-CLF in substantive amounts has limited progress. Herein we show that the *Gloeocapsa* KS-CLF can be expressed and purified in *E. coli* in exceptionally high titers. Further characterization has shown this KS-CLF to be uniquely stable under desirable laboratory conditions. Additionally, evidence from a new colorimetric assay indicates potential interactions between this KS-CLF and non-native ACPs. This presents the opportunity to mix-and-match biosynthetic pathways in a previously unexplored manner and could lead to the production of novel “unnatural natural products.” Computational methods are currently being pioneered for the future screening of reactive ACP-KSCLF partner pairs, which will subsequently guide strain selection for future wet lab work.

Brandon Lookfong
2018 Beckman Scholar
Biology (Neuroscience)
Texas A & M University

Engineering Ubx-based Fusion Proteins to Promote Growth Cone Extension Following Peripheral Nerve Injuries

The extension and reconnection of a distal nerve growth cone to a proximal nerve ending following peripheral injury requires complex biomolecular interactions and a conduit that maintains an environment complementary to regeneration. Molecules involved in this interaction are used in artificial conduits but diffuse readily when implanted. We propose the use of the *Drosophila melanogaster* Hox Protein Ultrabithorax (Ubx) because Ubx materials spontaneously self-assemble in mild buffers. This allows us to covalently attach active functional proteins at high concentrations through gene fusion. Ubx fibers have mechanical properties that can be tuned to match native nerves, they are electrically conductive, and fusion protein gradients can be made. Ubx fibers have a high affinity to Early differentiated 6J neural stem cells similar to native elastomeric extracellular proteins. Testing is underway to determine if Ubx fiber resistance to matrix metalloproteinase can be tuned since the environment post peripheral nerve injury is highly degenerative. Our early data indicates Ubx materials may be useful in the extension and guidance of the growth cone.

Kaitlin Malley
2018 Beckman Scholar
Chemistry (Biochemistry)
Boston College

Developing Better Tyrosyl-tRNAs for Genetic Code Expansion in Mammalian Cells

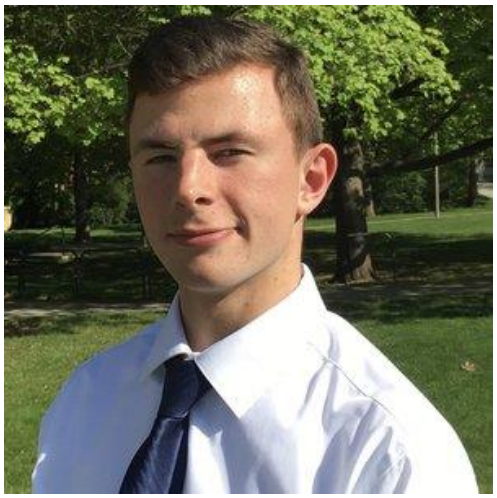
Genetic code expansion (GCE) is a technology that allows cells to site-specifically incorporate non-canonical amino acids (ncAAs) into proteins *in vivo*. Proteins containing ncAAs may have enhanced or novel activities, offering a wide variety of applications in biological systems. tRNA efficiency has been shown to be the limiting component in GCE technology, and evolution of tRNAs in mammalian cells poses several challenges. A novel platform for virus-assisted directed evolution of suppressor tRNAs (VADER) was developed to overcome these challenges by genetically encoding unnatural amino acids in adeno-associated virus (AAV). VADER was first shown to produce pyrrolysyl-tRNA variants with activity three-fold that of wild type. The platform was adapted for use with tyrosyl-tRNA variants by producing an azide-containing ncAA (LCA). LCA was genetically encoded in EGFP and AAV and expressed in HEK293T cells with two different amino-acyl tRNA synthetase variants. A mock selection was performed to demonstrate that active tRNA variants can be enriched relative to inactive variants using LCA with VADER.

Patrick McGeoghegan
2018 Beckman Scholar
Biology (Biochemistry)
Boston College

A Novel Graphene-based RNA Aptasensor for *xpt-pbuX* Riboswitch-Ligand Interactions

Riboswitches are a class of regulatory structures located in the 5' untranslated region of many bacterial mRNAs. Validating riboswitch-ligand interactions has historically been costly and low-throughput. Recently, graphene field-effect transistors (G-FETs) have emerged as effective biosensors in detecting interactions of such regulators with charged, high molecular weight analytes. However, a bottleneck still exists in detecting relatively neutral small molecules. The *Bacillus subtilis* guanine riboswitch (Xpt) within the *xpt-pbuX* operon contains a purine-responsive aptamer region with affinity for guanine, hypoxanthine, and other purine analogs. The G-FET sensor revealed successful detection of Xpt-hypoxanthine interactions at saturating concentrations. The specificity of Xpt was also demonstrated by a lack of signal detection when incubated with adenine. Therefore, such G-FET devices are effective in detecting aptamer binding to small, electrically-neutral molecules, which will allow for rapid screening of potential therapeutic ligands. G-FET riboswitch biosensors can thus provide an avenue for the discovery of novel antibiotics to combat the burgeoning antibiotic resistance crisis.

Jett Murray
2018 Beckman Scholar
Biology (Bioengineering)
University of Idaho



Evaluating the Role of Wnt/β-catenin Signaling in Tenogenic Stem Cell Differentiation

Tendon injuries are frequent and heal poorly, often resulting in long-term dysfunction. Regenerative treatments are needed, but are limited by a lack of information on how mesenchymal stem cells (MSCs) differentiate toward tendon (tenogenesis). Transforming growth factor (TGF)β2 regulates tenogenesis, and impacts levels of β-catenin and N-cadherin. β-catenin may both link cadherins to the actin cytoskeleton and translocate into the nucleus to facilitate Wnt signaling. Based on this, we hypothesized that β-catenin regulates tenogenesis in MSCs via Wnt/β-catenin signaling and cadherin interactions. To test this, MSCs were treated with TGFβ2, 6-bromoindirubin-3'-oxime (6BIO); an inactivator of β-catenin degradation, TGFβ2+6BIO, or vehicle controls. TGFβ2 significantly decreased cellular levels of β-catenin at 3 days, but levels were maintained with TGFβ2+6BIO. TGFβ2+6BIO altered tenogenic cell morphology. TGFβ2 decreased N-cadherin levels, which were not impacted by 6BIO. Immunofluorescence imaging demonstrated an increase in β-catenin nuclear translocation with TGFβ2 in 7 and 14 day timepoints. Overall, β-catenin appears to play a role in TGFβ2-induced tenogenesis. These findings improve our understanding of the β-catenin interactions in tenogenesis to advance tendon regeneration strategies.

