Biology Department

Honors Research and Summer Research Open House

Wednesday, January 22
7:00pm
Thompson Chemistry Room 123 (Wege)

Thursday, January 23
Lab Open House
9:30am – 3:30pm

Department Chair: Lois Banta
x4330

biology.williams.edu
or on Facebook at Williams biology

Biology Majors….

…learn about honors research opportunities, use the following resources:

- information session with faculty
- open house (see schedule below)
- department website

The deadline to apply to the honors program is February 7th. Applications can be found online at:

https://biology.williams.edu/research/honors-research-form/

Faculty accepting honors students for **academic year 2020-2021**: Derek Dean, Lois Banta, Matt Carter, Pei-Wen Chen, Sonya Auer, Cynthia Holland, Damian Turner, Luana Maroja, Joan Edwards, Tim Lebestky, Heather Williams, Ron Bassar, Manuel Morales, Martha Marvin, Allison Gill

Faculty accepting off-cycle honors students for **academic year 2020-2021**: Derek Dean, Cynthia Holland, Tim Lebestky, Heather Williams

Faculty accepting **summer** students for 2020: Lois Banta, Matt Carter, Pei-Wen Chen, Sonya Auer, Cynthia Holland, Damian Turner, Luana Maroja, Martha Marvin, Joan Edwards, Tim Lebetsky, Heather Williams, Ron Bassar, Allison Gill

Open House Schedule		
Faculty	**Time**	**Location**
Lois Banta	1:30 – 2:00	SSB 116
Matt Carter	1:00 – 1:30	TBL 018
Tim Lebestky	3:30 – 4:00 or by appt	SSB 203
Manuel Morales	10:30 – 11:00	TBL 011
Luana Maroja	2:00 – 2:30	SSB 213
Martha Marvin	9:30 - 10:00	MSL 128
Heather Williams	11:30 – 12:00	TBL 015
Cynthia Holland	11:00 – 11:30	SSB 114
Damian Turner	10:00 – 11:00	TBL 012

If you are interested in the following labs, please email the professor directly:

Professor Auer, *ska2@williams.edu*
Professor Bassar, *rdb4@williams.edu*
Professor Edwards, *jedwards@williams.edu*
Professor Chen, *pc7@williams.edu*
Professor Loehlin, *dwl1@williams.edu*
Professsor Claire Ting, *cting@williams.edu*
Professor Allison Gill, *gilla@umn.edu* ***(arriving summer 2020)***
Derek Dean, *ddean@williams.edu*

Biology Major Requirements

BIOL 101 The Cell
BIOL 102 The Organism
BIOL 202 Genetics
2 – 300-Level courses, both with a lab component
1 – 400-Level course
3 – additional electives at any level

Biology Major Requirements w/Honors

BIOL 101 The Cell
BIOL 102 The Organism
BIOL 202 Genetics
BIOL 493/494 Senior Thesis
2 – 300-Level courses, both with a lab component
1 – 400-Level course
2 – additional electives at any level

Sonya Auer

TBL 019 (laboratory), TBL 201 (office), x2808, ska2@williams.edu

Many organisms face novel conditions in an increasingly human-altered world. How do they cope with challenges imposed by climate change, altered nutrient cycling, biological invasions, and increased urbanization? These are timely questions given the current rapid pace of environmental change occurring across the globe. Research in the Auer lab uses question-driven observational, experimental, and comparative studies in both the field and laboratory to understand the role that physiology and behavior play in mediating responses to environmental change at the individual, population, and community levels.

Upcoming projects will focus on whether and how organisms cope with challenges associated with warming temperatures and reductions in food quality and availability:

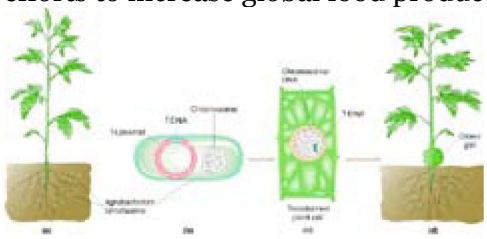
1. What role do rates of energy metabolism play in allowing organisms to cope with changes in diet quality?
2. Which physiological adaptations allow organisms to persist in resource poor environments?
3. How are upper thermal tolerance limits impacted by food availability?
4. Can the evolution of thermal tolerance limits permit species to cope with rapid climate change?
5. Are shifts in upper thermal tolerance a prerequisite for invading hot urban environments?
6. How is climate change impacting the distribution and abundance of local bird communities?
7. Can nutrient enrichment of small streams in the Scottish Highlands save Atlantic salmon from the negative impacts of climate change?

If any (or all!) of these research questions interest you, check out our website, www.sonyakauer.com, stop by (TBL 201), or email Prof A (ska2@williams.edu) for more information.

Lois Banta

SSB 116 (laboratory); TBL 213 (office), x4330, lbanta@williams.edu

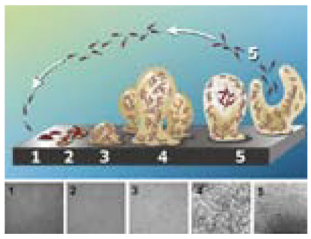
In the Banta lab, we study the interactions between the soil bacterium Agrobacterium tumefaciens and its host plants. In particular, we are interested in the transport of a large fragment of DNA across the membrane system surrounding the bacterium, and in the plant defense responses elicited by the bacterium. Infection of susceptible plants by A. tumefaciens results in crown gall tumor formation. The disease mechanism involves the transfer and integration into the plant genome of a specific DNA molecule (T-DNA) from a bacterial tumor-inducing (Ti) plasmid. Sequences on the T-DNA encode enzymes responsible for the biosynthesis of plant growth hormones; expression of these genes in the host plant leads to uncontrolled hormone production and hence unregulated plant cell division ("plant cancer"). This naturally occurring process of DNA transfer to plants is widely used to introduce new genes into plants, but its utility is limited by the fact that some plants, including the agriculturally important grains rice, wheat, corn and barley, are poor hosts. Thus, advances in our understanding of the mechanism of DNA delivery, and in particular the contributions made by bacterial proteins that are required for infection of some but not all hosts, may further the work of those scientists engaged in efforts to increase global food productivity.



Source: Griffiths, et al., An Introduction to Genetic Analysis (7th ed.)

Many bacteria including A. tumefaciens form biofilms, complex aggregates of bacteria, held together by polysaccharides, that are resistant to antibiotics and immune attack. Dental plaque and slime on rocks or metal in water are examples of biofilms; in the lungs of cystic fibrosis patients, biofilms serve as a clinically significant reservoir of bacteria. Derrick Spencer '20 has been exploring how the Type VI Secretion System (T6SS), implicated in virulence in several other human pathogens, plays a key role in Agrobacterium's ability to form biofilms. We will continue to investigate why bacteria deficient in the T6SS exhibit enhanced attachment to biotic and host plant surfaces.

We also discovered that this T6SS mutant is less able than its wild-type parent to infect host plants efficiently, and we believe this is because substrates secreted by the T6SS are needed to dampen host defenses. Additional data from our lab have led us to hypothesize further, however, that those same substrates can also trigger defense responses through a previously unknown mechanism. Future students will have the opportunity to continue the work of current Honors student David Gorestki '20 and WS students Sofia Neaher '22 and Amy Wang '23, who are comparing the defenses mounted by Arabidopsis plants against T6SS mutant versus wild-type bacteria. The goal of our research in the coming year is to further characterize this novel pathogen-recognition pathway, using protein biochemistry, plant genetics, and molecular and cell biology approaches.



