Biology Department

Honors Research and Summer Research Open House

Tuesday, January 19th
7:00pm
Thompson Biology Room 112

Wednesday, January 20th
Lab Open House
1pm – 4pm

Department Chair: Joan Edwards
x2472

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 12th. Applications can be found online at:

http://biology.williams.edu/research/honors-research/

Faculty accepting honors students for **academic year 2016-2017**:

Lois Banta, Ben Carone, Dawn Carone, Pei-Wen Chen, Derek Dean, Joan Edwards, Tim Lebestky, Dan Lynch, Luana Maroja, Martha Marvin, Manuel Morales, David Smith, Claire Ting, Damian Turner, Heather Williams

Faculty accepting **summer** students for 2016:

Lois Banta, Dawn Carone, Pei-Wen Chen, Joan Edwards, Tim Lebestky, Dan Lynch, Luana Maroja, Martha Marvin, Manuel Morales, David Smith, Damian Turner, Heather Williams

Open House Schedule		
Faculty	**Time**	**Location**
Joan Edwards	1:00 – 2:30	TBL 217
Lois Banta	2:30 – 4:00	TBL 301
Martha Marvin	2:30 – 4:00	MSL 126
Dan Lynch	2:00 – 4:00	BSC 260
Luana Maroja	3:00 – 4:00	BSC 163
Tim Lebestky	3:00 – 4:00	BSC 032
Heather Williams	2:00 – 3:00	TBL 019
Claire Ting	3:00 – 4:00	TBL 214
Derek Dean	2:00 – 4:00	BSC 240
David Smith	3:00 – 4:00	TBL 205
Damian Turner	1:00 – 2:00	BSC 136

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

Professor Art, *henry.w.art@williams.edu*
Professor Carter*, mc10@williams.edu*
Professor Morales, *mmorales@williams.edu*
Professor Dawn Carone, *dmc5@williams.edu*
Professor Ben Carone, *brc1@williams.edu*
Professor Chen*, peiwenchn@gmail.com*

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

Hank Art

Class of 1966 Env. Center 203 (Office), Rosenburg Center (Laboratory), x2461
hart@williams.edu

350 Years of Carbon Sequestration in an Old-Growth Forest: The Beinecke Stand in the Hopkins Memorial Forest represents one of the best examples of an old-growth woodlot in the region. Although during the 18th and early 19th centuries there may have been some limited tree cutting in this 12-acre site, the structure of this patch of forest indicates that the stand has never been intensively used by humans. The collection of quantitative data on this tract was started by the U.S. Forest Service in the 1930s and has been continued at 5-year intervals over the past several decades. This project involves the analysis of the patterns in carbon distribution and sequestration through analysis of forest population history, tree-ring patterns, mapping the spatial distributions of trees in the stand and measurement of organic matter concentrations in live vegetation, litter-fall, and soil components.

P.S. Prof. Art is teaching a Winter Study course in California during January, 2016. Please contact him via email at HArt@Williams.edu if you are interested in the project and would like more details before his return to campus in February.

Matt Carter

BSC 019 (Laboratory) TBL 218 (Office), x2196, matthew.carter@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. Which neural populations and neural networks in the brain play an important role in maintaining homeostasis, and how does their activity affect animal physiology and behavior?

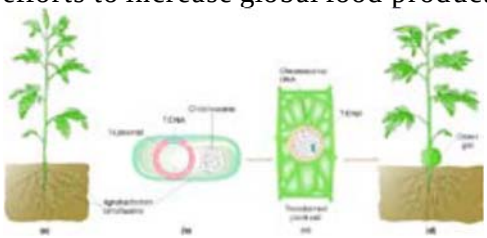
To address these questions, my lab combines mouse behavioral experiments with a variety of approaches. Neuroanatomical and electrophysiological methods demonstrate which brain regions are active during specific behavioral states. Cutting-edge optogenetic and pharmacogenetic methods allow us the ability to stimulate or inhibit specific neurons in the brain in a freely moving, behaving animal to test hypotheses about the role of these neurons in behavior.