Kartik Nath
2018 Beckman Scholar
Biology (Neuroscience)
Union College

Biomarker and cognitive improvements for MCI patients after neuro-exergaming: Pedal and play for brain health (iPACES v2.5 and 2.75)

There is a dementia epidemic that is affecting the older adult population, and researchers are exploring accessible ways to ameliorate the cognitive decline associated with Alzheimer's Disease and related dementias. Non-pharmacological interventions such as interactive physical and cognitive exercise are being investigated to understand the physiological and cognitive effects in older adults. Twenty-seven older adults were enrolled in a single-bout neuro-exergaming intervention of the interactive Physical and Cognitive Exercise System (iPACESv2.0), a neuro-exergame that consists of pedaling an under-desk elliptical while playing an interactive video game. The study explores the cognitive and biomarker outcomes in participants with mild cognitive impairment (MCI). The intervention featured a neuropsychological battery and salivary analysis to measure changes in executive function and biomarkers associated with neuroplasticity. Analyses revealed a significant increase in executive function and salivary alpha-amylase in the MCI population, suggesting cognitive improvements occurred after the intervention. This study provides encouraging preliminary support for the use of interactive exergaming interventions as clinical treatments to ameliorate the cognitive decline associated with Alzheimer's disease.

Kevin Pataroque
2018 Beckman Scholar
Chemistry (Chemical Engineering)
Case Western Reserve University

Degradation of Perfluoroalkyl Compounds by Interfacial Reactions Between an Electrolytic Non-equilibrium Plasma and Water

Advanced oxidation processes (AOPs) can degrade contaminants for water treatment. These processes create radical species such as hydroxyl radicals (OH) by ultraviolet (UV) radiation or ozonation. Currently, AOPs are expensive, energy-inefficient, and form toxic byproducts. One alternative is electrical discharges in gases or plasmas that produce UV radiation, electrons, ions, and other non-equilibrium species. The combination of species can degrade species without addition of other chemicals or catalysts.

In the first set of studies, we generated an electrolytic, atmospheric-pressure plasma at the surface of aqueous solutions containing perfluorooctanoic acid (PFOA). Our studies demonstrate that PFOA at environmental concentrations are degraded increasingly with time, with a maximum of 29% after two hours of treatment.

We examined the species in solution to understand the reaction mechanisms for PFOA degradation. By using terephthalic acid, we have developed a procedure to measure OH in solution. Using scavenger species and a split-cell reactor, we have observed these radical species, as well as their degradation capability. We hope to understand the formation pathway of oxygen-derived radical species.

Ryan Rahman
2018 Beckman Scholar
Biology
Texas A & M University

Elucidation of Polyphosphate and Phagocytosis Signaling Pathways in *Dictyostelium discoideum*

Immune cells called macrophages engulf and kill bacteria such as *Mycobacterium tuberculosis* (*Mtb*), the bacteria that causes tuberculosis. But when *Mtb* are engulfed by macrophages they prevent the macrophages from killing them. How *Mtb* causes this is poorly understood. Macrophages can be modeled by *Dictyostelium discoideum*, a soil-dwelling amoeba that engulfs and kills bacteria. *Mtb* requires chains of phosphates called polyphosphate to survive in macrophages, and we found that polyphosphate acts as an extracellular signal to prevent *Dictyostelium* from killing ingested bacteria. I found that to sense the polyphosphate signal, *Dictyostelium* cells do not need the Ras family proteins RasC and RasG, polyphosphate kinase Ppk1, TORC2 subunit PiaA, PI3K proteins PikA and PikB, arrestin protein AdcC, and G-protein components Gα3 and Gβ. However, two proteins were needed for *Dictyostelium* to sense polyphosphate. Pharmacological inhibition of either of the human homologs of these two proteins might prevent macrophages from sensing the polyphosphate signal from *Mtb*, and thus allow them to kill engulfed *Mtb*.

Alice Sardarian
2018 Beckman Scholar
Biology (Systems Biology)
Barnard College

Age of Alcopops: Understanding the Impact of Flavorants on Adolescent Alcohol Consumption

High-risk alcohol use leads to nearly 50,000 annual deaths amongst underage consumers. To reduce the aversive sensory qualities of ethanol—i.e., bitter taste, aversive odor, and burning sensation—beverage manufacturers often mix it with sweet flavorants. We sought to determine whether these flavorants would enhance the flavor and intake of ethanol in adolescent rats. Experiment 1 evaluated rat licking responses to various flavored ethanol solutions during brief-access lick tests. Rats initiated licking more quickly and at higher lick rates for flavored than unflavored ethanol, indicating that the flavorant improved the naso-oral sensory attributes of ethanol. Experiment 2 examined voluntary consumption of the same solutions over 8 days. Rats consistently consumed more flavored than unflavored ethanol. Following this exposure period, rats were offered unflavored ethanol for three additional days. Their daily ethanol intake dropped precipitously. Thus, sweet flavorants increase ethanol intake in adolescent rats by improving its flavor.