Formation of bacterial biofilmsSource: biology.binghamton.edu/davies/research.htm

Ron Bassar

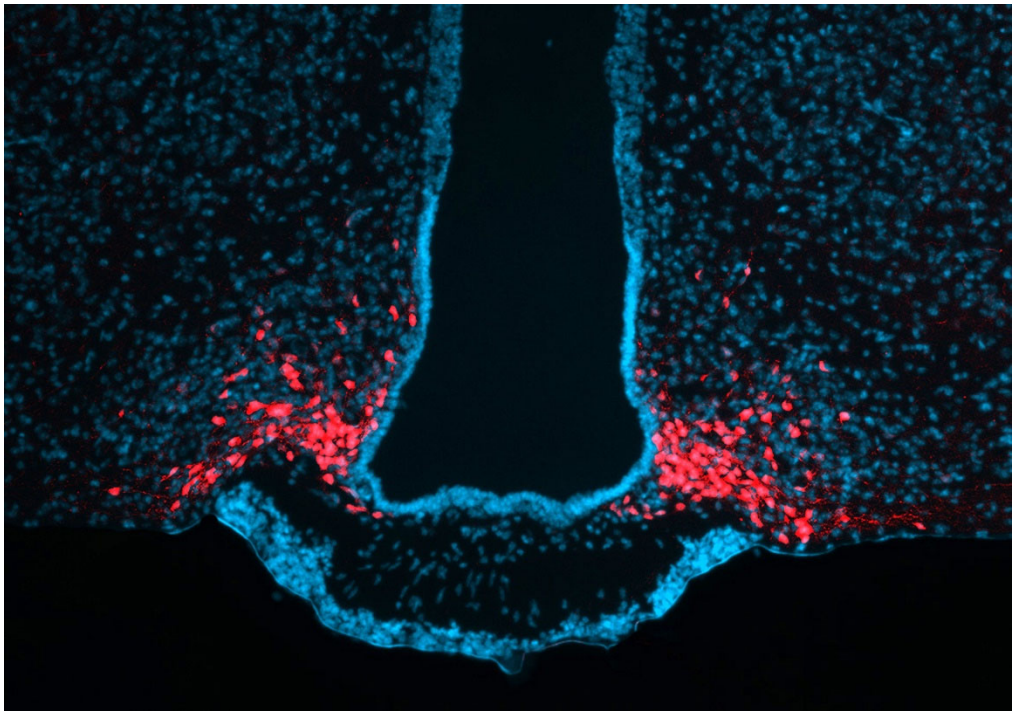
TBL 019 (laboratory); TBL 204 (office), x2119, rdb4@williams.edu

Darwin thought that evolution by natural selection occurred very slowly, over hundreds if not thousands of years. Evolutionary biologists now know that evolutionary changes in species can happen very quickly, over a relatively few generations. The consequence of this rapid evolutionary change is that ecological and evolutionary processes interact on the same timescale, sometimes drastically altering the outcomes of each. Research in the Bassar lab focuses on developing theory and conducting empirical research aimed at understanding the causes and consequences of this interaction in the generation and maintenance of biological diversity. Past research has demonstrated the role of biotic interactions in life history evolution, how these biotic interactions and their evolutionary outcomes alter community and ecosystem structure, and how abiotic factors, such as climate change, alter these dynamics. Current research is building upon this theme by testing the influence of short-term evolutionary change on species coexistence in structured populations. All research involves an ongoing synergism between theory and data using Trinidadian stream communities. We develop theory and then test predictions from theory with experiments in natural populations, semi-natural mesocosms, and the laboratory. As such, there are opportunities to conduct research in using any of these approaches.

Matt Carter

TBL 018 (laboratory); TBL 218 (office), mc10@williams.edu

To ensure that an animal obtains an optimal amount of sleep, food, and water, the brain must sense the internal and external environment and influence behavior by producing sensations we describe as “tired/awake,” “hungry/full,” and “thirsty/quenched.” The ultimate goal of my lab is to elucidate the neural basis of these homeostatic systems and behaviors using mice as a model organism. Which neuronal populations and neural networks in the brain play an important role in maintaining homeostasis, and how does their activity affect animal physiology and behavior?



Appetite-inducing neurons in a mouse brain. Neurons in the mammalian hypothalamus that produce the Agouti-related protein (AgRP) neuropeptide sense nutritional information in the blood and orchestrate an increase in food-seeking behavior. In this photomicrograph, AgRP neurons are transduced with red fluorescent protein and appear red. All cells are labeled with a DAPI stain and appear blue. In some lab projects, we selectively stimulate or inhibit AgRP neurons and measure changes in food intake behavior.

To address these questions, my lab uses classical and cutting edge neuroscience techniques. Neuroanatomical, imaging, and electrophysiological methods demonstrate which brain regions are active during specific behavioral states. Optogenetic and chemogenetic methods allow for the ability to stimulate or inhibit neurons in the brain of freely moving, behaving animals. Neuroanatomical and microscopy techniques show the structure of neural circuits. Taken together, these approaches allow us to dissect neural systems and circuits that regulate behavior.

By taking an integrative approach and performing experiments at the anatomical, molecular, physiological, and behavioral levels of investigation, we hope to make substantial contributions to understanding these homeostatic behaviors, and ultimately how they affect the health of the entire organism.

Pei-Wen Chen

SSB 110 (laboratory); SSB 130 (office), x3536, pc7@williams.edu

Concurrent remodeling of cellular membrane and actin cytoskeleton occurs in many biological processes such as cytokinesis, phagocytosis and cell migration. Broadly, my lab is interested in understanding the mechanisms underlying the coordinated change in various cellular membrane and actin structures as this coordination is fundamental for normal physiology and often disrupted in pathological conditions like cancer cell invasion and metastasis.

Specifically, we use focal adhesions (FAs) in mammalian cells as a model structure to investigate the role of Arf GTPase-activating proteins (Arf GAPs) in regulating dynamics of membrane and actomyosin networks (Fig 1). FAs are mechanosensing organelles that not only mediate cell adhesion to the extracellular matrix (ECM) but also sense and activate signaling crucial for cell survival, proliferation and differentiation. We use a combination of approaches including molecular cloning, biochemical and biophysical analyses, quantitative microscopy and cell biology techniques in our studies.

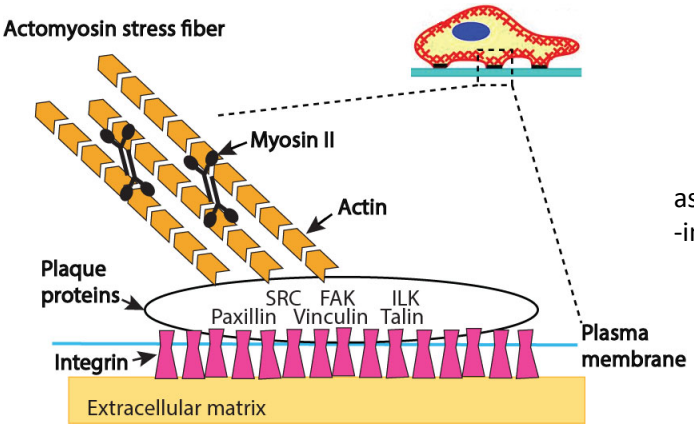


Figure 1 Components of focal adhesions.

