Microbial Sciences 22nd Annual Symposium

Friday, November 7, 2025

Symposium Program

1:00 – 2:40 pm	**Session 1 speakers**

Kazuki Nagashima – Assistant Professor, Department of Molecular and Cellular Biology, Harvard University

High Resolution View of Immune Modulation by the Gut Microbiome and Diet

Speaker Bio:

Kazuki Nagashima grew up in Tokyo, Japan. His childhood experience with food allergies drove his interest in the gut immune system and motivated him to go to medical school at the University of Tokyo, where he was inspired by a *Clostridium difficile* infection caused by dysbiosis of the microbiota. He was fascinated by the mysterious intestinal ecosystem in which the immune system permits diet and microbiome and eliminates pathogens.

To learn immunology research, he did his Ph.D. in the Hiroshi Takayanagi Lab at the University of Tokyo. He addressed a longstanding question in the host-microbe interaction – how antigens of the microbiome are recognized by the host's immune system and initiate an IgA response. He discovered a previously uncharacterized mesenchymal cell subset that induces epithelial microfold (M) cells and promotes the antigen-specific IgA response.

To explore the host-microbiome interaction from a microbial perspective, he joined the Michael Fischbach Lab at Stanford University as a postdoc, where he developed a new technology to understand the high-resolution view of immune modulation by the gut microbiome.

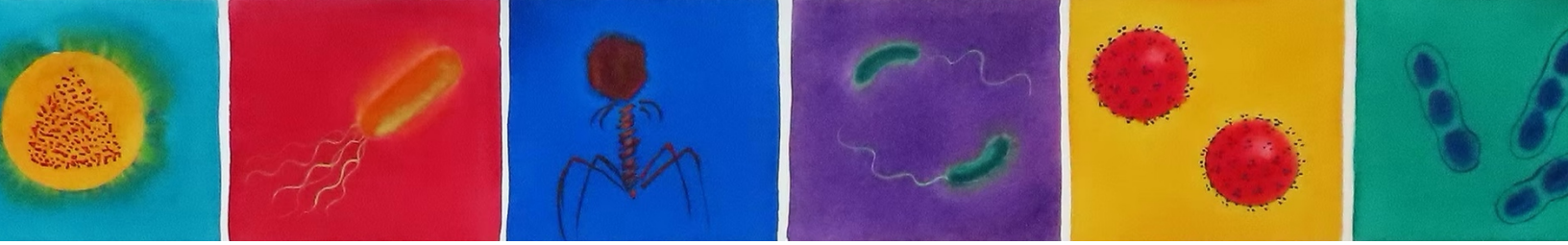
In 2024, he joined the Department of Molecular and Cellular Biology at Harvard University as an Assistant Professor. The Nagashima Lab aims to understand human immunology, microbiome, and diet at the level of molecular mechanisms.

Ben Taylor – Associate Professor,
Department of
Organismic & Evolutionary Biology and the
Arnold Arboretum, Harvard University

The microbes that mediate soil carbon responses to warming temperatures

Abstract:
Surface soils represent the largest active carbon pool on Earth, globally holding more carbon than the atmosphere and vegetation combined. So, even small proportional changes to the inputs and outputs of soil carbon can have large impacts on the global carbon budget and the subsequent pace of climate change. How soil carbon will change as global temperatures warm presents a particularly challenging question because multiple simultaneous mechanisms could serve to increase carbon inputs into the soil (e.g., increased plant growth) and increase carbon loss from soils (e.g., increased soil respiration). Because free-living and root-associated microbes in the soil drive the majority of soil carbon processes, their responses to soil warming are particularly important to understand. Working in a set of long-term soil warming experiments at the Harvard Forest, we have found dramatic changes in how strongly different trees rely on their belowground microbial partners for nutrient uptake, and that shifts in this reliance fundamentally alter the pathways of plant carbon entering the soil. We also find that shifts in plant carbon into the soil alter the soil microbial community and function. Finally, we find that increases in particular forms of plant carbon entering the soil (e.g., root exudates) do not always increase soil carbon, and that the functional impact of plant carbon inputs on the soil microbial community holds the key to whether new carbon inputs will lead to net soil carbon gain or loss. These findings underscore the complexity of soil carbon responses to warming temperatures and highlight the importance of focusing on the responses of the soil microbial community when trying to predict how global warming will impact soil carbon storage.

Speaker Bio / Lab overview
The Taylor lab's research focuses on understanding how belowground partnerships between plants and soil microbes will impact the ability of plants and soils to capture and store carbon under future global change scenarios. Our work spans natural ecosystems from tropical rainforests to the arctic tundra and combines theoretical ecology, manipulative experiments, and large-scale data syntheses to identify key ecological and biogeochemical mechanisms that will allow us to better predict the future carbon storage capacity of terrestrial ecosystems.



Smita Gopinath – Assistant Professor, Department of Immunology and Infectious Disease, Harvard T.H. Chan School of Public Health

Vaginal microbiome and antiviral immunity

Speaker Bio:

Dr. Gopinath completed her graduate training in Dr. Monack's laboratory in Stanford University where she worked on a mouse model of Salmonella transmission, studying the immune responses of asymptomatic supershedders. She carried out her postdoctoral work in Dr. Iwasaki's group at Yale University where she worked on vaginal immunity to genital herpes infections and uncovered a surprising antiviral effect of commonly used antibiotics. Her independent research group at the Harvard School of Public Health investigates the effect of vaginal microbiome on host immunity and resistance to sexually transmitted infections with the goal of developing microbiome-informed therapeutics and vaccine approaches.