By taking an integrative approach and performing experiments at the behavioral, anatomical, physiological, and molecular 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.

Lois Banta

TBL301 (Laboratory), TBL213 (Office), x4330, lbanta@williams.edu

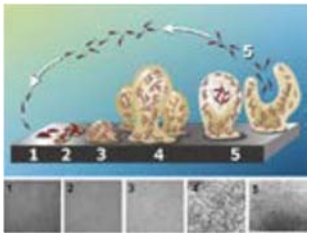
In the Banta lab, we study the interactions between the soil bacterium Agrobacterium tumefaciens and its host plants. In particular, we are interested in the transport of a large fragment of DNA across the membrane system surrounding the bacterium, and in the plant defense responses elicited by the bacterium. 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. David Rogawski '08 discovered that a newly identified secretion "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 are currently investigating why bacteria deficient in the T6SS exhibit enhanced attachment to 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 students Aubrey Kenefick '16, Jacob Kim '16, and Breanna Nguyen '16, as well as Adam Resnick '17 and Ruby Froom '17, 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 characterize this novel pathogen-recognition pathway, using protein biochemistry, plant genetics, and molecular biology approaches.



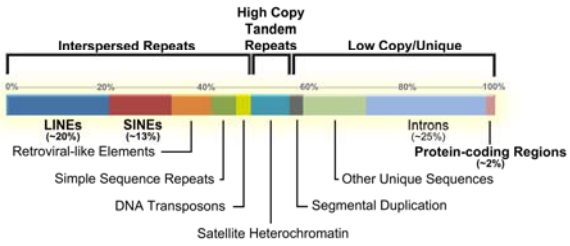
Formation of bacterial biofilmsSource: biology.binghamton.edu/davies/research.htm

Dawn Carone

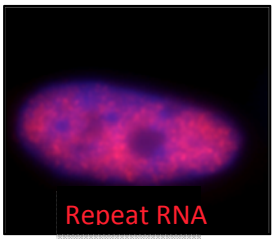
BSC236 (Laboratory), BSC223 (Office), x2244, dmc5@williams.edu

My lab studies human nuclear structure and the elements that contribute to maintaining nuclear integrity. We use a targeted combination of approaches including state of the art molecular cytology with quantitative microscopy, molecular biology and genomics in our investigations.

Uncovering functions for the junk of the human genome: Over ten years ago, the human genome was sequenced, however there is still much of the genome sequence that is a mystery. High-copy repetitive elements comprise roughly half of our genome, and the bulk of these are unexplored and understudied. The goal of my research is to uncover the many potentially important functions for the repetitive half of the genome as it relates to nuclear structure and gene regulation. As cutting-edge genomics studies are increasingly generating large amounts of data on the interactions between DNA, RNA and protein, it is becoming increasingly apparent that there is widespread transcription of repetitive sequences and these have critical gene and nuclear regulatory functions. As these functions are uncovered, it is becoming clear that misregulation of repeat-derived transcripts has wide-ranging implications for cancer, and many other diseases. We are developing new techniques to release this nuclear-



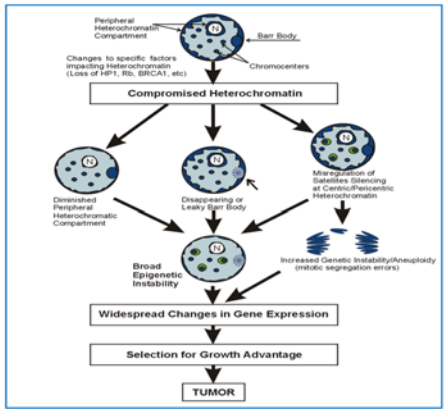
High-copy number repeats comprise the left half of the genome typically considered "junk DNA."



Heterogeneous Repeat RNA detected in situ is abundantly expressed in normal human fibroblasts.

bound repeat RNA in order to sequence, study, and, ultimately, manipulate it. In order to do this, we have developed quantitative methods to compare in situ nuclear RNA signals to extracted RNA.