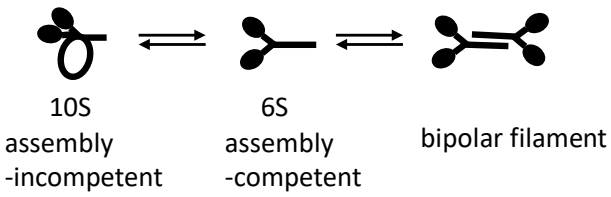


Figure 2 Conformations of Myosin II.

I. Molecular basis for the formation of Myosin II-Arf GAPs complex

Initial work will focus on one Arf GAP called ASAP1 because of its clinical relevance to cancer. ASAP1 is amplified in many human malignancies and elevated expression of which is implicated in cancer invasion and associated with poor prognosis. However, the mechanism by which ASAP1 contributes to cancer progress remains elusive. Through proteomic screens and subsequent biochemical, microscopic and functional analyses, we have identified the actin-associated motor, Myosin II as a novel binding partner and effector for ASAP1. Direct association of ASAP1 with Myosin II is essential for ASAP1 function in controlling actin remodeling, FAs and cell migration. We will generate, produce and purify mutants of ASAP1 recombinant proteins to determine the structural components in ASAP1 responsible for Myosin II-binding. We will also test if the formation of Myosin II-ASAP1 complex is modulated by other known binding partners of ASAP1, phosphoinositide PI(4,5)P2 and Arfs. By the end of the study, we will have defined the interacting motif/residues and a role of lipid in regulating Myosin II, which will position us to determine the biological function of the complex and rationally design small molecules that perturb the complex to block migration or invasion.

II. Regulation of Myosin II structural changes and bipolar filament formation

Myosin II assumes three forms: a folded assembly-incompetent monomer, an extended assembly-competent state and self-assembled bipolar filaments (Fig 2). The transition among the three forms regulates Myosin II ability to bind ATP and actin, which confers actin cross-linking and motor activity of Myosin II to generate contractility and cytoskeletal patterning in cells. Currently, there are no tools to detect Myosin II filament formation in live cells. Regulation of Myosin II filament formation in non-muscle cells has been centered on the phosphorylation of the regulatory light chain. Based on our result showing that siRNA-mediated knockdown of ASAP1 disrupted Myosin II structures in cells, we hypothesize that ASAP1 and perhaps a subset of Arf GAPs bind and control assembly of Myosin II filaments in specific time and space in cells. We will develop Föster resonance energy transfer (FRET) - based spectroscopy and microscopy assays to measure Myosin II filament formation and structural changes. We will first use purified Myosin II under conditions known to affect filament formation and computational modeling to establish the assay. We will then expand the study to live cells to test our hypothesis of Arf GAPs as a new class of Myosin II regulators.

III. Regulation of membrane and actin dynamics by Arf GAPs in cancer invasion and metastasis

There are multiple ways that ASAP1 may contribute to cancer invasion and metastasis. We will examine alternative hypotheses that can explain the effects of ASAP1 on cell movements and invasion. Given the known role of Arfs in membrane traffic, ASAP1 may control the secretion of collagen I and/or metalloproteases or delivery of integrin receptors to modulate cancer cell invasion. It is also possible that ASAP1 may regulate or under the regulation of signaling pathways such as RhoA and ROCK to affect actin dynamics and cell migration. Several cell-based assays, immunoblotting and immunofluorescence staining will be used in these projects.

Derek Dean

SSB 207 (laboratory); SSB 224 (office), x2004, ddean@williams.edu

Broadly speaking, my lab studies *Drosophila* genetics to study seizure disorders and wing development. I also have specific educational goals for students working in my lab that should be relevant whether they are planning on medical school, graduate school, or some other post-graduate endeavor. I hope to train students in the standard "genetic tool kit" available in flies (RNAi, GAL4, GAL80, *etc.*), which will be very useful foothold for understanding the molecular genetics of many other model systems.

I. *julius "seizure"*

The *Drosophila* "bang-sensitive" (BS) mutants respond to a mechanical jolt, cold shock, or even strobe lighting with a behavior that is behaviorally and physiologically similar to the seizures of mammals. This similarity, along with the wealth of genetic tools available in flies and their sequenced genome makes *Drosophila* an excellent model system to dissect the genetics that underlie seizure sensitivity.

Left vial in each panel, wild type flies. Right vial in each panel, mutants for the *jus* gene. After vortexing the culture vials, wild type flies do not appear to be affected, yet mutants have a seizure and then are paralyzed for 30-90 seconds.

It is becoming increasingly clear that insulin signaling affects the sensitivity of animals to seizures. For example, diabetes and hyperglycemia can induce seizures in humans, and mutations in the insulin pathway gene Akt1 lower the seizure threshold in mice. Our lab focuses on the bang-sensitive locus *julius seizure* (*jus*), named after the Roman emperor who reportedly suffered from epilepsy. Starting with flies that carry this mutation, we are asking how insulin signaling affects bang-sensitivity. We have found that mutations in *dfoxo*, a component of the insulin pathway, block the seizures of *jus* mutants. *dfoxo* encodes a Forkhead transcription factor that is upregulated under poor dietary conditions, and the genes that it targets have been uncovered in genomic studies by other labs. Using these findings as a point of information, we intend to identify the steps upstream and downstream of *dfoxo* that act to modulate bang-sensitivity. We also are working to determine the point of development when—and the tissue where—insulin signaling affects bang-sensitivity (*i.e.* if this is a developmental or acute effect, and whether insulin signaling acts directly on the CNS or indirectly through another tissue).

The Jus protein has a no clear homology to other known proteins, and so we are also interested in understanding the direct function of the protein. Using GFP-tagged alleles, we are characterizing the expression pattern and protein binding partners of Jus. Genes encoding binding partners will be tested for genetic interaction with *jus*. We have also made lines that express GAL4 in the pattern of the *jus* gene. This will enable us to better understand the function of *jus*-expressing neurons.

II. The role of IP3 signaling in wing development

The *Drosophila* wing has proven a useful tissue for study of signal transduction: it is not required for survival and its surface location on the animal make it useful in genetic interaction screens. *wavy*, a mutation causing crumpled wings, was initially described nearly 90 years ago but the associated gene was not identified until our Genetics class did so in 2014-15. The *wavy* gene encodes an inositol 1,4,5-trisphosphate (IP3)-kinase, an enzyme that phosphorylates IP3 to IP4. IP3 is a broadly conserved signaling molecule in nature—you may remember it from Biology 102 as a factor that causes the release of calcium from the ER during fertilization. Using the *Drosophila* genetics toolkit, we are working to determine the pathway surrounding *wavy*, ultimately to determine why loss of IP3-kinase function causes a crumpled wing. Current evidence suggests that Wavy and the IP3 receptor may interact to control levels of autophagy, a process by which the cell actively degrades certain components of itself. Misregulation of autophagy has been implicated in certain illnesses including cancer and autoimmune disorders, and so like our seizure model, study of *wavy* may be informative to medical research.

Left, wild type *Drosophila*. Right, mutant for *wavy*. (The eye color difference is due to a separate, unrelated mutation.)