Shira Weingarten-Gabbay – Assistant Professor, Department of Microbiology, Harvard Medical School; Associate Member, Broad Institute

Illuminating the viral dark proteome to advance our understanding on antiviral immunity

Abstract:
Viruses are among the most fascinating biological entities on Earth. With genomes 10,000 times smaller than ours, they somehow manage to hijack entire cells and execute remarkably complex life cycles. This paradox raises a key question: how well do we really understand the coding capacity of viruses?
In my talk, I will describe a new technology that combines synthetic biology with ribosome profiling to map viral translation across thousands of viral sequences in parallel. Using this approach, we unveiled more than 4,000 previously unknown microproteins across nearly 700 viruses. Among them are unexpected targets for T cells and regulatory elements that fine-tune viral gene expression. Shedding light on this new universe of viral proteins could reshape our understanding of the viral life cycle and antiviral immunity.

Speaker Bio & Lab Overview
Dr. Shira Weingarten-Gabbay is an Assistant Professor of Microbiology at Harvard Medical School and an Associate Member of the Broad Institute. She earned her B.Sc. in Medical Sciences from the Hebrew University, and her M.Sc. in Molecular Genetics and Ph.D. in Systems Biology from the Weizmann Institute of Science. She completed her postdoctoral training in virology at the Broad Institute and The Rockefeller University.
In 2025, she established the Laboratory of Systems Virology at Harvard Medical School, where her team integrates virology, synthetic biology, immunology, and bioinformatics to develop high-throughput technologies that decode viral genomes and reveal how viruses interact with the immune system. She is the recipient of multiple awards, including the Blavatnik Regional Award, the Edward Mallinckrodt Foundation Award, the RNA Society Award for Innovation in High-Throughput Biology, and the Eric S. Lander Prize for Scientific Excellence. In 2020, she co-founded the international Systems Virology Journal Club to spotlight new concepts and methodologies in virology.

David Johnston – Betty Wold Johnson Foundation Professor of Earth and Planetary Sciences, Harvard University

Aerobic respiration: a gateway to estimating global oxygen production

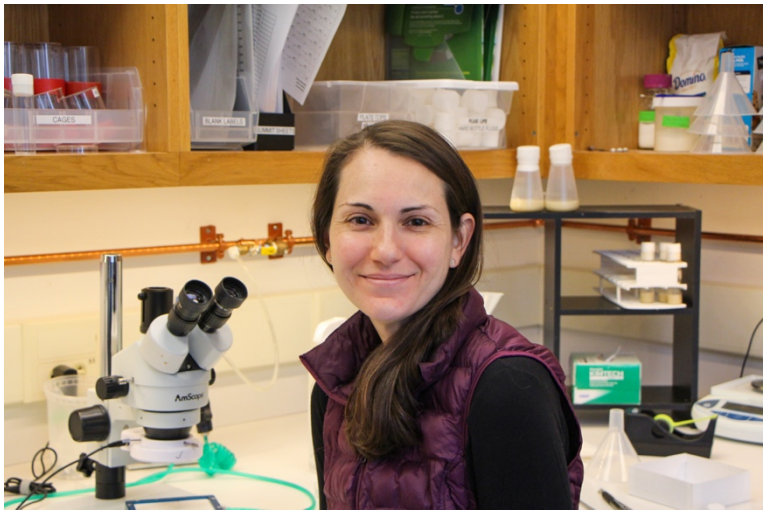
Abstract:

Primary production in the surface ocean is a critical component of Earth's carbon and oxygen cycles, modulating the uptake and release of CO_2 and O_2, respectively. Quantitatively estimating these exchanges remains challenging. Of the methods available, leveraging the triple oxygen isotope composition of O_2 in seawater (and the atmosphere) is one of the more robust approaches to this problem. Under the hood of this approach is a suite of presumptions – some rooted in physics and others in biogeochemistry. In this talk, we take aim at the central importance of aerobic respiration (and associated isotope effects) as the key to refining estimates of gross oxygen production on Earth. This can be simplified to a series of questions: What are the physiological controls on the oxygen isotope effects associated with oxic respiration? How are these effects reflective of the inner workings of a cell's respiratory chain? Are all respiring microorganisms created equal from an isotope perspective? We use E Coli. (both WT and mutants) to start addressing these questions.

Speaker Bio / Lab overview

The primary goal within the group is to better understand the relationship between microorganisms and Earth surface evolution. Our work ranges from geologically rooted questions, where we aim to track the onset or environmental expression of different metabolic processes and follow the inventory of atmospheric/oceanic oxidant budgets, through to modern processes and environments (such as experimental work with extant organisms, purified protein, work in the modern ocean water column, and early diagenesis in marine sediments). A common theme through these various scientific paths is the use of stable isotopes, and often more novel isotope systems, to unlock Earth's storyline.

Carolyn Elya – Assistant Professor, Department of Molecular and Cellular Biology, Harvard University



The last of fung(us): Mechanisms of fruit fly behavioral manipulation by the killer fungus Entomophthora muscae

Abstract:

Many parasites are known to manipulate the behavior of their animal hosts, but how this occurs remains poorly understood. As a graduate student, I discovered a strain of the mind-controlling pathogen *Entomophthora muscae* in wild fruit flies and developed robust methods to culture the fungus in the model organism *Drosophila melanogaster*. Before sunset on their final day of life, infected flies perform the "zombie" behaviors characteristic of *E. muscae* infection: they climb to a high location (a behavior known as "summiting"), extend their proboscises, and raise their wings in a pose that facilitates spore dispersal. The "death at sunset" phenotype has been of particular fascination to me. I will share our recent work using the fruit fly toolkit and fungal genomics and transcriptomics to understand how this eerie punctuality emerges.