Jamison Takashima
2018 Beckman Scholar
Chemistry (Biochemistry)
University of Arizona

APEX2-Mediated Proximity Labeling in Dictyostelium discoideum

Characterizing the signaling mechanisms controlling directed cellular migration, or chemotaxis, is critical for understanding and combating the spread of metastatic cancer. Dictyostelium discoideum is an excellent model organism for the study of chemotaxis due to its powerful chemotactic response to the signaling molecule cAMP. However, methods for the identification of new protein-protein interactions in Dictyostelium's signaling pathways are limited. Here, we describe an optimized protocol for proximity labeling in Dictyostelium using the engineered ascorbate peroxidase APEX2. This protocol was adapted from existing APEX2 procedures developed for mammalian cells and demonstrates that in Dictyostelium, cell permeabilization is required for APEX2-mediated labeling. These preliminary findings pave the way for large-scale studies of chemotactic signaling networks in Dictyostelium. The described research was supported by the National Institutes of Health (NIH) under award number R01GM131200-01A1, the American Cancer Society under award number 127940-RSG-15-024-01-CSM, and the Arnold and Mabel Beckman Foundation.

Brooke Van Wyk
2018 Beckman Scholar
Biology (Molecular & Cell Biology)
Hope College

Post-hatch Ontogeny of Melanopsin Gene Expression in the Brain of Breeder Ducks.

The hypothalamic-pituitary-gonadal axis (HPG) is known to be regulated by daylength through the deep brain photoreceptor (DBP) system. DBPs are known to respond to light and to activate the HPG via a pathway that involves the thyroid axis. The thyroid axis has numerous functions not only for reproduction, but also for post-hatch neuronal and somite development. It is currently unknown if thyroid axis activity during posthatch development is influenced by DBPs, nor is the posthatch ontogeny of any of the DBPs known. We set out to determine the ontogeny of OPN4 and OPN5 gene expression relative to GnRH and GnIH using qRT-PCR. Data were analyzed between sexes at each age using an independent T-test. Interestingly, results showed that on the day of hatch (Day 0) ducks showed adult-like levels of relative OPN4 gene expression but not again until week 19. OPN5 maintained low levels until week 10, as did GnRH. GnIH maintained constant levels at all ages. These observations suggest that DBPs may have differential functions depending upon the age of the duck.

Ana Verma
2018 Beckman Scholar
Biology (Neuroscience)
Amherst College

Exploring inner ear phenotypes of Nfe2 Δ/Δ KO zebrafish larvae and their response to oxidative stress

Oxidative stress caused by factors like aging and loud noise induces damage in hair cells, the sensory receptors of the ear. Nfe2, a transcription factor recruited in the oxidative stress response (OSR) is expressed in the larval zebrafish inner ear. This project aimed to explore the effects of oxidative stress and *nfe2* loss on the function of hair cells in the larval zebrafish ear. To assay whether mechanotransduction was disrupted, we recorded ear microphonics and quantified FM1-43 (fluorescent dye) uptake by hair cells both at basal conditions and after exposure to a pro-oxidant. Given that *nfe2* morphants show abnormalities in ear development, we hypothesized that without the potentially protective and developmental cues from Nfe2, microphonics and FM1-43 labeling in the Nfe2 KO would be reduced. Our preliminary data showed that at basal conditions, microphonics and FM1-43 levels in the KO were similar to those in WT controls. However, because Nfe2 is involved in the OSR, we anticipate that these phenotypes may be revealed after pro-oxidant exposure. Future work will assess the larvae following oxidative stress.

Catherine Weibel
2018 Beckman Scholar
Biology (Evolution & Population Biology)
University of Arizona

More Exquisitely Adapted Species Have Higher Structural Disorder in Vertebrate Protein Domains

Protein structural disorder helps avoid misfolding and aggregation, but in impeding protein folding might also impede function. The balance between these two selective pressures on protein biophysics might vary among species as a function of the effectiveness of weak selection. We predicted the Intrinsic Structural Disorder (ISD) of Pfam domains across 118 fully sequenced vertebrate species and estimated the effect of species identity on to control for differences in Pfam composition across species. We compared this to each species' Codon Adaptation Index of Species (CAIS), a metric we developed to quantify for effectiveness of selection from synonymous codon usage, corrected for total genomic GC content and amino acid composition, to be comparable across species. Simple correlations between ISD and CAIS indicate that well-adapted species tend to have high ISD. To correct for phylogenetic confounding and resulting pseudoreplication, we transformed CAIS and ISD species effect data using Phylogenetic Independent Contrasts (PIC). Phylogenetically controlled linear models confirmed that better-adapted species have higher ISD, indicating selection for higher disorder across protein domains of vertebrate species.

Shoshana Williams
2018 Beckman Scholar
Chemistry (Biochemistry)
Barnard College

Investigation of Fused-Rubredoxin AlkBs

Alkane monooxygenase (AlkB) enzymes play a critical role in the global carbon cycle by catalyzing the conversion of linear alkanes to terminal alcohols. AlkB proteins have different subunit structures, including one in which AlkB is covalently bound to an essential electron transfer partner, a rubredoxin. This class of AlkB enzymes is called “fused-rubredoxin” AlkBs. An exploratory bioinformatic analysis was performedyan to examine the distribution of fused-rubredoxin AlkBs across bacterial species. One fused-rubredoxin AlkB was cloned from the bacterial species *Dietzia cinnamea* and expressed in *E. coli*. Its activity on alkane and alkene substrates was tested in a partially purified system and compared to an AlkB without a fused rubredoxin, cloned from *Alcanivorax borkumensis*. The *alkB* gene from *D. cinnamea* was truncated and expressed in *E. coli* to examine the activity of this AlkB with and without the rubredoxin domain. The point mutation V91W was made in the full-length *alkB* from *D. cinnamea* to examine the effect of a single amino acid residue on protein activity.