Joan Edwards

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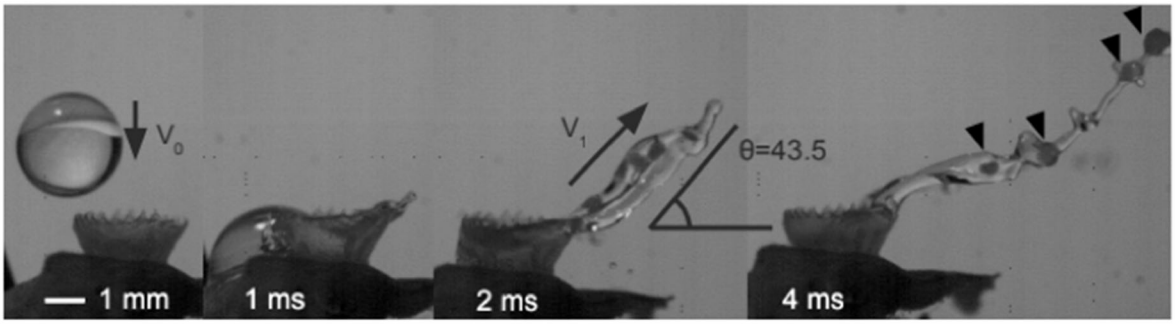


The gemmae cups of the liverwort, Marchantia, disperse gemmae by capturing the energy of a falling raindrop.

My research covers the areas described below:

Evolution of the biomechanics and adaptive behavior of ultra-rapid movements in plants. Examples of study plants include

a) Splash-cup dispersal by raindrops in *Marchantia*,
b) Use of plant "poppers" to propel seeds in wood sorrel (*Oxalis* spp.),
c) walking, jumping and gliding spores of horsetails (*Equisetum* spp.),
d) catapulting pollen in gaywings (*Polygala paucifolia*), stinging nettle (*Urtica* spp.) and bunchberry (*Cornus canadensis*), which has the fastest blooming flower (opens in <0.05ms!),
e) fruit explosion in touch-me-not (*Impatiens* spp.),
f) sphagnum moss (*Sphagnum* spp.), which has a spore-filled capsule that explodes open propelling the spores over 15cm into the air using a vortex ring.

We use high-speed cameras (filming at up to 100,000fps), microscopy (including SEM and EM), and field studies that focus on understanding the biomechanics and adaptive significance of these rapid movements.

Conservation of flowers and their pollinators. Pollinators and their flowers are part of the 6th extinction and in a worldwide decline primarily due to habitat loss. In New England, forests are increasing whereas field habitats where many of our most spectacular asters and goldenrods grow, have decreased. Using permanent plots in Hopkins Memorial Forest, we are testing how different mowing patterns affect the abundance and diversity of flowers. Changes in the floral resources, in turn, can affect pollinator populations. We are testing to determine the best management plan for fields to maximize resources for flowers and their pollinators.
Pollination Networks. Plant-pollinator systems have classically been defined by tight co-evolutionary links between flowers and their pollinators. Our current understanding of pollination systems has been based on sampling for brief periods (e.g., direct observation or net captures). We have developed a long-term time-lapse system that allows recording near-complete records of visitors to flowers as well as recording simultaneously at several different locations. These complete records are changing the way we think of pollinators and their flowers. The diversity of insect visitors is much higher that we thought based on the shorter observations. The taxa of insect visitors also differed among sites with important implications for gene flow.

Evolution and behavior of the sawfly, *Empria obscurata*. These remarkable larvae turn the color of whatever they eat so that they remain cryptically colored even when eating very different colored foods. So far, our studies have shown that larvae that eat both flowers (yellow) and leaves (green) have higher survivorship, achieve a larger adult size and develop more quickly that larvae fed on either flowers or leaves alone. We have also demonstrated that they

can complete their entire life cycle on alternate host plants—thus opening up the possibility of speciation by host-shift.

Long-term plant population studies of a) the invasive plant, *Alliaria petiolata* (Garlic mustard) in different successional stands in Hopkins forest—now in its 16th year— and b) the growth, survivorship and reproduction of arctic plants growing at the southern edge of their range on Isle Royale National Park, Lake Superior.

Phylogeography of arctic plants

This project is in collaboration with Professor Luana Maroja. Please see the description in her section.

Allison Gill

Arriving summer 2020

My lab investigates how plant-microbe interactions influence the movement of carbon and nutrients throughout terrestrial ecosystems. These processes are important for understanding how ecosystems will respond to ongoing global changes such as increasing atmospheric CO2 concentrations, warming temperatures, and anthropogenic nitrogen deposition. Approaches in my research group integrate long-term field studies, laboratory experiments, and data synthesis activities. This summer, there are opportunities for students in my lab to collect pre-treatment field data (litterfall, plant community composition, soil respiration, soil chemistry) associated with a new long-term nitrogen and carbon substrate addition experiment at Hopkins Forest. We will also conduct lab-based analyses on soils collected from a forest fertilization experiment at Cedar Creek Ecosystem Science Reserve in central Minnesota. This experiment has been treated with multiple forms of nitrogen and carbon-containing fertilizer (ammonium nitrate, protein, glucose) for fifteen years. We will assay rates of microbial respiration and extracellular enzyme production to evaluate how fertilizer treatments have influenced the activity of the soil microbial community and size & composition of the soil carbon pool. These lab-based analyses could be a great source of data for a senior thesis project or independent study!

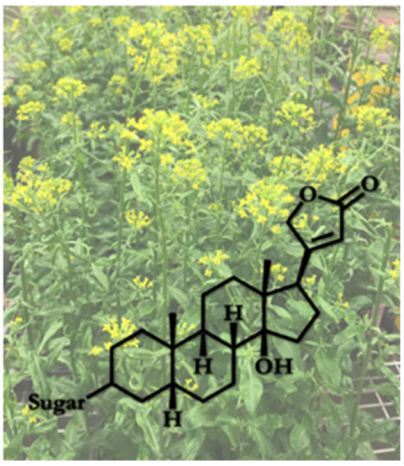
Cynthia Holland

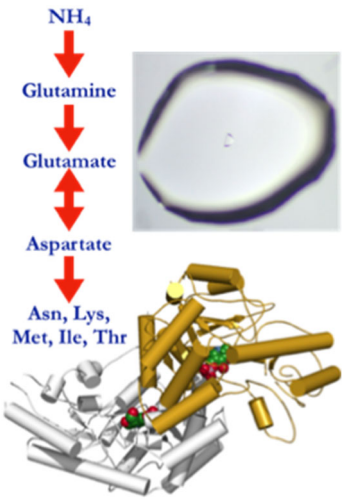
SSB 114 (laboratory); SSB 132 (office), x2746, ckh2@williams.edu

Plants are chemists that have spent the past 425 million years evolving enzymes to generate compounds that they use to grow, develop, communicate, reproduce, and defend themselves. There are numerous instances where an enzyme from primary metabolism will pick up a single point mutation that introduces a new function, which can sometimes lead to the biosynthesis of new compounds. Research questions in the Holland laboratory focus on the evolution of enzyme function and regulation in primary nitrogen metabolism and in defense metabolism. Discoveries from this research have potential biotechnology-related applications in agriculture, human health, and the environment.

Herbivore defense metabolism in wallflower

To defend themselves against insect predators, twelve plant families have independently evolved the ability to generate toxins known as cardenolides. Extracts from cardenolide-producing plants (wallflower in Asia, foxglove in Europe, and milkweed in North America) have been used to treat heart arrhythmias in the past and are currently being investigated for treating certain cancers. To date, the biosynthetic pathway for cardenolides is unknown. Using wallflower (*Erysimum cheiranthoides)* as a model, current research that correlates tissue-specific gene expression to cardenolide abundance is being used to identify candidate genes.Using a combination of functional genomics and biochemistry techniques, we hope to find genes involved in cardenolide biosynthesis and determine how this metabolic pathway evolved.