Speaker Bio:

Carolyn received her Ph.D. in 2017 from UC Berkeley (go bears!) working with Dr. Michael Eisen where she accidentally discovered zombies in her backyard. She developed the zombie fruit fly (Drosophila melanogaster-Entomophthora muscae) lab system based on this encounter, and brought it with her to Dr. Benjamin de Bivort's group at Harvard University where she completed her postdoc investigating the neuromechanistic basis of zombie behaviors. Carolyn started her own group in 2024, the MCB Department at Harvard University, to dive even deeper into the zombie fruit fly system to answer questions related to behavior manipulation, host-parasite interactions, and fundamental biology of an early-diverging terrestrial fungus.

3:00 – 4:45 pm	**Session 2 speakers**

Yonatan Grad – Professor, Department of Immunology and Infectious Disease, Harvard T.H. Chan School of Public Health

How antibiotic use shapes microbial lineage dynamics

Speaker Bio / Lab Overview:

Our lab studies how pathogens evolve and spread. We use experimental and computational tools to test our hypotheses and collaborate with clinical and public health institutions. Our overall aim is to improve diagnostics, therapeutics, and clinical and public health strategies to aid in the control of infectious diseases.

Samantha Miranda – Research Scientist, Broad Institute

Translating the Message: Functional Impacts of Quorum Sensing Diversity

Abstract:
Pseudomonas aeruginosa is a versatile pathogen with an arsenal of virulence factors regulated by three interconnected quorum sensing (QS) systems. Although QS has been well-studied in laboratory strains, we have only recently begun to understand the diversity of QS genotype and phenotype in clinical isolates, particularly beyond those from people with Cystic Fibrosis. To address these gaps, we previously used coevolution analysis to identify amino acids responsible for signal selectivity and sensitivity, thereby moving us closer to our goal of predicting QS signal and function from DNA sequence. Recently, we sequenced the genomes of 104 P. aeruginosa isolates from 92 patients with ocular infections, nearly doubling the number of publicly available ocular isolate genomes. We observed significant genetic diversity among the isolates, including a high frequency of mutations in the QS receptors LasR and RhlR, adding to growing evidence that such mutations are common across multiple types of infection. Preliminary functional characterization of common RhlR variants showed the most common substitutions result in loss of function while a substitution in a selectivity residue results in increased activity and decreased selectivity. Within our collection of ocular isolates, we also observed diversity in exotoxin genotype and within-host variation in alginate production and mucA genotype. Our research highlights the genomic and functional diversity of clinical P. aeruginosa isolates and paves the way for future studies to fully understand the impact of this strain-level diversity on pathogenesis.

Speaker Bio / Lab Overview:
Dr. Samantha Miranda is a Research Scientist at the Broad Institute interested in uncovering the impact of genetic variation in bacterial isolates on microbe-microbe interactions and pathogenicity. She earned her PhD in Chemical Biology from Harvard University where she investigated novel inhibitors of Mycobacterium tuberculosis. Her recent postdoctoral research at the University of Washington, supported by a Helen Hay Whitney Foundation Fellowship and an NIGMS K99/R00 Award, focused on the evolution of bacterial social behaviors. This work revealed significant diversity in signaling sensitivity and selectivity across both species and strains. Dr. Miranda's current work builds on this foundation, investigating microbial interactions during infection with an emphasis on determining the functional consequences of genetic variation in clinical isolates.

Thomas Bernhardt – Professor, Department of Microbiology, Harvard Medical School

Control of peptidoglycan synthesis during polar growth

Abstract:

Bacterial cells are surrounded by a peptidoglycan (PG) cell wall that protects them from osmotic lysis. Elongation of the wall in rod-shaped bacteria is commonly achieved by one of two mechanisms: dispersed elongation or polar (apical growth). The dispersed mode of growth is used by most well-studied model organisms like Escherichia coli and Bacillus subtilis. Polar elongation is carried out by some alpha-proteobacteria and most if not all actinobacteria. I will discuss our past work focused on elucidating the control mechanisms governing dispersed cell elongation in E. coli by the conserved machinery called the Rod complex (elongasome). As a point of comparison, I will also present our recent work on the regulation of polar growth. Here, we are using Corynebacterium glutamicum as a model system to uncover the fundamental principles of polar PG elongation in members of the Mycobacteriales order of bacteria, which includes major pathogens like Mycobacterium tuberculosis.

Speaker Bio:

I performed graduate studies at Texas A&M University with Ry Young where I investigated the mechanisms by which phages induce host cell lysis. My postdoctoral work was with Piet de Boer at Case Western Reserve University where I investigated the spatiotemporal control of bacterial cell division. I started my lab in the Microbiology Department at Harvard Medical School in 2007.

Lynn Bry – Professor, Department of Pathology, Brigham and Women's Hospital; Director, Massachusetts Host-Microbiome Center

Talk title TBA

Markus Basan – Associate Professor, Department of Systems Biology, Harvard Medical School

Homeostasis of bacterial biomass density

Abstract:
The cell wall is an essential cellular component of bacteria and the target of many antibiotics. However, how bacteria regulate the rate of cell wall biosynthesis as growth rates change remains unresolved. In E. coli, cell wall growth is thought to proceed independently from turgor pressure1, the osmotic pressure that the cytoplasm exerts on the cell wall. Here, by modulating turgor pressure and measuring the rate of cell wall biosynthesis, we find that turgor pressure directly controls cell wall biosynthesis rate. Quantifying turgor pressure using osmotic shocks, we uncover an increase in turgor pressure with growth rate caused by an increase in intracellular potassium concentration. We propose a biophysical model that explains how turgor pressure is generated and regulated via biomass counterions and how it affects cell wall expansion rate via hydrolase-mediated cell wall fluidization. Elegantly, this model explains how bacteria achieve homeostasis of cytoplasmic crowding and simultaneously how they regulate their rate of cell wall biosynthesis in coordination with growth rate.

Speaker Bio:
After undergraduate studies in physics at ETH Zurich and Harvard University, Markus obtained a PhD in theoretical physics working with Jean-Francois Joanny and Jacques Prost at the Curie Institute. He went on to do postdoctoral studies in the labs of Terry Hwa at the University of California at San Diego and Uwe Sauer at ETH Zurich before joining the Department of Systems Biology at Harvard Medical School.