Katherine Yan
2018 Beckman Scholar
Chemistry (Chemical Engineering)
Case Western Reserve University

Investigation of the Antifouling Properties of Polyproline Self-Assembled Monolayers on Biomaterial Surfaces – Towards Preventing Post-surgical Adhesions

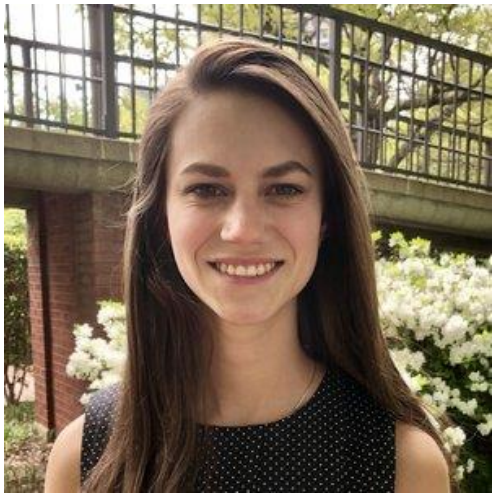
Biofouling is a major concern for the surfaces of medical devices and biosensors. The goal of this research was to quantify protein adsorption onto polyproline to determine its capabilities in preventing biofouling on those surfaces. A quartz crystal microbalance with dissipation (QCM-D) was used to measure the protein adsorption onto a gold sensor functionalized with a polyproline self-assembled monolayer. The adsorption of bovine serum albumin (BSA) and human plasma fibrinogen onto the coating was measured by examining the change in frequency shift, which is directly proportional to the change in mass. The measured change in frequency due to BSA adsorption was approximately ten times less on a polyproline SAM than on bare gold.
The change in frequency due to fibrinogen adsorption was reduced by 73% compared to bare gold. The data indicate that polyproline has the potential to repel proteins and therefore reduce biofouling. Moreover, the use of polyproline demonstrates that peptides can be used to further examine properties of antifouling surfaces, as different modifications of this peptide can be tested using this methodology.

Sahar Amin
2019 Beckman Scholar
Chemistry (Organic Chemistry)
San Francisco State University

Chemical investigation of a new meroterpenoid produced by the deepwater sediment-derived *Streptomyces* sp. CP55-76

Our group has investigated the cytotoxic secondary metabolites with significant prostate cancer selectivity produced by the deepwater sediment-derived *Streptomyces* sp. CP55-76. Up to date, we have isolated a new naphthoquinone meroterpene (**1**) together with a series of known napyrodiomycin derivatives from a non-polar fraction (80% MeOH in water) obtained from reversed-phase flash column chromatography. In order to further investigate the non-polar fraction as well as polar fractions, we have initiated a scale-up culture (90 L) for the strain CP55-76. The organic extract obtained from the culture was separated into five fractions (20%, 40%, 60%, 80%, 100% MeOH in water) through reversed-phase flash chromatography. UV chromatogram-guided high-performance liquid chromatography (HPLC) separation of the 80% MeOH fraction and the 40% MeOH fraction led to isolation of two new meroterpenoid designated as arromycin B (**2**) and arrophenazine A (**3**), respectively. The strictures of the two new meroterpenoids have been firmly determined on the basis of spectroscopic methods. The details of the isolation methods and structure elucidation of **2** and **3** will be seen in this presentation.

Alicia Caughman
2019 Beckman Scholar
Biology (Microbiome, Proteomics & Metabolomics)
Georgia Institute of Technology



Coral microbiome changes over the day-night cycle

Host microbiomes play important roles in coral health and metabolism; therefore, it is critical to understand factors that change the microbiome, such as daily fluctuations in environmental conditions. For certain parameters (temperature, pH), the magnitude of diel fluctuation can exceed that observed in mean values over seasons, especially on shallow reefs. Such short-term environmental heterogeneity can affect long-term trends, possibly influencing the extent of acclimatization to stress. This study examined diel microbiome dynamics in three coral species (*Porites lutea, Porites cylindrica*, and *Pocillopora damicornis*) from a shallow reef in Mo'orea. We assessed microbiome taxonomic composition and relative transcriptional activity using 16S rRNA genes and transcripts from six time points over 48 hours for each coral species. Results showed that both community composition and relative transcriptional activity change over a diel cycle, possibly driven by environmental conditions and/or stochastic effects of low abundance members. These results also identify specific microbes for future studies of host-microbe interaction and confirm that daily variation should be considered when designing studies.

Ryan Clark
2019 Beckman Scholar
Biology (Bioengineering)
University of Virginia

Immunogenicity of Focused Ultrasound Thermal Ablation in Metastatic Breast Cancer

Ryan A. Clark[1], Natasha D. Sheybani[1], Alexander S. Mathew[1], Richard J. Price[1]
[1] Department of Biomedical Engineering, University of Virginia, Charlottesville, VA

Focused ultrasound (FUS) is a non-invasive, non-ionizing technique for tumor damage and destruction. Its thermal bioeffects have been demonstrated to elevate immunological activity against breast cancers, suggesting that it may augment other immunotherapy regimens. In this study, we sought to determine whether FUS thermal ablation of murine breast cancer cells *in vitro* increases their immunogenicity and primes an anti-tumor immune response.

FUS treatment decreased cell viability *in vitro* in FUS-treated 4T1 breast cancer cells compared to 4T1 cells that received sham treatments at 0 and 8 hours. Priming mice with 4T1 cells thermally ablated with FUS significantly extended overall survival after tumor challenge. Future directions will evaluate whether this improvement in mouse survival following priming with FUS-treated cells is linked to decreased metastatic burden in the lungs and/or immune-mediated control therein.

Acknowledgements: Supported by the Arnold and Mabel Beckman Foundation.