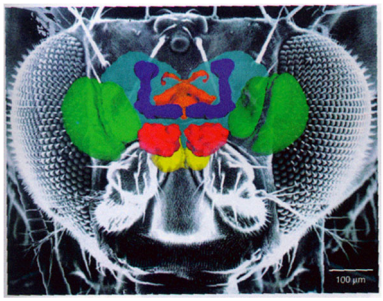


Plant nitrogen metabolism

Nitrogen is an essential nutrient for plant growth and is used by the plant to generate amino acids, which are components of enzymes and proteins. While a great deal of research has focused on the uptake of nitrogen, the enzymes at the interface of nitrogen assimilation and amino acid metabolism remain to be studied. Using a combination of plant genetics, biochemistry, and structural biology, our goal is to characterize the enzymes involved in aspartate and asparagine metabolism in the model plant *Arabidopsis* and soybean. Because many of these metabolic enzymes use intermediates from the citric acid cycle as substrates, we predict that we may uncover interesting links between central carbon metabolism and amino acid metabolism.

Tim Lebestky

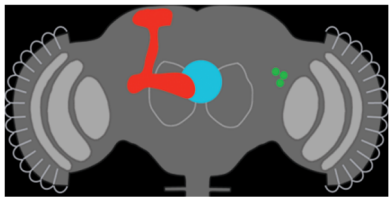
SSB 203 (laboratory); SSB 226 (office), x4508, timothy.lebestky@williams.edu

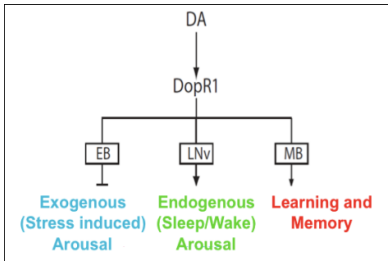


In the Lebestky lab, we utilize the genetic model system of Drosophila melanogaster for the study of behavioral genetics and molecular neurobiology techniques to understand arousal and sensory integration. Animals use their senses to learn about their immediate environment, parse the relevant information, and react in a meaningful way. If the sensory inputs are not interpreted correctly, this can cause inappropriate reactions, such as exaggerated behavioral responses to innocuous non-threatening stimuli, or by not reacting strongly enough to real threats. These concepts also translate into human biology, as imbalances in arousal and sensory gating are linked to pathologies, such as insomnia, attentional disorders, autism, and anxiety.

I. Behavioral Gating Mechanisms and Dopaminergic Circuitry in Arousal

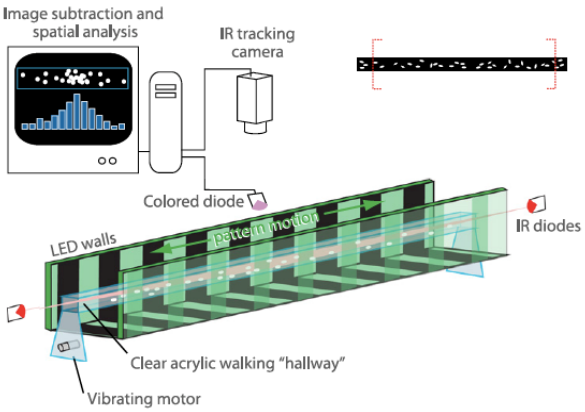
My lab has used the mechanical startle assay to identify the Dopamine Receptor (DopR) as an important component of the gating mechanism for "stress-based" arousal in the Central Complex region of the brain (blue circle) and we will extend the analysis to more deeply investigate the role of Dopaminergic circuits as well as try to identify and characterize additional molecular components. Mammalian studies of the basal ganglia suggest that DA oppositely regulates locomotion based on separate subclasses of post-synaptic neurons, also implicating the complex relationships between D1 and D2 family DA receptors. However, nothing is known of the interplay between these type I and II receptor families in Drosophila, and our behavioral assays allow for precise functional characterization and analyses currently unavailable in mammalian systems. To investigate these interactions in Drosophila, we will use multiple molecular, genetic, and behavioral techniques to separate and compare different forms of dopaminergic signaling in the brain. By coupling functional circuit manipulations with traditional immunohistochemical imaging techniques, we will try to unlock the many functions of multiple brain regions and evaluate our insights for relevant comparative studies of higher vertebrates.





II. Sensory Integration of Vision and Arousal State

There are very few examples of well-defined circuitries and molecular mechanisms in any model system, for the integration of arousal state and output behaviors. Therefore, in order to understand how arousal states translate into modulation of a simple sensory-based behavior, we use "the fly stampede" that measures visual responses to motion by tracking walking behavior. The arena of LED arrays create a pattern of moving light bars that elicit rapid reflexive walking behaviors in a freely moving population of flies. Furthermore, visual stimuli can be modulated to drive locomotor responses towards either the middle, or the ends of the arena. It was anecdotally noted in preliminary experiments that the fidelity and magnitude of the locomotor response is largely dependent on the animals' arousal state, since animals that receive no mechanical startle prior to the visual stimuli perform poorly in responding to motion. Also, given my earlier analysis of arousal phenotypes of DopR mutants, we have



tested their performance in the visual arena, and these mutant animals are indeed compromised in their ability to perform visual tasks. The visual system in Drosophila is well characterized and the extensive control of both stimuli parameters and genetic manipulation of specific cell types allows exact precise separability of potential hypotheses. We will functionally dissect the circuit requirements for DopR in vision and arousal by utilizing Gal4 lines as performed previously for separating sleep/wake and startle-based arousal (Figure in section I). These studies, coupled with new genetic screens, may provide new candidates and methods for understanding the molecular nature of disorders involving regulation of impulsive motor behaviors due to altered attentional or arousal states.

III. The Role of Serotonin in OCD and Autism

The primary molecular target for pharmacological treatment of depression and anxiety disorders is the human Serotonin Transporter (hSERT/SLC6A4). However, the mechanisms as to how blockade of hSERT results in therapeutic changes are not known. Human genetic studies have identified risk alleles that can provide critical clues about the molecular pathways responsible for disease. Moreover, the replication of these alleles in model organisms allows the experimental study of their activity in vivo, and testing of therapeutic strategies to mitigate their pathophysiological effects. Several highly conserved residues in SERT have been shown to be critical for its subcellular localization, and mutation of these sites may contribute to both obsessive-compulsive disorder (OCD) and autism. dSERT transgenes containing identical SERT mutations of interest can be used to test their ability to rescue the phenotype of a dSERT null mutant allele. Additionally, genetic model organisms such as Drosophila are highly amenable to directed genetic interaction studies and large-scale genetic screens. Such strategies may identify compensatory mutations that reduce the pathophysiological effects of the risk alleles, and help determine the cellular pathways required for the normal function of hSERT.

David Loehlin

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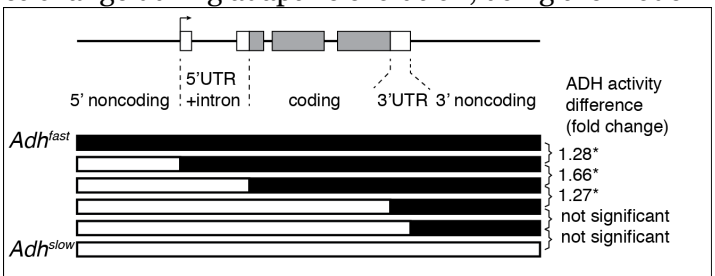
The Loehlin lab studies how adaptive evolution shapes gene function in multicellular organisms. Identification of the underlying principles is essential to our ability to predict the phenotypic consequences of mutations and variation from whole genome sequences.