Braden Tierney – Executive Director, Two Frontiers Project; Director of Exposomics and Microbial Data Science, Harvard Medical School

Walking the line between human and environmental microbiology

Abstract:
Microbes are ubiquitous, yet we often study them in ecological silos. Whether in the human gut or benthic sediments, these systems—while spatially distinct—share deep functional and evolutionary links that are easy to overlook. In this talk, I will draw on anecdotes from my work and the broader literature to argue for breadth alongside depth in microbiology. From "methodological arbitrage," the repurposing of tools across clinical and environmental research, to the shared biochemical strategies that drive resilience in both coral and human holobionts, I will show how connecting these worlds clarifies the principles of microbial life and strengthens each field through mutual insight.

Speaker Bio:
Braden Tierney is the co-founder and Executive Director of the Two Frontiers Project, a nonprofit research organization dedicated to scaling naturally-evolved, microbial machinery from geochemically diverse environments to address challenges from bioremediation to food sustainability. A microbiologist and data scientist, Dr. Tierney earned his PhD from Harvard Medical School, where he developed large-scale, computational methods to discover novel microbiome diagnostics and therapeutics. He has led work on microbiome-based therapeutics for conditions ranging from constipation to coral bleaching, including clinical trials via industry partnerships. Since founding Two Frontiers in 2022, he has led over a dozen expeditions across four continents and helped discover one of the most efficient organisms for carbon sequestration.

Poster Session Abstracts

1. Is it a feature or is it a bug? Leveraging Lambda phage to investigate the mechanisms and consequences of ribosomal frameshift errors

Kristopher Kennedy[1], Ann Hochschild[1]

[1]Department of Microbiology, Harvard Medical School

Although ribosomal frameshift errors are thought to be relatively rare, recent work from our lab suggests that the error frequency is higher than previously assumed. The overall impact of ribosomal frameshift error on cellular function remains unknown, and models for predicting an mRNA's frameshift propensity are lacking. To address this, I've developed *Escherichia coli* bacteriophage Lambda as a tool for identifying frameshift-prone mRNA sequences. Lambda gene *GT* undergoes programmed ribosomal frameshifting to produce two distinct polypeptides that are coordinately required for phage morphogenesis. The shift to the –1 reading frame is induced by a 7-nucleotide 'slippery' motif in the *GT* mRNA. I observe that genetic suppressors of inviable slippery site mutant prophages rescue viability by acquiring alternative frameshift-prone sequences in *GT.* I plan to comprehensively analyze frameshift-prone sequences by constructing DNA libraries containing *GT* homology and randomized 12-nucleotide stretches at strategic sites. Inviable *GT* mutant lysogens will be transformed with these libraries by Lambda Red recombineering. Recombinant phages acquiring frameshift-prone sequences will be enriched and identified by deep sequencing. The resultant list of frameshift-prone sequences will be analyzed to predict novel frameshift sites in *E. coli* and bacterial pathogens, exposing hidden mechanisms and consequences of gene expression error.

Keywords: Bacteriophages, genetics, molecular mechanisms

2. Polyunsaturated Fatty Acids Promote Appetite via the Microbiome–Gut–Brain Axis

Yi Jia Liow[1,2], Shusei Eshima[3], Mustafa Talay[4] Vladimir Yeliseyev[5], Lynn Bry[5], Rachel N. Carmody[1]

1. Department of Human Evolutionary Biology, Harvard University, Cambridge, MA, USA
2. Department of Human Ecology, School of International Health, Graduate School of Medicine, The University of Tokyo, Bunkyo City, Tokyo, Japan
3. Independent Researcher
4. Department of Molecular & Cellular Biology, Harvard University, Cambridge, MA, USA
5. Massachusetts Host–Microbiome Center, Department of Pathology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

Appetite is regulated by nutrient-sensing systems that integrate long-term signals from energy stores and short-term cues from dietary intake, yet this regulation is increasingly disrupted by industrialized diets. Although the physiological effects of industrialized diets are well documented, the continued rise in metabolic and eating disorders underscores a critical gap in our understanding of how these diets shape neurological regulation of eating behavior. Here, we tested how distinct properties of industrialized diets alter brain neurochemistry and change appetite. We probed the properties of an industrialized diet through contrasts targeting the overall diet pattern (Western vs. control), enriched macronutrients (fat vs. sugar), and isocaloric trade-offs of macronutrient variants (saturated fatty acids vs. polyunsaturated fatty acids [PUFA]). The most salient effects emerged from the finest-grained contrast: PUFA conditioning increased appetite through a mechanism involving elevated brain 5-hydroxyindoleacetic acid (5-HIAA), a primary serotonin catabolite associated with the gut microbiome. Fecal microbiota transplants into germ-free mice confirmed that the PUFA-conditioned gut microbiome carries an appetite-enhancing signature. Together, our findings delin- eate a diet–microbiome–gut–brain axis through which dietary components enriched in industrialized diets can modulate appetite and contribute to altered eating patterns.