Shaoni Dasgupta
2019 Beckman Scholar
Biology (Genetics)
Clemson University

Carnitine Acetyltransferases Influence the Virulence of the Fungus *Cryptococcus neoformans*

Cryptococcus neoformans, an invasive pathogen of the CNS, is the most frequent cause of fungal meningitis. Acetyl-CoA is essential for numerous cellular and biosynthetic processes, and defects in its synthesis and utilization display reduced virulence in *Cryptococcus*. For utilization, the amphiphilic acetyl-CoA must be transported into the mitochondria. Carnitine Acetyltransferases (Cat) play a key role in the export of acetyl units from the cytosol into the mitochondria. Three open reading frames (CNAG_00537, CNAG_06551, CNAG_05042) that could encode for Cat have been identified in the *C. neoformans* genome. Gene knockout mutants of CNAG_00537 and CNAG_06551 are unable to grow on acetate as a carbon source, as would be expected for a Cat mutant. Preliminary results indicate both knockout mutants have reduced survival in macrophages, suggesting a role in virulence for both Cat enzymes. We are generating a gene deletion of CNAG_05042 using Crispr-Cas9 gene editing. As proof of principle, we used the TRACE system to disrupt the Ade2 gene locus. Further characterization of these knockout mutants will elucidate the role of Cat in *C. neoformans* pathogenesis.

Alexis Davison
2019 Beckman Scholar
Biology (Biochemistry)
Pennsylvania State University

Identification and Characterization of Inhibitors of *trans*-Translation

The global phenomenon of antibiotic resistance is projected to lead to more deaths than cancer, by 2050. This powerful reality results from pathogens surviving in the presence of antibiotics and spreading their resistant mechanisms within their population. This work targets *trans*-translation for novel antibiotic development. It is an essential pathway in many bacterial pathogens that rescues stalled ribosomes during translation due to the formation of nonstop complexes. These form when no stop codon is present at the 3' end of an mRNA message. This disables the termination of the message needed to produce a functional protein. If *trans*-translation is activated, its main machinery, tmRNA and SmpB protein, identifies the stalled ribosome and tags the protein for degradation. The project focused on identifying and characterizing inhibitors of *trans*-translation, specifically, since these would promote cell death. Efforts to outline the molecular mechanisms occurring during *trans*-translation were explored via ribosome profiling in *Caulobacter crescentus*. Advancement in these endeavors will aid in the movement to combat antibiotic resistance.

Jasmine Esparza
2019 Beckman Scholar
Biology (Molecular & Cell Biology)
University of California, Los Angeles

Investigating the Role of cAMP-Dependent G-Protein Coupled Receptor (GPCR) Cellular Signaling in the Murine Hair Cycle

Hair follicle stem cell (HFSC) activity is partially responsible for maintaining the homeostasis of the hair follicle. The mechanism that gives HFSCs the ability to regulate the hair cycle is not understood. HFSCs were shown to be an origin of cutaneous squamous cell carcinoma (cSCC) in mice. Canonical G-protein coupled receptor (GPCR) signaling has been implicated in SCC progression through the cAMP-response element-binding (CREB) pathway. In this study, GPCR signaling was manipulated to study HFSC homeostasis and hair cycle regulation. Literature has shown that ablation of CREB, a transcription factor downstream of cAMP signaling, inhibits skin papilloma formation. Emerging work has shown that topically applied small-molecule drugs can accelerate the hair cycle via GPCR/CREB signaling. The mechanism that explains how upregulated pCREB expression induces hair cycle acceleration is not yet known. Here, I show work that aims to characterize this mechanism. We hypothesize that pCREB induces metabolic changes that activate HFSCs and thus, induce hair cycle activation. This relationship was defined by analyzing gene and protein expression as well as metabolic enzyme activity.

Lucas Frye
2019 Beckman Scholar
Chemistry (Inorganic Chemistry)
University of Virginia

Synthesis of Stilbenes by Rhodium-Catalyzed Aerobic Alkenylation of Arenes via C–H Activation

Arene alkenylation is commonly achieved by late transition metal-mediated C(sp^2)- C(sp^2) cross-coupling, but this strategy typically requires pre-functionalized substrates and/or the presence of a directing group on the arene. Transition metal-mediated arene C–H activation and alkenylation offers an alternative method to functionalize arene substrates. This project is centered on the development of a rhodium-catalyzed oxidative arene alkenylation from arenes and styrenes to prepare stilbene and stilbene derivatives. Our methodology improves upon existing synthetic routes because it does not require the use of labile functional groups or directing groups to achieve good yields and selectivity, improving step efficiency and atom economy. The reaction is successful with several different functional groups on the arene and the olefin. Reactions of mono-substituted arenes are selective for alkenylation at the *meta* and *para* positions, with approximately 2:1 *m*:*p* selectivity. Two compounds with reported pharmaceutical properties, resveratrol and *(E)*-1,2,3-trimethoxy-5-(4-methoxystyryl)benzene (DMU- 212), are synthesized by this single step approach in high yield.

Kathleen Imbach
2019 Beckman Scholar
Biology (Bioinformatics)
Georgia Institute of Technology

Understanding the Effect of Induction Therapy for Pediatric ALL One Single Cell at a Time

In order to understand how immune and leukemic cells are affected by induction in pediatric ALL, we performed a pilot investigation utilizing single-cell RNA-sequencing (scRNA-seq) on the 10X Genomics Chromium platform. Samples from seven patients were collected, four of whom exhibited measurable residual disease (MRD) after induction, and three patients who did not. Leukemic cells were separated from peripheral immune cells using flow cytometry and ~1000 single cells were sequenced from peripheral immune cells before treatment, peripheral immune cells after treatment, leukemic cells before treatment, and leukemic cells after treatment. The goal of this study was to discern how the immune and leukemic cell populations and gene expression vary both before and after treatment and between those patients who did or did not respond to induction. Our results highlight a comparative increase in erythrocytic cell populations in MRD-negative patients while MRD-positive patients demonstrated higher levels of T cell populations. This work also demonstrates that leukemic cells resistant to therapy tend to have gene signatures of cell activation, immunological responses and resistance to cell death.