Misregulation of satellite DNA in cancer and heterochromatin instability: Another project in the lab is focused on a subset of repetitive elements, satellite DNA, which are tandemly repeated near the centromeres of all human chromosomes. We have identified a specific satellite sequence that is aberrantly expressed in a wide range of human cancer cell lines and tissues, and may be a potential biomarker of cancer. This satellite is not only aberrantly expressed, but accumulates within nuclei of cancer cells and binds regulatory proteins, which is linked to genome methylation status. We are currently trying to understand the mechanisms underlying the satellite misregulation and the impact this has on regulation of the cancer genome more broadly. Satellite misregulation is a potential read-out for global misregulation of highly-packaged and normally compartmentalized heterochromatin, as detailed below.



Heterochromatin instability in cancer may be common and important to cancer genesis. Changes to heterochromatin maintenance could cause over-expression of satellite RNAs and generate a diversity of potentially neoplastic expression profiles. (Carone & Lawrence, Seminars in Cancer Biology 2013).

Steve Swoap

BSC168 (Laboratory), BSC166 (Office), x3336, sswoap@williams.edu

The cardiovascular state of animals is remarkably dependent on the environment. Foraging of food, consumption of food, presence of predators, procuring a mate, ambient temperature, and general activity are just a few examples of external stimuli that have a substantial impact on homeostasis of the cardiovascular system. Research in the Swoap lab examines the underlying mechanisms for cardiovascular adaptations to both changes in ambient temperature and lack of food availability.

Our approach is an integrative one; combining molecular biology, thermal physiology, and cardiovascular physiology. Body temperature, blood pressure, and heart rate measurements are made in genetically modified animals using a telemetry-based system. This allows for accurate physiological measurements in animals that are conscious, unrestrained, and freely moving. The use of mice with known germline mutations allows us to directly test hypotheses that relate caloric intake, ambient temperature, and metabolism with cardiovascular function.

Dan Lynch

BSC262 (office); BSC260 (laboratory); x2330; daniel.v.lynch@williams.edu

Sphingolipids have been demonstrated to play important roles as both membrane components and as signaling molecules involved in regulating cellular processes in eukaryotes. Only recently has it been established that sphingolipids are quantitatively important components of specific membranes in higher plants and appear to serve as signaling molecules in plants. While the majority of these studies have been carried out using the model angiosperm plant Arabidopsis thaliana, research in the Lynch lab employs the moss Physcomitrella patens for studies of sphingolipid metabolism and function. Moss species were some of the first land plants, and their simpler morphology and growth patterns facilitate study. The genome of this moss has been sequenced, and methods for transforming moss allow us to investigate the roles of sphingolipids in the plants and provide insight into plant sphingolipid metabolism. These studies incorporate aspects of molecular biology, biochemistry and plant physiology.

Pei-Wen Chen

New faculty member starting Fall 2016

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.

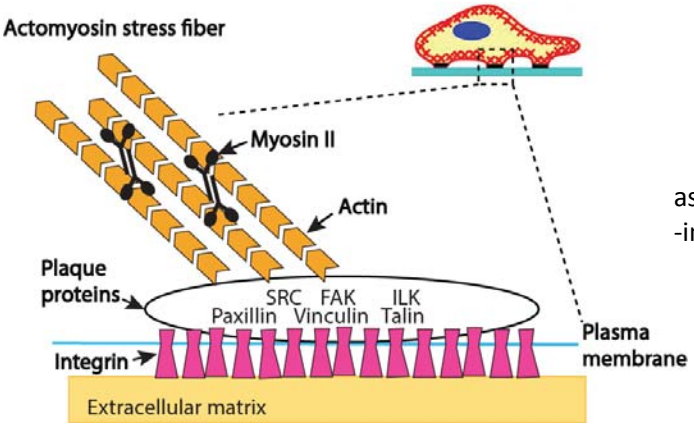


Figure 1 Components of focal adhesions.