Keywords: Microbial Ecology, Microbiomes - non-human, Science Communication

3. Selective Elimination of *Vibrio* Pathogens via the Synergy of a Type Six Secretion System and a Natural Phenazine Antibiotic

Sarah Bier[1], William Robins[1], John Mekalanos[1]

[1]Department of Microbiology, Harvard Medical School, Boston, MA 02115

Vibrios are most often studied in the context of human disease; multiple *Vibrio* species, including *Vibrio cholerae*, are widespread mammalian pathogens. In this poster, we describe the isolation of a vibriocidal strain of *Aeromonas dhakensis*, named A603. We determine that its vibriocidal activity comes from a synergy between A603's Type Six Secretion System and a synthesized phenazine antibiotic, AdPhen. Remarkably, non-*Vibrio* taxa resist this killing. A603's T6SS activity overcomes efflux-mediated AdPhen resistance in newly-generated *V. cholerae* mutants, likely through membrane potential disruptions. A603 uses both AdPhen and its T6SS to protect the host from invading *Vibrio* pathogens, like toxigenic strains of *V. parahaemolyticus*. A603 guards aquatic hosts from vibriosis-related microbiome disruptions without significant host colonization or changes to non-*Vibrio* native flora. A603's easy application, low colonization of hosts, and minimal alteration of microbiome composition or function makes it a promising new probiotic against and treatment of vibriosis in aquatic hosts. While A603 cannot colonize mammalian hosts, its vibriocidal systems may be engineered into human commensals to provide long-term protection from *Vibrio* diseases, including cholera. Furthermore, the modulation of AdPhen resistance by T6SS activity may reveal new roles for microbiota in antibiotic treatments of gastrointestinal disease.

Keywords: Antibiotics, Natural Products, Toxins/Virulence Factors, Microbiomes - non-human Microbial Ecology, Molecular Mechanisms, Microscopy/Imaging

4. Regulation of Virulence Gene Expression by Serum Albumin in *Listeria monocytogenes*

Bri Manning; Jacquelle Joseph-Lainez; Jimmy Regeimbal; Daniel Grubaugh; Darren Higgins

Harvard Medical School

Intracellular pathogens remain a tremendous cause of morbidity and mortality worldwide. *Listeria monocytogenes* (*Lm*) is an intracellular bacterial pathogen and a leading cause of death by a food-borne pathogen. *Lm* infections affect immunocompromised individuals, the elderly, pregnant people, newborns, and infants. A paramount concern is the ability of *Lm* to infect the brain, causing life-threatening meningitis and encephalitis, or crossing the placenta to cause stillbirth of the fetus. While numerous studies have explored how *Lm* invades, replicates, and spreads cell to cell within host cells, fewer studies have examined how *Lm* survives in various niches within a host but outside of host cells (*in vivo* extracellular). *Lm* colonization of distal sites such as the brain or spread to the developing fetus necessitates dissemination in the bloodstream within host cells. Nonetheless, an understudied area of *Lm* pathogenesis is the adaptation of extracellular bacteria to residence in the bloodstream. We hypothesize that *Lm* senses components of blood and responds by altering gene expression to facilitate growth, survival, and subsequent intracellular infection of host cells. We have observed that serum albumin, a major component of blood, is sufficient to upregulate *Lm* virulence gene expression at a transcriptional level. Our studies suggest that the increase in virulence gene transcription is mediated by PrfA, a DNA-binding transcriptional activator. Furthermore, we have also discovered that albumin upregulation of virulence gene expression can be controlled at a post-transcriptional level and the ability of albumin to induce virulence gene expression is dependent on the mammalian species of origin. To date, there have been no studies on how sensing of a blood component can induce virulence gene expression at a post-transcriptional level in *Lm.* Therefore, our work is to gain insights into the serum albumin-induced post-transcriptional upregulation of virulence gene expression.

Keywords: Pathogenesis, Host-pathogen interaction

5. Evidence of coordination between host and microbiome to shape calcifying fluid chemistry in the Eastern oyster (*Crassostrea virginica*)

Andrea Unzueta-Martínez[1], Jennifer A. Delaney[1], Kate Morkeski[2], Abby Ross[3], Zhaohui Aleck Wang[2], Peter R. Girguis[1]

[1]Department of Organismic and Evolutionary Biology, Harvard University, Cambridge, MA, 02138
[2]Marine Chemistry and Geochemistry, Woods Hole Oceanographic Institution, Woods Hole, Massachusetts, USA
[3]Institute of Arctic and Alpine Research, University of Colorado Boulder, Boulder, CO, 80303

Marine animals that build shells, such as oysters, carefully regulate the chemistry of their internal calcifying fluids, but the molecular mechanisms behind this control, as well as whether microbes play a role in calcification, are poorly understood. To better understand oysters' molecular mechanisms and the role of their calcifying-fluid microbes, we conducted experiments that simulated a tidal cycle, measured calcifying fluid pH and total dissolved inorganic carbon, and characterized host and microbial gene expression via transcriptomics. These experiments showed that calcifying fluid pH remained relatively stable throughout tidal pH fluctuations, with corresponding increases in oyster transcripts for ion transport and acid-base regulation. These data provide direct evidence that tidal fluctuations drive rapid changes in oyster calcifying fluid chemistry. Most surprisingly, increases in microbial transcripts related to nitrogen and sulfur cycling correlated to higher calcifying fluid DIC, and co-expression network analysis revealed coordinated patterns of gene expression that linked oyster immune and neural pathways to microbial redox processes, providing molecular evidence of potential host modulation of microbial metabolism. Together, these results reveal that oysters actively regulate their calcifying fluid pH over short timescales, and the endemic microbiome metabolic responses can yield metabolites that influence calcifying fluid pH, alkalinity, and ultimately calcification. These data offer a new perspective on oyster physiological capacity and, most importantly, the role of microbes in oyster calcification. In light of more rapid changes in ocean pH and temperature, oysters provide a new model for studying animal-microbial responses to environmental acidification and coordination in biomineralization.