Angelica Lang
2019 Beckman Scholar
Biology (Molecular & Cell Biology)
University of Kansas

The Role of Basement Membrane Proteins for Proper Q Neuroblast Migration in *C. elegans*

Neuronal migration is crucial for proper nervous system development. In *C. elegans*, neuronal migration can be modeled in the two Q neuroblasts, QR and QL. They originate in approximately the same location in the worm but, during development, QR migrates anteriorly and QL migrates posteriorly. DPY-17 and SQT-3, collagen proteins found in the cuticle and basement membrane of the worm, were recently identified to influence the direction of Q cell migration. My work suggests that collagen heterotrimers of DPY-17 and SQT-3 within the basement membrane provide directional information to the migrating neuroblasts, likely through an interaction with the known Q cell receptor PTP-3. This hypothesis is supported by the finding that Q neuroblast migration is dependent upon other structural basement membrane proteins such as type IV collagen and laminin as well as basement membrane components such as perlecan and hemicentin. My work suggests that structural components in the basement membrane serve not only as a substrate for migrating neurons, but also influence the direction of migration.

Vennela Mannava
2019 Beckman Scholar
Chemistry (Organic Chemistry)
University of Chicago

Carbon dioxide utilization in plastic production: Development of a nickel catalyst

Carbon capture and utilization (CCU) aims to incorporate atmospheric CO_2 into commodity chemical syntheses. An attractive target is sodium acrylate, the building block of superabsorbent sodium polyacrylate found in many common goods. Researchers have sought a reaction coupling CO_2 and ethylene, which could produce acrylate from sustainable starting materials. Nickel catalysts have shown promise for enabling this coupling but suffer from low efficiency, due to a nickelalactone intermediate with a stable ring structure that resists the release of sodium acrylate from the catalyst. My project aims to develop supporting ligands that provide appropriate steric bulk and electron density to the nickel center to promote nickelalactone ring-opening. Current work focuses on N-heterocyclic carbene (NHC) ligands, which are very electron-donating and highly modular. Preliminary experiments support the instability of a simple bis(NHC) nickelalactone. Computational investigation of other systems with varying electronic and steric properties also helps to inform ligand design. These NHC ligands could be the key to efficient nickel catalysts coupling CO_2 and ethylene for sodium acrylate production, thus contributing to global CCU efforts.

Nathan Matzko
2019 Beckman Scholar
Biology (Genetics)
Clemson University

Novel Functions of Human SSB1 and SSB2 in Homology Directed Repair

Double-stranded DNA breaks (DSBs) are the most deleterious form of DNA damage sustained by the cell. Unrepaired DSBs are lethal, and misrepair may lead to cell death and genomic instability. To repair DSBs with high fidelity, cells utilize the homologous recombination (HR) pathway, which repairs DSBs by utilizing a homologous DNA template for accurate repair. Successful DSB repair through HR is dependent on the catalytic activities of the recombinase RAD51 and its presynaptic filament, which are tightly regulated by various accessory proteins, such as single-stranded binding proteins (SSBs). Throughout HR, SSBs are responsible for protecting ssDNA from nuclease degradation, preventing the formation of secondary structure, and recruiting HR proteins. Human SSB1 and SSB2 are SSBs that previously have been implicated in the DNA damage response but remain uncharacterized in HR. Here, we present novel evidence that both hSSB1 and hSSB2 catalyze homologous DNA pairing and strand invasion activities, which suggests their potential significances in HR.

Silas Miller
2019 Beckman Scholar
Biology (Synthetic Biology)
Whitman College

ShadowAuxin: Optimization of Quenching FRET Pairs for a Fluorescent Auxin Biosensor

Auxin is a hormone crucial in many aspects of plant growth and development. Advancing our understanding of auxin signaling may provide needed tools for agricultural scientists to help feed a growing population in the face of global climate change. However, existing auxin biosensors have significant shortcomings that limit their utility in plants. We are building and testing a novel auxin biosensor, ShadowAuxin, to address these shortcomings. Our design relies on dimerization of two fluorescent proteins capable of Forster Resonance Energy Transfer (FRET). Our biosensor utilizes a quenching fluorescent protein in the FRET pair; when this quenching FRET pair are held in proximity by fused dimerization domains, the fluorescent signal dims. Pilot experiments in yeast have revealed the importance of dimer-domain choice and controlled expression levels. New inducible promoters have enabled us to control expression levels of each component of the biosensor to maximize FRET quenching. Next, we will increase FRET efficiency with new heterodimerization domains. Ultimately, this FRET system will be coupled with an auxin-sensing domain to generate a rapidly-responding biosensor with wide dynamic range.

Alexandra Moore
2019 Beckman Scholar
Biology (Medical Sciences)
Whitman College

Differences in cardiac mitochondria in conditions of exercise stress versus heart attack

The energetic demands of the constant work the heart must maintain means that cardiomyocytes have large populations of mitochondria. Changes in these essential organelles have major implications for the heart and its ability to function. After a myocardial infarction occurs, there is an onslaught of cell and tissue damage in the heart. The process of mitochondrial fission that occurs due to these hypoxic conditions results in cell death, toxin productions, inflammation, and reduced mitochondrial function. While hypoxia-induced fission can be highly pathological, it has also been shown to be beneficial in another low-oxygen condition: exercise. In this context, physiological-induced fission improves mitochondrial oxygen consumption, energy production, and leads to an overall increase in exercise capacity. Because the same process occurs during a heart attack and exercise but results in different outcomes, we sought to determine how the mitochondria's morphology, membrane potential, and viability changed with exercise or heart attack simulation.

Emi Nakahara
2019 Beckman Scholar
Biology (Immunology, Virology & Infectious Disease)
University of California, Los Angeles

Exploring Roles of Flagellar Proteins in Signaling of *Trypanosoma brucei*

Trypanosoma brucei is a protozoan parasite endemic to Sub-Saharan Africa, where it causes sleeping sickness in humans and nagana in cattle. *T. brucei* uses its flagellum to sense its environment as it traverses different hosts, but mechanisms driving this sensing remain poorly understood. Our lab has found that Social Motility (SoMo), the ability of *T. brucei* to move in a coordinated manner on surfaces, may be modulated by cAMP signaling at the flagellar tip. We knocked down three proteins localized at the tip (SRR 60, SRR 70, and HP400) to investigate their possible role in modulating SoMo. Data suggest that reduction of HP400 affects the proliferation rate of the parasite, but does not affect SoMo. In addition to the flagellum tip, we are interested the BBSome, a protein complex at the flagellar base that controls trafficking signaling proteins in and out the flagellum. We used APEX2-proximity proteomics and identified multiple protein candidates that are likely assisting the BBSome with this trafficking process, such as intraflagellar transport proteins; their functional analysis remains pending.