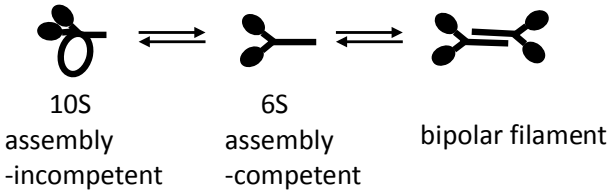


Figure 2 Conformations of Myosin II.

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

BSC240 (Laboratory and Office), x2004, ddean@williams.edu

How metabolism affects seizure sensitivity. I use the fruit fly, Drosophila melanogaster, as a model system to study seizure disorders. The Drosophila "bang-sensitive" (BS) mutants respond to mechanical shock with a behavior that is 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.

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 mutation sda[iso7.8] in the aminopeptidase N gene slamdance. 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 sda[iso7.8] 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).

We are excited about these findings in and of themselves, as well as their potential for informing the medical community. 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. In addition, my lab has imported a neurophysiology technique to quantify the voltage necessary to induce seizures. This could be a valuable experience for those interested in neuroscience.

Ben Carone

BSC136 (Laboratory); TBL216 (Office); x2266; brc1@williams.edu

The human body is composed of ~30 trillion cells, all with the same genes and same DNA sequences. Despite this, our bodies contain cells with wildly different morphologies and functions, leading us to wonder how the same genic content can be interpreted so differently.

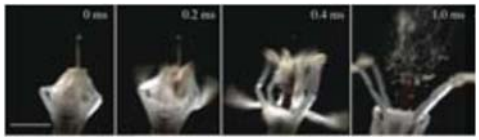
My laboratory works in the field of Epigenetics: the inheritance of phenotypic changes in the absence of corresponding changes in DNA sequence. Often this phenomenon is the result of specific chemical modifications of DNA or modification of proteins that interact with DNA. Experiments in my lab focus on developing the technology to rewrite the epigenetic code and understanding how the deposition of specific epigenetic marks affect gene activity. To accomplish this work, we work with the model organism S cerevisiae which is easy to genetically manipulate and has a very well characterized chromatin organization. Students interested in this project can expect to learn advanced molecular techniques, tools for genetic engineering, and develop a strong understanding of epigenetic phenomenon.

Joan Edwards

TBL012 (Laboratory); TBL217 (Office); x2472; jedwards@williams.edu

My research covers four broad areas described below:

Evolution of floral diversity including mechanisms and adaptive behavior of ultra-rapid movements in plants. Examples of study plants include a.) bunchberry (*Cornus canadensis*), which has the fastest blooming flower (opens in <0.05ms!), b.) sphagnum moss (*Sphagnum* spp.),hich has a spore-filled capsule that explodes open propelling the spores over 15cm into the air using a vortex ring, c) fruit explosion in touch-me-not (*Impatiens* spp.), which use a slingshot mechanism to propel seeds away from the parent plant, d.) catapulting pollen in gaywings (*Polygala paucifolia*), and stinging nettle (*Urtica* spp.). e.) Spash-cup dispersal by raindrops in *Marchantia*. These studies use high-speed cameras (filming at up to 100,000fps), microscopy (including SEM and EM), and work in the field that focuses on understanding the plants *in situ*.



Pollination Networks. Plant-pollinator systems have classically been classified by tight co-evolutionary links between flowers and their pollinators. This has led to the identification of pollination syndromes: bee flowers, bird flowers, butterfly flowers, *etc.* Increasingly, ecologists have observed visitors from many different taxa visiting a given flower species. Working with the flowers in the boreal forests and those in fields in Williamstown, we are identifying pollinator behaviors and describing ways in which flowers can use insects from multiple taxa to effect efficient pollination.

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.

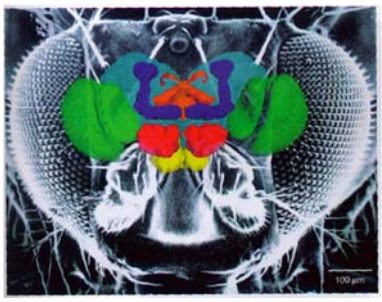
Conservation of fall-blooming asters and goldenrods. In New England, forests are increasing whereas field habitats where many of our most spectacular asters and goldenrods grow, have decreased. Using permanent plots in Hopkins Memorial Forest, we are testing how different mowing patterns affect floral diversity. We are testing how changes in the flowerscape, in turn, affect pollinator populations.