Keywords: Microbiome – non-human

6. What Makes a Plasmid Successful in a Bacteria?

Samantha Capehart, Sophia Wiesenfeld, Fernando Rossine, Michael Baym

Antibiotic-resistant pathogens are an urgent global health threat that grows worse with each passing year. In 2019, 5 million people were killed by antibiotic-resistant infections and the World Health Organization estimates that resistant infections will kill 10 million people a year by 2050 ((Chan, 2022) Lin et al., 2017). Critically, genes that confer antibiotic resistance are increasingly spread on plasmids, which are extrachromosomal mobile genetic elements commonly found in bacteria (Kaul et al., 2025). Thus, research into plasmid evolution and fitness will shed light on what facilitates this horizontal spread, which may help us design strategies to mitigate plasmid-mediated antibiotic resistance. For example, if existence of a native plasmid of the same type prevents plasmid spread, potential development of a 'probiotic plasmid' without any antibiotic resistance could outcompete plasmids that spread antibiotic-resistance. The project presented by this poster takes the first steps toward such a plasmid by determining key aspects of plasmids which make them more successful within a cell. Key to understanding plasmid competition is understanding that it occurs at two distinct levels: within-cell, in which plasmid variants compete with one another to clonally fix within a cell, and between-cell, where host cells containing different plasmid compositions compete with each other (Coluzzi et al., 2022). Historically, study of both of these levels has been challenging, because there has been no way to measure the within-cell fitness of plasmids. In 2025, Rossine et al created a method where plasmid heterodimers are introduced into a bacterial cell containing an arabinose-inducible FLP recombinase (Rossine et al., 2025). Activating this recombinase converts the plasmid dimers into monomers which then begin to compete. Because this method ensures a starting 1:1 ratio of each plasmid, subsequent changes in the number of plasmids per cell can be calculated over time to show plasmid competitive fitness. My research used this competition technique to investigate what makes plasmids successful in a cell. Using a diverse sample of plasmids, we found that both plasmid origins and Rom proteins influence success, cell health, and plasmid coexistence.

Keywords: Antibiotics, microbial evolution, plasmids, mobile genetic elements

7. Ultrasmall Episymbionts within the human microbiome utilize unique Type 4 Pili to bind bacterial hosts

Alex S. Grossman[1], Lei Lei[1,2], Deepak Chouhan[1], Jack M. Botting[3,4], Jett Liu[1,5], Nusrat Nahar[1], João Gabriel S. Souza[1,6], Jun Liu[3,4], Jeffrey S. McLean[7,8,9], Xuesong He[1], and Batbileg Bor[1#]

1. Department of Microbiology, ADA Forsyth Institute, Cambridge MA, 02142, USA
2. West China Hospital of Stomatology, Sichuan University, Chengdu Sichuan, 610093, China
3. Department of Microbial Pathogenesis, Yale School of Medicine, New Haven CT, 06536, United States
4. New Haven Microbial Sciences Institute, Yale University, West Haven CT, 06516, United States
5. Institute for Medical Engineering and Science and Department of Biological Engineering, Massachusetts Institute of Technology, Cambridge MA, 02139, USA
6. Department of Periodontology, Dental Research Division, Guarulhos University, Praça Tereza Cristina, Guarulhos, São Paulo 07023-070, Brazil
7. Department of Microbiology, University of Washington, Seattle WA, 98109, USA
8. Department of Periodontics, University of Washington, Seattle WA, 98195, USA
9. Department of Oral Health Sciences, University of Washington, Seattle WA, 98195, USA

Ultrasmall Patescibacteria, also known as the Candidate Phylum radiation, are prevalent in diverse microbiomes, including mammalian guts and oral microbiomes, arthropod guts and epithelia, and coral surfaces. Patescibacteria observed to date grow episymbiotically on the surface of bacterial or archaeal hosts. Culturable representatives from Saccharibacteria have been shown to dramatically alter their bacterial host's growth rate, metabolism, morphology, and immunological impact within the human microbiome. Because so few ultrasmall bacteria have been cultivated, little is known about the molecular mechanisms they utilize to identify host bacteria, bind them, and manipulate their cellular processes. Type 4 Pili (T4P) are complex polymeric filaments that we hypothesized may be vital mechanisms for host-binding. We systematically targeted T4P genes in Saccharibacterium *Nanosynbacter lyticus* TM7x to characterize these extracellular filaments and their contribution to episymbiotic host-binding. We found that *N. lyticus* produces two distinct T4P: a thick pilus that drives twitching motility and is essential for survival; and a thin pilus that contributes to initial host-binding and has a smaller diameter than any known T4P (1.8 nm). Disruption of the thin T4P through deletion of its major pilin (PilA2), its extrusion ATPase (PilB2), or its putative tip adhesin (PilX2) significantly inhibited host-binding and delayed stable episymbiosis with host cultures. Loss of PilA2 or PilX2 compromised *N. lyticus*' competitive fitness when grown alongside another Saccharibacteria, illustrating how important host recognition is for episymbiont success. To study the localization of T4P binding we expressed and purified the tip adhesin proteins from both T4P (PilX1 and X2). Both episymbiont derived adhesins clearly associated with host bacteria, and in dot blots PilX1 bound host peptidoglycan while PilX2 bound purified cell wall polysaccharides. Finally, we identified that thin T4P defective mutants were incapable of binding human epithelial cells and being internalized, suggesting that these appendages drive both prokaryotic and eukaryotic host binding. Our results provide mechanistic insights into the largely unknown host-binding mechanisms of episymbiotic microbes, describe the unique T4P produced by Saccharibacteria, and give new insights into the ecology of episymbiont competition and co-infection.

Keywords: Microbial Ecology, Genetics, Microbial Motility, Host-Pathogen Interaction, Anaerobes, Episymbiosis

8. Identifying natural inducers of gene transfer agent synthesis in Caulobacter crescentus

Ryan Pianka, Kevin Gozzi

Rowland Institute at Harvard University

Caulobacter crescentus is an Alphaproteobacterium extensively studied for its asymmetric division and elaborate cell cycle. Recently, we discovered it produces lethal, yet nonvirulent, phage-like entities called gene transfer agents (GTAs) in a subset of the population during stress. We have since demonstrated that GTAs increase the population's tolerance for antibiotic-induced DNA damage by providing a pool of templates for homology-directed repair. In this project, we examine the regulation of GTA synthesis, describing a two-component system essential for GTA production and identifying the stringent response as a key regulator. We have also identified an essential operon containing a luxR-like regulator that may play a role in GTA-mediated death. This project suggests a unique viral domestication where preexisting systems co-opted the lytic cycle of a phage, harnessing it as a stress-induced genetic exchange mechanism.