Benjamin Neubert
2019 Beckman Scholar
Biology (Systems Biology)
University of Virginia

Optimizing the Biosynthesis of Therapeutic Compounds in *E. coli* using Computational Modeling

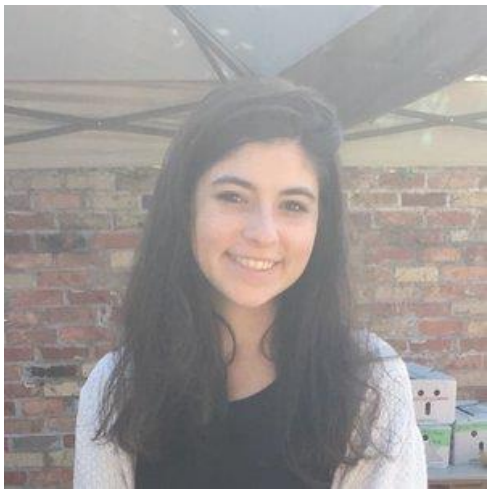
Genome-scale metabolic network reconstructions (GENREs) are a powerful computational tool for mathematically modeling the metabolic processes within a cell at a systems-level. The development of improved curation methods through strategic data integration would improve our ability to use GENREs to understand metabolic diseases and to inform metabolic engineering. To this end, we developed a novel data-driven GENRE curation pipeline using a combination of well-established packages and experimental data. Production sub-networks were created using weighted parsimonious flux balance analysis with different objective functions based upon single products across candidate media conditions with varied carbon sources. We were able to generate a prioritized list of media conditions that induced the greatest variation among ensemble members, representing the conditions for which gathering metabolomics data would be most informative. The resulting data-driven GENRE was applied to determine the optimal dietary input for the generation of therapeutic compounds by *E. coli* K-12. This study developed a novel data-driven GENRE curation pipeline for determining the optimal biosynthesis of therapeutic compounds with reduced uncertainty in network structure and increased curation efficiency.

Jeffrey Rasmussen
2019 Beckman Scholar
Biology (Neuroscience)
University of Connecticut

Investigating the Role of Adipose Tissue in the Prognosis of Amyotrophic Lateral Sclerosis

Motor neuron diseases such as amyotrophic lateral sclerosis (ALS) and spinal muscular atrophy are devastating diseases often result-ing in premature death of patients. While several mutations have been associated with ALS, the exact pathogenesis underlying the disease remains unclear. One such mutation is the mutation of the nuclear localization signal of the Fused in Sarcoma protein, which has been shown to result in its aggregation in the cytoplasm of juvenile-onset ALS patients. Normally, FUS is also found in the nucleus, where it regulates minor intron splicing, but mutated FUS aggregates sequester the minor spliceosome components U11 and U12 small nuclear RNA (snRNA) to the cytoplasm. To test whether loss of minor spliceosome function contributes to the pathology observed in patients with juvenile-onset ALS, we inhibited the minor spliceosome by ablating U11 snRNA at postnatal day 15. In comparison to their wildtype counterparts, these mutant mice die prematurely and weigh significantly less. Moreover, mutant mice show motor impairments, as indicated by an altered gait and increased hindlimb clasping.

Megan Rodriguez
2019 Beckman Scholar
Chemistry (Biochemistry)
University of Chicago



Nanoscale Coordination Polymers for Peptide Delivery and Synergistic Cancer Therapy with Immune Checkpoint Blockade

Nanoscale coordination polymers (NCPs), composed of metal ions coordinated to polydentate ligands in the core and surrounded by an asymmetric lipid bilayer shell, are a novel class of cancer nanomedicines which overcome drawbacks of many current therapeutic delivery systems owing to their tunable sizes, enhanced bioavailability, and increased circulation time. The NCP delivery system has not yet been utilized for peptide therapeutics. This project focuses on expanding the use of the NCP platform to peptide therapeutics in order to overcome previous limitations of using free peptides as therapeutics, as they have poor stability and short half-lives. The NCP platform was optimized to encapsulate a small peptide targeting MUC1, a protein overexpressed in various carcinomas with downstream signaling effects which influence cell proliferation and survival. The NCP-peptide was studied both *in vitro* and *in vivo,* and determined to induce toxicity and influence protein expression, specifically expression of PD-L1, more effectively than the free peptide. In addition, anti-tumor efficacy results suggest that the NCP-peptide combined with anti-PD-L1 may be a promising method to treat carcinomas.

Bradley Scholten
2019 Beckman Scholar
Biology
Calvin University

Unmanned aerial vehicles do not affect tree swallow stress responses

Visual and acoustic disturbances can cause physiological stress in animals. Human-induced stress may be particularly problematic for birds as new technologies, such as drones, increasingly invade their air space. Although drone usage is increasing rapidly, there is little information on how drones affect avian behavior and physiology. We examined the effects of drone activity on behavior and physiology in adult, box-nesting tree swallows (*Tachycineta bicolor*). We monitored bird behavior during drone flights and in response to a control object, and measured telomere lengths and corticosterone levels as indicators of longer-term physiological stress. Swallows responded more aggressively towards drone presence than a control object, but were slower to approach the drone initially and more reluctant to use nest boxes during drone activity. Swallows also habituated to the presence of the drone and control object at similar rates. Drone activity did not affect telomere length, corticosterone levels, mass, or fledging rates. Our results indicate that a small number of short, targeted, drone flights do not impact tree swallow health or productivity differently than a non-invasive control object.