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

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.

Tim Lebestky

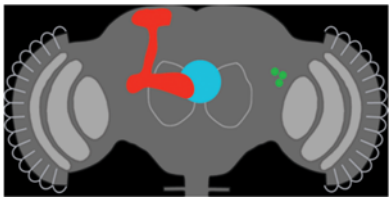
BSC029 (Laboratory). TBL201 (Office), x4508, timothy.lebestky@williams.edu

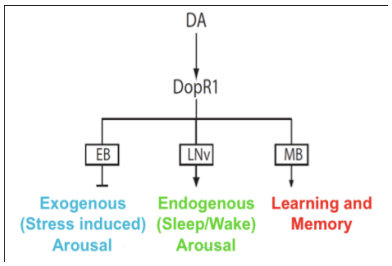


In the Lebestky lab, we utilize the genetic model system of Drosophila melanogaster for the study of behavioral genetics and molecular neurobiology techniques to understand arousal and sensory integration. Animals use their senses to learn about their immediate environment, parse the relevant information, 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

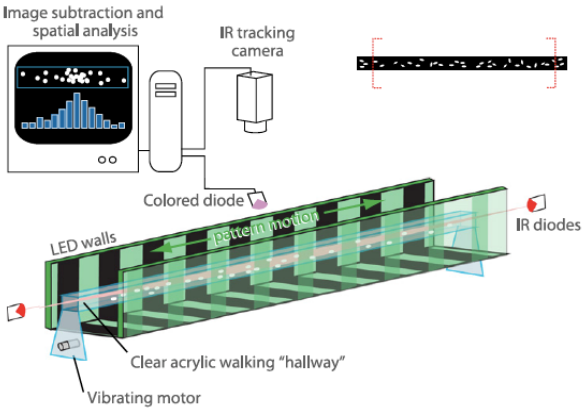
My lab has used the mechanical startle assay to identify the Dopamine Receptor (DopR) as an important component of the gating mechanism for "stress-based" arousal in the Central Complex region of the brain (blue circle) and we will extend the analysis to more deeply investigate the role of Dopaminergic 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.

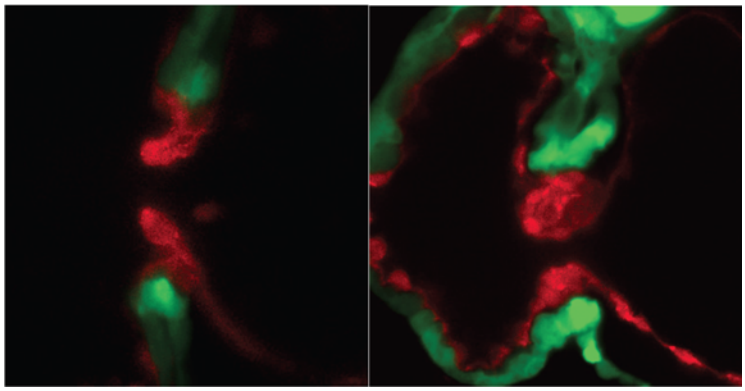
Martha Marvin

MSL126 (Laboratory); MSL126 (Office); x3546, mmarvin@williams.edu

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

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 hope to soon have fish with a mutation in *fkbp5*, a stress-modulating gene. We will study their behavior with larval and adult stress response tests that we are developing in the lab.

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.



Atrio-ventricular valves (red) in *hspb7* knockdown embryos (B) are enlarged and misshaped compared to control embryos (A).

Small heat shock proteins defend the organism against excess heat and toxins, but have essential functions in normal development as well. The small heat shock protein *hspb7* is essential for motility of the cilia that establish laterality, as well as limiting the size of heart valves (see figure). Loss of *hspb7* causes the valves to become thickened and stiff. We are developing Crispr/Cas9 tools to target hspb7 and other genes in the heart valve development pathway.