One universal aspect of gene function evolution that has been largely unexplored is quantitative– how much protein or enzyme activity is produced by a gene. This is of particular interest in animal genomes, due to their complex gene regulation and the link to human biology. Open questions about quantitative gene evolution include: Do all aspects of gene structure contribute to adaptive functional change? When parallel quantitative adaptations occur in different lineages, do these follow similar paths, changing the same gene structures or nucleotides? What are the relative contributions of protein coding changes, *cis*-regulatory substitutions, and gene duplications? Do the same rules apply at different scales – is variation within populations representative of differences between species?

Research in the lab focuses on how genes change during adaptive evolution, using the model trait of alcohol metabolism in *Drosophila* flies. Most *Drosophila* species feed on fermenting fruits, but some species have adapted to low-alcohol foods like mushrooms whereas others actually prefer the alcohol-rich environments of breweries and wine cellars. We study how the *Alcohol dehydrogenase* (*Adh*) gene changed in these species.



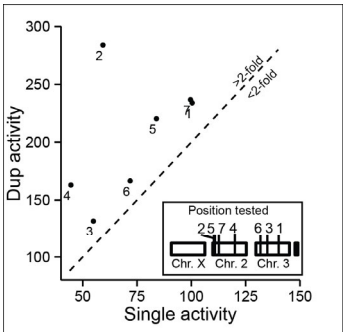
Gene components contributing to the difference between two *D. melanogaster* alleles. Recombinant constructs were constructed at the specified breakpoints. Fold change in ADH activity between adjacent constructs is shown.

The lab uses techniques of molecular cloning and transgenics, combined with high-throughput enzyme and gene expression assays to precisely measure the quantitative differences in enzyme activity that have accompanied these shifts in diet. This is a fertile research area, with multiple paths to investigate depending on student interest.

One early insight is that the *Adh* gene seems to have changed in activity in different species through changes in many parts of the gene – both in the coding sequence and regulatory regions. However, there is some evidence that there is a hotspot of repeated evolution in the core promoter. To follow up on this, a student might investigate how the promoter has diverged in multiple species and determine if canonical eukaryotic promoter elements such as TATA Box and Initiator are contributing.

A second major research area is trying to make sense of the observation that tandemly duplicated genes in *Drosophila* often do not produce 2-fold higher output than single copy genes (Loehlin and Carroll 2016). Basically, tandem duplicates of the whole *Adh* gene, or of unrelated reporter constructs, show enzyme activity and transcript levels that are *greater than twice that* of the single copy.

Currently, we are investigating if this excess expression occurs for other fly genes (using the CRISPR/Cas9 gene editing technique) or if some other pattern (less than twofold?) holds for other genes. Other aspects of this project that could be pursued are mechanistic aspects, such as copy-specific expression, as well as what the pattern of tandem duplicate expression is in yeast.



Expression (B-galactosidase activity) of single copy and tandem duplicate *vgQ-lacZ* reporter genes in seven chromosomal *attP* locations. Duplicate activity is significantly greater than twice single activity at each site.

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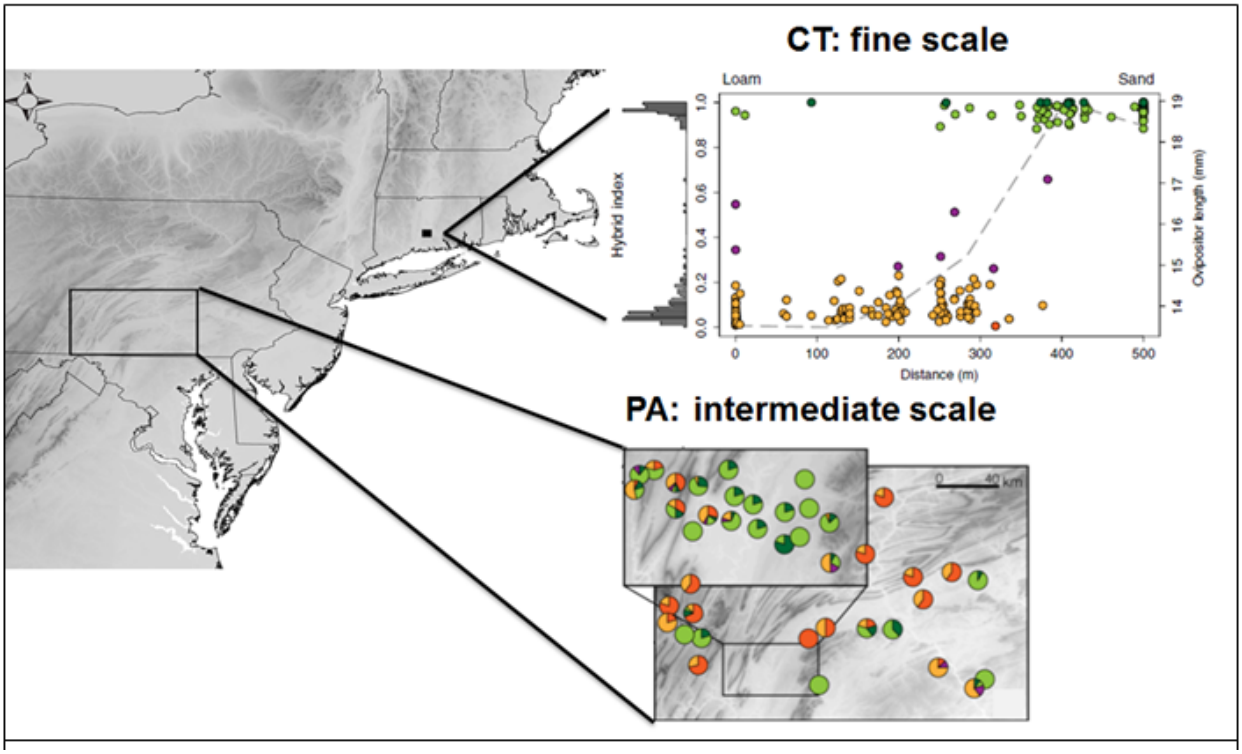
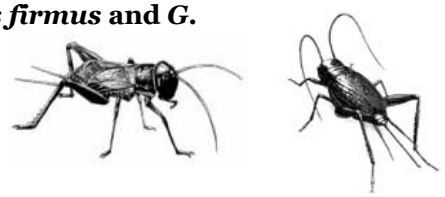
Gene flow between species: Can we find genes responsible for speciation and species isolation?



I am currently working in two species complexes, crickets and fruit flies. In both projects the aim is to help us understand the mechanisms that generate biodiversity. That is, how do two unique species evolve from one common ancestor? One way of examining this is to look at populations of closely related species that have recently diverged but are still able to mate with each other, producing hybrids and mapping families. What genes are responsible for the initial divergence and maintenance of species barriers? What are the mechanisms that impede such species eventually losing their identity through hybridization? Which genes are able to flow across the hybrid zone and which are limited to one species? What are the first genetic changes that lead to reproductive isolation?