Ekaterina Skaritanov
2019 Beckman Scholar
Biology (Neuroscience)
University of Connecticut

ETS-domain transcriptional regulators Pnt and Yan control Mmp2 expression and follicle rupture in *Drosophila*

From flies to mammals, follicle rupture requires proteolytic remodeling to liberate a mature oocyte from its surrounding layer of somatic follicle cells. During the last stage of oogenesis in *Drosophila* (stage 14), activation of the protease matrix metalloproteinase 2 (Mmp2) elicits degradation of posterior follicle cells and subsequent rupture of the oocyte out of its follicular epithelium into the oviduct below. It remains unknown what signaling mechanisms regulate precise spatiotemporal expression of Mmp2 in posterior stage-14 follicle cells. Here we identify a novel role for the transcriptional activator Pointed (Pnt) and its endogenous repressor Yan in regulating Mmp2 expression and follicle rupture. Pnt is localized to posterior follicle cells throughout late oogenesis while expression of Yan is rapidly downregulated at stage 14. Both the expression of Pnt and downregulation of Yan in stage-14 is required for proper follicle rupture and ovulation. Furthermore, a novel source of Mmp2 expression is identified in the calyx region of the oviduct, which is sufficient to compensate for ovulation when follicular Mmp2 is depleted.

Jonah Stiel
2019 Beckman Scholar
Chemistry
University of Kansas

Unexpected Reactivity During Synthesis of New 4,5-diazafluorene Ligands

Organometallic catalysis represents a promising means of economically converting carbon dioxide (CO_2) waste into carbon monoxide (CO), an important industrial feedstock. Tricarbonyl metal diimine complexes have demonstrated the desired reactivity and are competent electrocatalysts for this conversion in many cases. Complexes bearing the 2,2´-bipyridyl moiety have been extensively investigated, yet many details of their catalytic mechanism(s) are poorly understood. The prevailing theory suggests that CO_2 must interact simultaneously with both the metal center and the diimine ligand for catalysis to occur. It was envisioned that the instillation of steric bulk on a bipyridine analogue, 4,5- diazafluorene (daf), may function as a strategy for probing the proposed mechanism. 4,5- diazafluorene (daf) offers the interesting opportunity to install steric bulk perpendicular to the plane of the aromatic ring system via derivatization of the daf framework at the “9” position. The synthesis of daf-based compounds will be discussed, including details of unexpected reactivity encountered during preparation of the planned derivatives of daf.

Jacob Watts
2019 Beckman Scholar
Biology (Plant, Ecology & Environmental Sciences)
Colgate University

A case study on the epiphyte *Asplenium australasicum* and climate change

Asplenium australasicum is a basket forming epiphyte (a plant that grows on other plants) which thrives in the coastal forests of eastern Australia and helps regulate the canopy microclimate and forest nutrient cycling. Its habitat is seasonally dry but its basket forming morphology allows *A. australasicum* to capture rainfall and leaf litter during long periods of drought while also harboring approximately 50% of the arboreal insect diversity. However, even considering such adaptation, its distribution is predicted to change as a result of climate change. To determine the physiological limitations of this keystone epiphyte species and the resultant effects of climate change, each part of its lifecycle must be considered in light of a changing climate. This project examines the stress physiology of the entire development of *A. australasicum*, from the small, single cell-layer thick gametophyte lifestage to the large, vascularized sporophyte lifestage. Findings indicate that increased temperatures will drastically inhibit gametophyte growth while both immature and mature sporophytes are strongly drought tolerant, suggesting that the gametophytes will be most affected by climate change.

Katherine Xia
2019 Beckman Scholar
Biology
Santa Clara University

Greening Polymer Coupling Reactions Using Benign Reducing Agents and Radical Traps

Atom transfer radical coupling (ATRC) has proven to be an effective way to transform halogenated polymer chains into new structures, such as macrocycles. These structures have numerous applications, including light harvesting and drug delivery. However, ATRC reactions face barriers in being implemented on an industrial scale due to its reliance upon transition metal catalysts, which are costly, environmentally harmful, and difficult to dispose of. One method of significantly reducing the amount of metal used in atom transfer reactions relies on activators generated by electron transfer (AGET). In AGET, an environmentally benign reducing agent, such as L-ascorbic acid, can be used to generate and then continuously regenerate the active metal catalyst from its more oxidatively-stable state. In this work, AGET was combined with a radical trap assist (RTA) in ATRC reactions to couple end-brominated polymers of major vinyl polymer classes: polystyrene, poly(methyl methacrylate) and poly(methyl acrylate). This process, AGET-RTA-ATRC, minimized the total metal content used by more than 97% of what was being used in standardized reactions.

Taylor Yount
2019 Beckman Scholar
Biology (Biochemistry)
Pennsylvania State University

Vibrio fischeri Responds to Autoinducers Produced by Neighboring Populations in the Squid Light Organ

Animals form long-term, intimate associations with bacteria that express specific traits that promote normal host physiology. Many bacterial symbionts associate with host epithelial tissue, thereby creating a microscopic ecosystem. The extent to which bacterial symbionts impact the physicochemical properties of this ecosystem remains poorly understood. To address this question, we examined the symbiosis between the bacterium *Vibrio fischeri* and the Hawaiian squid *Euprymna scolopes*. *V. fischeri* cells colonize several habitats within the host, and the resulting populations produce bioluminescence that camouflages the squid from predators. Intercellular signaling mediated by small molecules called autoinducers that are synthesized by *V. fischeri* induces bioluminescence production. Autoinducer binds to a receptor that activates transcription of the genes necessary for bioluminescence. Using a transcriptional reporter for these genes, we found that transcription is activated in each bacterial population *in vivo* by neighboring populations, suggesting that autoinducers diffuse across host tissues and affect multiple bacterial habitats. This finding suggests that the chemical composition of a bacterial habitat is influenced by the signals produced by symbionts located elsewhere in the host.