Cardiac valve growth is promoted by Notch signaling and regulated by prostaglandins, which are more widely known as pro-inflammatory signals. We are investigating the roles of these signals and their interaction with *hspb7* to clarify the role played by the versatile yet mysterious family of small heat shock proteins.

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.

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

These projects aim 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? These are some of the questions we can answer, as we examine the barriers to gene exchange in closely related cricket species *Gryllus firmus* and *G. pennsylvanicus.*

Recently diverged species, such as *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 trying to test 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.

Phylogeography of arctic plants

This project is in collaboration with Professor Joan Edwards

Phylogeography is the study of genetic variation over space. It provides important information to understand demographic history and mechanisms of evolutionary processes in nature (e.g. population expansion, contraction, migration patterns, selection). In this project we will look at population genetic structure of a disjunct arctic plant species located in Isle Royale National Park, Lake Superior and Newfoundland, Canada. These populations are remnant populations of cold adapted plants that were once widespread during the last glaciation maxima – now the species only occur in the arctic and in Isle Royale (all other connecting populations have been extinct and the Isle Royale populations are likely threatened due to climate change). In this project we will use genetic markers (chloroplast and nuclear markers - microsatellites) to analyze several populations to understand how climatic changes are shaping genetic diversity in these populations.

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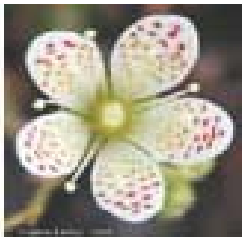

David C. Smith

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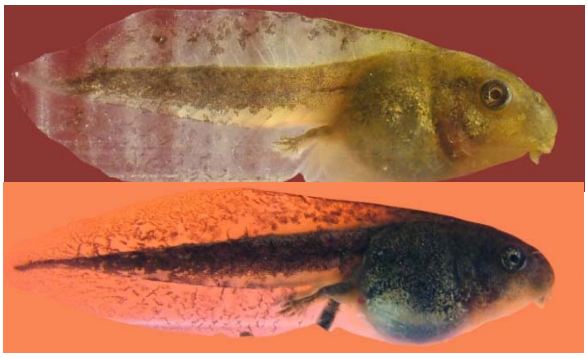
I'm interested in the dynamics of microevolution and ecology that control the distribution and abundance of natural populations, especially vertebrates. My research focuses on population of the boreal chorus frog on Isle Royale, a wilderness National Park in Lake Superior, Michigan. This population is relatively undisturbed, and it provides a model not only for frogs, which are now seriously declining in numbers, but also for natural populations in general. My work combines field experiments and long-term observations (over 30 years) on both evolution and ecology.

Chorus frog adults are terrestrial and live in the forest – body length, 1.2 inches.

My first area of research focuses on the population dynamics of the frogs. We know from our earlier experiments that tadpole numbers are controlled by predation, competition, and environmental disturbances. We are now interested in how these factors relate to larger scale patterns in population abundance. Our long-term census data indicate that the populations cycle in numbers, and that the tadpole distribution among pools is strongly controlled by the quality and spatial pattern of pools available for breeding. These patterns provide us a starting point to dissect a number of ideas about how the local control of tadpoles maps into the persistence of the frog population as a whole, as well as to judge the prospects of the population in the face of regional climate change.

My second area of interest is in how phenotypic attributes of tadpoles and their developmental flexibility are shaped by natural selection, and what explains the limits to local adaptation on the part of the tadpoles. Chorus frog tadpoles are mostly restricted to temporary pools with low abundance of predators, yet individual tadpoles can modify their behavior and body shape developmentally in ways that appear appropriate to habitats that have higher food levels and more predators. My work focuses on quantitative traits and their genetic basis, with particular attention to how these traits are inherited, and on how natural selection shapes these attributes in different habitats occupied by the tadpoles.



Chorus frog tadpoles shift phenotype according to habitat - the upper grew in a pool with predatory dragonfly nymphs (note taller tail fin, green color), and the lower in pools without dragonflies (note shorter rounder body and black color).