Keywords: Bacteriophages, genetics, molecular mechanisms

9. RNA guided nucleases enable the gene drive of insertion sequences in plasmids

Kepler Mears, Michael Baym

10. Determinants of within-cell plasmid competitive fitness

Sophia Wiesenfeld, Fernando Rossine, Michael Baym

Plasmids are extrachromosomal, frequently multi-copy mobile genetic elements. In bacteria, they are frequently the source of rapid genetic flexibility: entire virulence genes, metabolic pathways, or multidrug resistance can be gained and lost via the gain or loss of a plasmid. Interestingly, plasmids' multicopy trait leads to multi-level selection. Plasmids undergo two phases of competition: within-cell competition, when a new mutant plasmid or invading plasmid must establish itself, sometimes against a resident plasmid or the wildtype, and between-cell competition, when bacteria with different plasmid compositions compete. Critically, plasmid traits that provide a benefit in the between-cell phase (such as aligning fitness interests with its host cell) are not necessarily beneficial in the within-cell competition phase.

Within-cell competition of plasmids has been understudied, despite its critical role in plasmid ecology, because experimental techniques to look at the varying levels of competing plasmids had not been created. Our lab designed an experimental tool to provide direct experimental observation of this phase and verified that this level of competition directly impacts the success or failure of a plasmid to outcompete others.

For example, we have shown a trade-off between resistance gene transcription and replication ability and therefore within-cell competitive fitness of the plasmid: plasmid variants that have slower copy-number recovery after division are at a disadvantage. We hypothesize that this should be true of any replication speed or carrying capacity determinant, and so have moved our attention from plasmid cargo to the innate regulators of copy number in plasmids. This work seeks to explore determinants of within-cell competitive fitness using ColE1 plasmids as a model system, by competing plasmid variants with mutated primer/repressor RNAs and repressor of replication (ROP) proteins.

We report experimental results suggesting that the ROP proteins of coexisting plasmid variants act as a private good to regulate plasmid copy number within a cell, rather than a public good, and are currently simulating models of ROP spatial segregation to see if we can represent experimental results. We have begun to show that environmental modulations and synthetic engineering of the ROP protein which cause it to act more in trans results in it acting as a public good, abolishing a plasmid variant's competitive advantage and resulting in competitor-dependent plasmid fitness.

Finally, we show that nonlinear competitive dynamics emerge in as small a difference as a single SNP in the RNA primer/repressor region. These data encourage us to pursue a high-throughput competitive screen of primer/repressor RNA and ROP protein mutants to determine trends of within-cell plasmid competitive fitness. Results of this screen will characterize plasmid traits that lead to their success at the within-cell competitive phase, shaping the between-cell plasmid competition we observe that can ultimately contribute to or block multidrug resistant plasmid spread.

Keywords: Microbial evolution, mobile genetic elements

11. Effects of prophages on evolutionary paths to antibiotic resistance in S. Typhimurium.

Amy Zamora[1], Siân V. Owen[2], Shreyas Pai[1], & Michael Baym[1]

1. Department of Biomedical Informatics and Laboratory of Systems Pharmacology, Harvard Medical School, Boston, MA.

2. New York State Department of Health, Wadsworth Center, Albany, NY.

Naturally occurring bacteria commonly contain prophages integrated into their genome. These temperate phages are typically induced by the SOS response, resulting in phage replication and host death. DNA-damaging antibiotics can activate the SOS response and therefore trigger prophage induction, even at sub-inhibitory concentrations. However, the mechanism by which prophage-induced sensitization might affect resistance evolution is less clear. To investigate this relationship, we selected spontaneous resistant colonies of prophage (+) and (-) S. Typhimurium from a gradient of Ciprofloxacin. We quantified these mutants, measured their Ciprofloxacin MIC, and sequenced a subset of the isolates. Prophage(+) strains showed higher minimum inhibitory concentrations of Ciprofloxacin compared to isogenic prophage(-) strains. Interestingly, prophage(+) bacteria had a lower frequency of Ciprofloxacin resistance mutations, which tended to be more resistant. Sequencing results showed higher prophage(+) resistance was the result of an altered breadth of mutations, focused mostly in direct drug targets, which drove increased resistance. Further, the resistance-conferring role of mutations was characterized through fluorescent tracking of the SOS response. Mutations related to CIP and the induction of the SOS response were determining factors in prophage involvement in resistance evolution, per these results. Finally, to interrogate if this effect applied generally to other DNA-damaging antibiotics, we followed up by repeating our previous tests with Trimethoprim and Mitomycin C. For MitC, we noted similar trends in prophage effects on sensitivity. However, we see for TMP that the previously observed antibiotic sensitization and subsequent evolutionary phenotypes with prophage(+) strains were lost. This may be due to the temporal dynamics of DNA damage from each antibiotic's mechanism of action. Taken together our results indicate that although prophages sensitize their hosts and constrain their immediate paths to resistance, they do not necessarily constrain the evolution of high-level resistance.