Reproductive isolation between two field crickets, *Gryllus firmus* and *G. pennsylvanicus*



Recently diverged species, such as he crickets *G. firmus and G. pennsylvanicus*, share the majority of their DNA. This is both due to the short time they have been evolving independently and also because they can still exchange genes by producing hybrid offspring. Recently, some SNPs unique to each species and unable to pass the species barriers have been described. The very interesting observation is that most of the loci unable to cross the species barriers seem to be located in the X-chromosome, which might indicate a large X-effect in speciation or the presence of a single important X-linked locus. We are testing if any of these genetic locations determine whether the offspring of a heterospecific cross will be viable or not, to do this we will use population crosses between the two species and use next generation sequencing to scan SNPs in surviving offspring and parents that yielded fertile crosses. We will also use next generation sequencing to get a full sequence of the X chromosome and locate genes that seem to be important for speciation.

Martha Marvin

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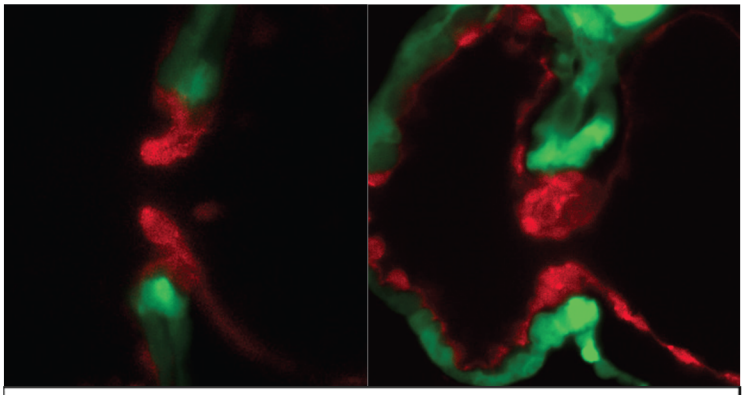
Our chief research interests are in **cardiovascular development in zebrafish** and the molecular mechanisms underlying variations in **stress reactivity** in embryos and adults.

Adult levels of stress reactivity are in part governed by early life experience of stress. We are investigating the genes that are modulated by early life exposure to stress, with a particular focus on genes that may undergo permanent epigenetic changes in expression levels from embryonic exposure through adulthood. These candidates could be key genes in setting the stress "thermostat" throughout life. We created mutations in *fkbp5*, a stress-modulating gene, using CRISPR/Cas9 mutagenesis. We study their motion and biochemical responses following stimuli to observe how the presence or absence of fkbp5 affects their stress response.

Zebrafish are an excellent model in which to study the developing heart, the most common organ to suffer birth defects in humans. The zebrafish heart begins beating at 24 hours, but is not required for survival for the first week, permitting the study of serious defects.



Deformed zebrafish embryo heart valves caused by estrogen exposure, viewed by confocal microscopy.

Cardiac valve growth is regulated by Notch signaling and by prostaglandins, which are more widely known as pro-inflammatory signals. Zebrafish exposed to exogenous estrogen or estrogen-like compounds causes the loss of heart valves. We are investigating the roles of signals such as Notch and prostaglandins, and their interaction with two estrogen receptors—the canonical nuclear receptor (ER) as well as the G-protein coupled estrogen receptor (GPER)—to clarify the developmental risks posed by exogenous endocrine disruptors.

Manuel Morales

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The overarching goal of my research program has been to understand the ecological and evolutionary dynamics of mutualism. My research addresses this goal using a variety of study systems, but focusing on the interaction between ants and the treehopper Publilia concava. In this mutualism, treehoppers feed on the phloem (sap) of the host-plant Tall Goldenrod (Solidago altissima) which is nitrogen poor and carbohydrate rich. Treehoppers filter large quantities of sap to meet their nutritional needs, and the carbohydrate-rich excrement (honeydew) is collected by ants as a food resource. In return, ants protect treehoppers from predators, and the act of removing honeydew facilitates feeding by treehoppers. Below, I highlight two projects that illustrate the current direction of my research program.

Tri-trophic population dynamics of mutualism.

The main project that I am involved with is an NSF-funded study to understand the consequences of mutualism in a community context. I have addressed this question using both modeling and empirical approaches. For example, a simple model of mutualism involving ants, treehoppers, treehopper predators, and host-plants shows that by reducing the impact of predators on treehoppers, protection by ants can allow treehoppers to overexploit their host plants. Thus, while ant protection can provide short term benefits, it can generate population cycles over the long term. I have begun to test these model predictions in the field. Early results suggest that treehoppers do have strong negative effects on host-plant quality between years but that treehopper mothers avoid these plants when deciding where to oviposit.

The European Fire Ant

A third project that I am involved in is a collaboration with colleagues at Skidmore College and the University of Connecticut to assess the role of mutualism in the spread of invasive species. In the spring of 2003, I discovered the invasive European Fire Ant (Myrmica rubra) in Williamstown MA, previously recorded outside of its native range almost exclusively along the coast of northern New England. Research in my lab found that this population of M. rubra appears to be concentrated along the Hoosic River watershed from North Adams, MA to Hoosic Falls, NY.

Interestingly, the presence of this ant species is correlated with the abundance of a second invasive species, the plant Japanese knotweed. Japanese knotweed has extrafloral nectaries that attract ants who defend these plants against their natural enemies. While there are few herbivores of Japanese knotweed in its introduced range, a third invasive species, Japanese beetles, can inflict high levels of herbivory. In these cases, ants effectively defend plants from beetle herbivory. Ongoing research is aimed at identifying how mutualistic interactions can affect the population dynamics of participants in these invaded communities.

Claire Ting

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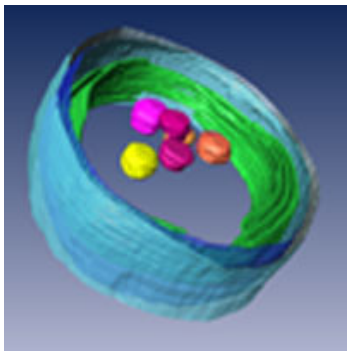
Photosynthesis is a fundamental biological process upon which the majority of Earth's life depends. How do differences at the genome level between closely related photosynthetic organisms translate into selective physiological advantages in photosynthetic capacity and in tolerance to abiotic stress? What is the significance of existing molecular/physiological diversity for the ecology of photosynthetic organisms and the evolution of niche differentiation?



In order to address these questions my laboratory is focusing on the ecologically successful marine cyanobacterium, *Prochlorococcus* (image on the left depicts a *Prochlorococcus* cell visualized by the Ting Lab using cryo-electron microscopy). This microbe is thought to be the most abundant photosynthetic organism on our planet. In certain regions of the oceans, more than 10,000 cells can be found in a single drop of sea water. *Prochlorococcus* plays a key role in primary production and in global energy cycles, and is an excellent model for plant photosynthesis. The projects in my lab are interdisciplinary and integrate tools and concepts from fields including genomics, biochemistry, cell biology, ecology, and evolution.

Photosynthetic Physiology and Environmental Stress Response Mechanisms
Through comparative studies of closely related isolates, we are investigating the photosynthetic physiology and environmental stress response mechanisms of *Prochlorococcus*. The availability of 12 complete *Prochlorococcus* genome sequences has enabled us to formulate specific hypotheses regarding how isolates and ecotypes will respond to key environmental factors, such as light and temperature. These studies will contribute to our understanding of the survival and distribution of *Prochlorococcus* populations in the open ocean water column and how this important marine microbe will respond to global environmental change.

Comparative Genomics, Metagenomics, Metatranscriptomics
Our most recent grant from the National Science Foundation has funded our field work in the Sargasso Sea, an open ocean region where *Prochlorococcus* often dominates the bacterioplankton population. We are conducting metagenomic (characterization of genes/genomes isolated from environments) and metatranscriptomic (characterization of gene expression in natural communities) analyses in order to understand how key environmental factors impact community composition and biological activity in open ocean waters.