Dragonfly-free pools for chorus frogs on Isle Royale lack emergent vegetation around the edges due to recurrent wave wash from Lake Superior.

My third focus is on how Pleistocene invasion history and present-day population structure (especially subdivision among different islands) have shaped the genetic variability of the frogs, and how this variability in turn may control the evolutionary responses to selection by the tadpoles. Our work on selection suggests that multivariate genetic variability is relatively restricted in chorus frog populations. My work relies primarily on dissecting measures of genetic variability that we obtain from DNA markers, particularly mitochondrial haplotypes and microsatellite alleles. This work in molecular evolution is in part carried out in collaboration with the Maroja laboratory.

Claire Ting

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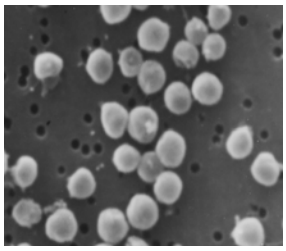
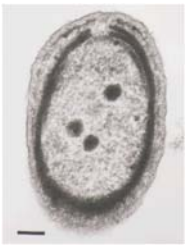
Photosynthesis is a fundamental biological process upon which the majority of Earth's life depends. Research in my laboratory focuses on photosynthetic processes and proteins and on the response of photosynthetic organisms to environmental stress. Projects are interdisciplinary in nature and integrate tools and concepts from fields including genomics, biochemistry, cell biology, ecology, and evolution.

Research in my lab is funded by the National Science Foundation. In one project we are addressing how differences at the genome level between closely related photosynthetic organisms translate into selective physiological advantages in photosynthetic capacity and in tolerance to abiotic stress. We are focusing on the environmentally important marine cyanobacterium, *Prochlorococcus*, which is thought to be the most abundant photosynthetic organism on our planet. In certain regions of the world's oceans, more than 10,000 cells can be found in a single drop of sea water. In particular, *Prochlorococcus* plays a key role in primary production and in global energy cycles, and is an excellent model for plant photosynthesis.

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 natural environments) and metatranscriptomic (characterization of gene expression in natural communities) analyses in order to further understand how key environmental factors impact community composition and biological activity in open ocean waters. As part of this project we are also focusing on photosynthetic proteins and structures, including an important "microcompartment" called the carboxysome, which permits photosynthetic bacteria to concentrate carbon dioxide in the vicinity of the enzyme Rubisco.

Because *Prochlorococcus* cells are tiny (approximately 100 cells can be lined up side by side across the width of a human hair!), students in my lab have the chance to learn how to use state-of-the-art microscopy techniques. My lab, in collaboration with the labs of Professors Lopes (Physics) and Park (Chemistry), recently received an NSF grant to purchase two atomic force microscopes for Williams College. Students who are interested can learn different microscopy techniques, including transmission electron microscopy and atomic force microscopy, to study cell structure and function.

A.  B. 

Scanning (A) and transmission (B) electron microscopy are techniques we use for visualizing the ultrastructure of photosynthetic organisms and can reveal important changes in cell morphology following the exposure of organisms to environmental stress. *Prochlorococcus* cells are depicted in the above micrographs.