Keywords: Antibiotics, Bacteriophages, Host-Pathogen Interaction, Microbial Ecology, Microbial Evolution

12. A directed approach reveals diversity of closely-related gene transfer agent systems

David Zahrah, North Ediale, Kristina Ruiz, Nathan Thewedros, Andy Barnett, Kevin Gozzi

Rowland Institute at Harvard

Gene transfer agents (GTAs) are bacteriophage-like particles that mediate gene transfer in a bacterial population. Recently, GTA production has been observed in the model oligotrophic α-proteobacterium Caulobacter crescentus. To enable thorough discovery and characterization of GTA systems across α-proteobacteria, we developed a directed approach to activate GTA production in new species with GTA-encoding loci. Using a bioinformatic screen of a panel of distantly related Caulobacterales, we identify and overexpress homologs of GTA-activating genes in their native strain to induce GTA production. With a combination of cell viability assays and time-course microscopy, we find that lysis and lethality of GTA production to producer cells is conserved amongst the Caulobacterales clade. By sequencing the genomic DNA packaged within the GTAs, we find that packaging length is well conserved while packaging content varies substantially across species. Using our method, we have established several new GTA systems in α-proteobacteria, uncovering a diversity of structural and functional properties of this poorly understood form of horizontal gene transfer. Future studies of this consortium will expand our understanding of the role GTAs play in the evolution and ecology of microbial communities.

Keywords: Gene transfer agents, Horizontal gene transfer, Genetics, Microbial Evolution Microscopy/Imaging, Bacteriophages

13. Site-Specialization of Human Oral Porphyromonas Species

Julian Torres-Morales[1]*, Jessica L. Mark Welch[1], Floyd E. Dewhirst[1,2], Gary G. Borisy[1]

1. ADA Forsyth Institute, Somerville, MA, USA

2. Harvard School of Dental Medicine, Boston, MA, USA

Microbial taxa have evolved to colonize distinct sites within the human oral cavity. This spatial organization reflects ecological pressures and adaptation mechanisms, including metabolic dependencies. The genus Porphyromonas is a key member of the human oral microbiome and is broadly distributed across sites. P. gingivalis and P. endodontalis are well-established as being enriched in subgingival plaque during periodontal disease. In addition, P. pasteri, P. catoniae, P. sp. HMT-275, and P. sp. HMT-278 are also recognized as human oral taxa. Yet, site-specific distributions and ecological adaptation mechanisms at the taxon and strain levels remain poorly understood.

To investigate site specialization among Porphyromonas taxa, we systematically analyzed 1,218 metagenomes from nine oral sites in healthy individuals and 24 subgingival plaque samples from individuals with periodontitis. Competitive mapping to reference genomes, combined with pangenomic and metabolic enrichment analyses, revealed distinct site-specific patterns, ecotype differentiation, and metabolic dependency.

P. pasteri was the most abundant and widespread taxon, comprising two ecotypes with distinct ecological preferences. One ecotype was primarily associated with the tongue dorsum, while the other was enriched in supragingival plaque. P. catoniae was restricted to healthy supra- and subgingival plaque, whereas P. endodontalis was consistently found in subgingival plaque across both health and disease. P. gingivalis was detected in only half of the disease-associated samples. Functional analyses revealed overlapping metabolic capacities between the P. pasteri ecotypes, although the supragingival plaque-associated ecotype was enriched in a methyltransferase potentially involved in gene regulation. P. gingivalis exhibited the broadest metabolic potential, which might confer a survival advantage during inflammation. In contrast, P. catoniae lacked several key metabolic pathways, including those involved in biosynthesis of serine and the essential vitamin cobalamine, suggesting nutritional dependency on other microbes or the host. These findings enhance our understanding of the biogeography and adaptation of Porphyromonas species in the oral cavity.

Keywords: Microbiomes – human, Oral microbiome, Site specialization, Porphyromonas

14. In-situ cryo-EM structures of sheathed flagella reveal mechanisms of assembly, rotation, and disassembly

Wangbiao Guo[1,2,*], Jian Yue[1,2,*,#], Jin Hwan Park3[, *] Valverde Mendez Diana[4,5], Jack M. Botting[1,2], Rajeev Kumar[1,2], Huaxin Yu[1,2], Avijay Sen[1,2], Jing Yan[4,5], Fitnat H. Yildiz[3,#], Jun Liu[1,2,#]

1. Department of Microbial Pathogenesis, Yale School of Medicine, New Haven, CT, USA

2. Microbial Sciences Institute, Yale University, West Haven, CT, USA

3. Department of Microbiology and Environmental Toxicology, University of California, Santa Cruz, CA, USA

4. Department of Molecular, Cellular &Developmental Biology, Yale University, New Haven, CT, USA

5. Quantitative Biology Institute, Yale University, New Haven, CT, USA

*These authors contributed equally to this work.

Corresponding authors: jian.yue@yale.edu; fyildiz@ucsc.edu; jliu@yale.edu

The sheathed flagellum is a specialized, self-assembling nanomachine crucial for the dual sessile and motile lifestyles of Vibrio cholerae, the causative agent of cholera. Using in-situ single-particle cryo-electron microscopy and cryo-electron tomography, we reveal how this specialized nanomachine assembles and rotates within the dynamic and complex bacterial envelope. First, we determine near-atomic structures of the sheathed flagellar motor in two distinct functional states, capturing conformational changes that coordinate assembly and disassembly. Second, we find that the motor anchors to the outer membrane via lipoprotein-based H- and L-rings without forming a pore, thereby coupling membranous sheath development with flagellar biogenesis. Third, the sodium-driven PomAB stator complex exhibits remarkable flexibility, engaging the flagellar protein MotX rather than peptidoglycan to enable torque generation while accommodating membrane fluctuations. Finally, we reveal that the motor maintains rapid rotation within the dynamic bacterial envelope via a unique sliding-rotating mechanism. Together, these findings define the architecture, assembly, and dynamics of the sheathed flagellum, providing a structural framework for understanding how this specialized nanomachine mediates transitions between the sessile and motile lifestyles of V. cholerae.

Keywords: sheathed flagella, rotary motor, bacterial motility, assembly, disassembly.