Ting Lab research assistants conducing field work in the Sargasso Sea.

Structural Characterization of Photosynthetic Microorganisms
Because *Prochlorococcus* cells are tiny (approximately 100 cells can be lined up side by side across the width of a human hair!), we are using state-of-the-art microscopy techniques to characterize the cellular structure and organization of *Prochlorococcus*. We have discovered that closely related isolates exhibit significant differences at the ultrastructural level, including in the number and organization of their internal membranes, where proteins involved in photosynthesis are localized.

Damian Turner

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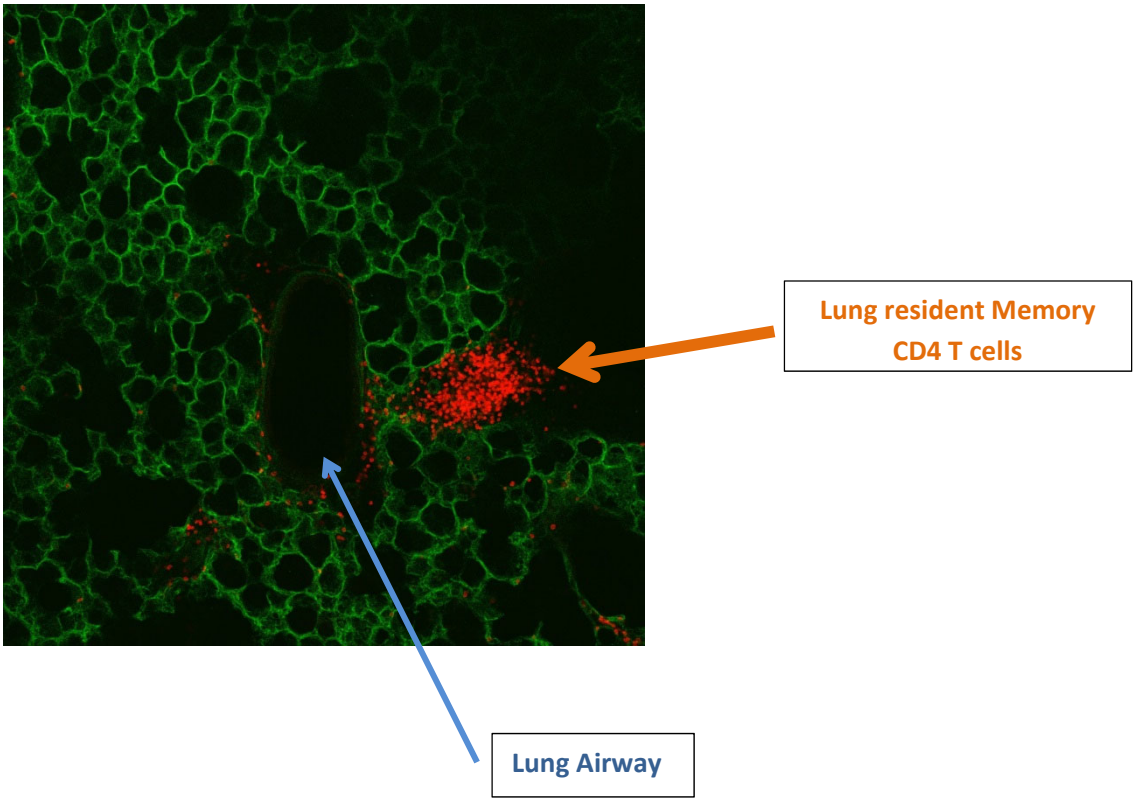
Resident memory T cells and the pathogenesis of asthma

Asthma is a chronic inflammatory disease of the lung which results in narrowing of the airways, breathing difficulties which can lead to death. According to CDC estimates, approximately 1 in 12 people (25 million) have asthma and asthma was responsible for 1.8 million emergency room visits in 2010. Current treatment strategies for asthma include inhaled corticosteroids that can control airway inflammation but do not cure chronic allergic asthma. Understanding the mechanisms leading to the development and chronicity of asthma is therefore critical to designing more effective therapies and to cure this disease.

Memory CD4 T cells play important roles in the initiation and regulation of asthma and have been shown to coordinate disease pathology through the recruitment and activation of effector cells like eosinophils and mast cells. Allergic asthma is driven by inhaled allergens that, over time, create populations of allergen-specific memory T cells. We have identified a new subset of tissue resident memory CD4 T cell (CD4 TRM) within the lung which are maintained independently of circulating populations and which exhibit peribronchiolar localization that ensure early exposure to inhaled matter. We have further found that CD4 TRM are generated in the lung of mice following long-term exposure to the common household allergen, house dust mite (HDM) allergen. We have found that allergen-specific TRM in the lung are rapidly activated and migrate into the airways upon re-exposure to the allergen. Lung TRM may therefore represent critical targets in new approaches to prevent chronic and recurrent asthma symptoms. I wish to investigate the role of lung TRM in the pathophysiology of allergic asthma. Furthermore I will use antigen specific immunotherapy to target the TRM population and assess the effect on disease severity and chronicity.



Heather Williams

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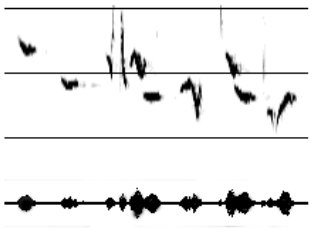
Research in the Williams lab focuses on how birds learn and use their songs, how variation in songs arises, and what that variation means.

Cultural evolution of song

Socially learned behaviors, such as songs, are transmitted and changed in ways analogous to and yet different from genes. Males may learn from their fathers, older neighbors, or even from males of the same age, and females may prefer certain song characteristics and so influence learning. We seek to understand how, in a wild population of Savannah sparrows, these factors combine to cause some parts of the song to be stable for decades, others to vary rapidly and randomly, and still other song segments to vary systematically over time. To address these questions, we use observation (tracking changes in song and relating them to characteristics of the singers), comparisons (contrasting the songs of different populations), experiments (exposing young birds to a variety of songs to determine which novel sounds are incorporated into the population), and modeling (collaborating with mathematicians to assess which processes best match the data).

Sexual selection and song complexity

House finches' songs consist of a fixed number of syllables that can be sung in different arrangements. The syllable sequence can "branch" and take different paths at specific points in the song, with two or more options for the next syllable. House finches often sing many songs in succession, and they tend to vary the syllable sequence from song to song. They also frequently "countersing": two males face each other and alternate songs. There are also specific syllables sung only when courting females. We study these variations in syllable order, an analog of syntax, and ask whether the variations have specific patterns, whether these patterns change when a male courts a female or countersings with another male, and how song patterns relate to other signals of male quality. The answers to these questions will inform our understanding of how signaling systems are organized and used.



Song organization

Like human speech, bird song can be divided into phonology and syntax. Birds learn phonological units (notes or syllables) from conspecific singers, and then assemble these subunits to form a song. The songs of different species appear to follow different syntactical rules; winter wrens' songs, though elaborate and complex in their phonology, have an invariant syntax, house finches have rules that define a variety of paths through their large syllable repertoires, and zebra finches have both a small syllable repertoire and a relatively simple linear syntax. We investige how syntax arises through 1) comparative studies of related species, 2) presenting young finches with variable syntax in model songs to determine whether abnormal syntax can be learned, and 3) tracking the responses of females to artificially constructed songs with either fixed or variable syntax.