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

Damian Turner

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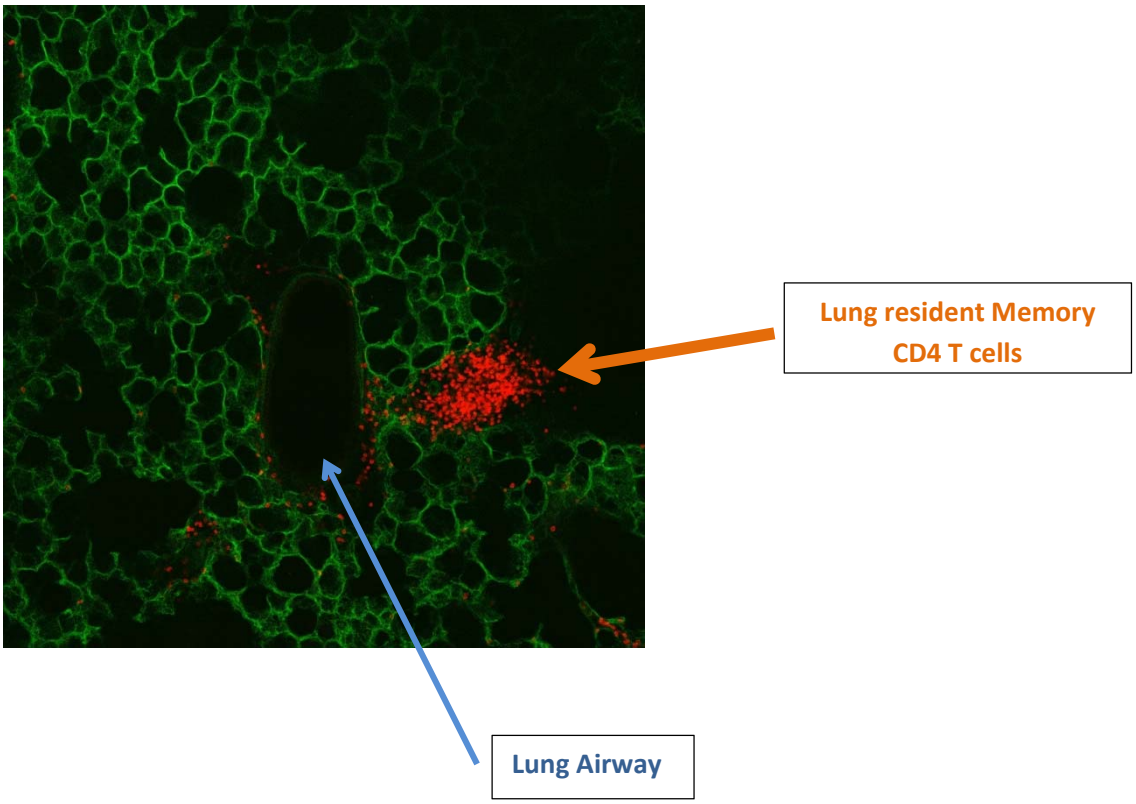
Resident memory T cells and the pathogenesis of asthma.

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 T_{RM}) 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 T_{RM} 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 T_{RM} in the lung are rapidly activated and migrate into the airways upon re-exposure to the allergen. Lung T_{RM} may therefore represent critical targets in new approaches to prevent chronic and recurrent asthma symptoms. I wish to investigate the role of lung T_{RM} in the pathophysiology of allergic asthma. Furthermore I will use antigen specific immunotherapy to target the T_{RM} population and assess the effect on disease severity and chronicity.



Heather Williams

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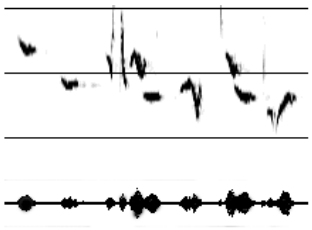
Research in the Williams lab focuses on how birds learn and use their songs, and how variation in songs arises and what it means.

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 are investigating 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.

How, when and why do birds shift their song organization?



House finches' songs consist of a fixed number of syllables that can be sung in different arrangements. Past work has shown that variation arises at specific points in the song where the sequence can "branch" - with two or more options for the next syllable. House finches often sing many songs in succession, and tend to vary the syllable sequence from song to song. They also frequently "countersing": two males face each other and alternate songs. Do the variations in sequence and the progressions through those variations have specific patterns, and do these patterns change when a male countersings with another whose pattern may be different? The answers to these questions will inform our understanding of how the signaling system is organized and used, and may also have implications for models of how the brain encodes song sequences.

Cultural evolution of song

Learned traits, such as songs, are transmitted and changed in ways analogous to genes. Males may learn from their fathers, older neighbors, or even from males of the same age, and females may prefer certain song characteristics. 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. The approaches we use are observational (tracking changes in song and relating them to characteristics of the singers), comparative (contrasting the songs of different populations), and experimental (exposing young birds to a variety of songs to determine which novel sounds are incorporated into the population).