TELLING THE STORY OF SCIENCE

Today's PhD researchers are finding their voice — building skills they need to describe their work to funding agencies, the noise-filled media, and the rest of us.

PHOTOGRAPHS BY BEN GEBO

Across the Graduate School's science disciplines, there is a growing recognition — often driven by students themselves — of the need to train young researchers to communicate complex or technical ideas in a way that makes them vivid and comprehensible to a broad audience. Whether that audience consists of federal agencies, hiring committees, or the general public, graduate students in the sciences are deeply interested in talking about their research with people outside of their immediate scholarly communities.

A workshop series held this January — called **ComSciCon Local** — exemplified the trend. The workshop was organized by Communicating Science, an organization founded and run by PhD students from Harvard and MIT. It seeks to encourage the kind of communication skills that students are increasingly hoping to acquire, sponsoring conferences that offer productive interaction with professional science communicators and lasting networks with peers. (See page 6 for details on the ComSciCon initiative, and visit www.comscicon.com.)

ComSciCon organizers asked the Harvard PhD students who participated in the January workshop to develop brief articles, aimed at a broad audience, that answered the question, **"What surprising role will your field take in explaining, shaping, or solving a problem faced by society this century?"** Four of the resulting pieces were selected for publication in *Colloquy*.

HOLLY ELMORE

The Story Behind the Story of Life

In my comparative genomics research, studying the genomes of fungi makes me feel like a detective getting to know a neighborhood. Sometimes the equivalent of graffiti on the walls or garbage in the streets can tell amazing stories — tales of trauma, death, desperate measures, and change that is occurring much faster than any of us once suspected. Take the fungal agricultural pathogen *Fusarium oxysporum*. I identified a possible defensive adaptation to a common pesticide without ever having studied the organism itself, just by following the leads in its genome.

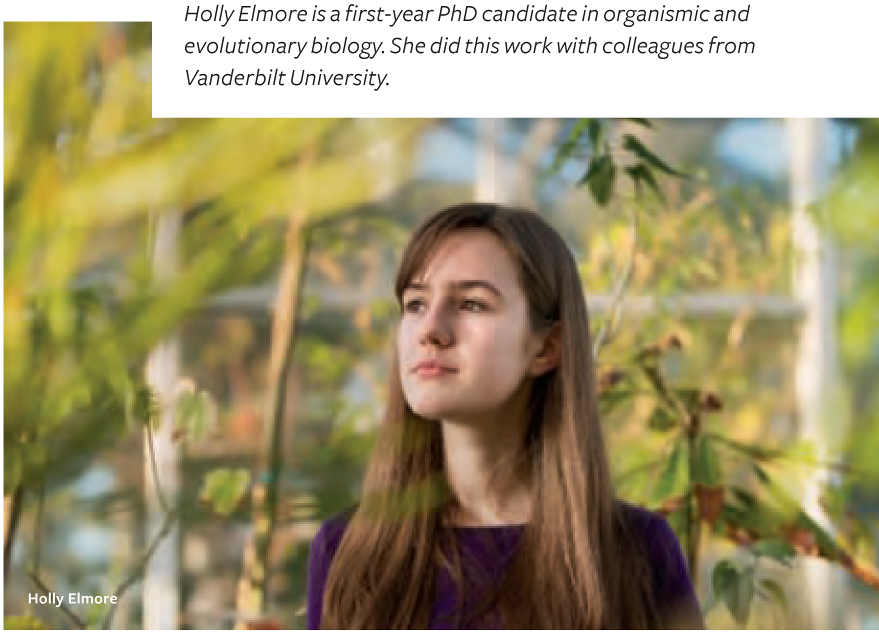
The characters in this story, the genes, can belong to a "family" of similar genes, a group of "colleagues" in the same metabolic pathway, and a "neighborhood" in the same physical location on the chromosome. Every strain of this fungus has the two genes that together combat this pesticide, but in some strains, the two are next-door chromosomal neighbors as well as colleagues. This physical proximity allows the genes to better work together, particularly when they are both needed on short notice to counteract a toxin. On top of that, this pair is ready to relocate together to new strains of the fungus on a mobile chromosome. Most chromosomes, like most neighborhoods, stay put. Mobile chromosomes, however, do not confine themselves to one lineage of parents and offspring, but can cross the borders between genetically distant individuals like a caravan, spreading the potential pesticide resistance to new strains. Their gain is our agricultural loss.

So, how did I piece all this together? Good, old-fashioned detective work aided by some fancy computational tools. Genomes are often described as a set of instructions to build and maintain an organism, but that is not the whole story. The working genes (the neighbors) represent only a sliver of the genome; the rest is a mixture of crucial genomic context (roads and buildings) and genetic garbage (trash and graffiti), that together form a historical record. I compare different genomes, all of which are variations on a common ancestor's theme, to better understand how evolution takes its many paths.

Curiosity drove me to investigate this case, but the results led me to some very practical conclusions. Before the genomic era, we did not appreciate how many avenues are available for resistance to evolve. The genes themselves are no different between strains, but their context — next-door neighbors on a mobile chromosome — can lead them to work together in very different ways, leading to differences in each strain's pesticide sensitivity.

Beyond even the practical lessons, there is something profound about exploring an organism's genetic environs. *F. oxysporum*'s genome bears the traces of the chaotic history behind an evolutionary arms race — a gripping and almost relatable account, for those who know how to interpret it. This kind of work was inconceivable just half a century ago, before we could read the genetic code. Through comparative genomics, I have the privilege of exploring a world that is both completely foreign and strangely familiar, following clues to solve mysteries that could lead to a better future and deeper understanding of the story behind the story of life.

Holly Elmore is a first-year PhD candidate in organismic and evolutionary biology. She did this work with colleagues from Vanderbilt University.


Holly Elmore

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Grigori Guitchounts

GRIGORI GUITCHOUNTS

The Neuroscience Society

Despite the recent media frenzy about all things *neuro*, from neurolaw to neuromarketing and brain games, drinks, and apps, most neuroscience research today is conducted with the ultimate goal of curing brain diseases, which take a great economic and emotional toll on our society.

Curing disease is of paramount importance, but it may turn out to be one of the simpler endeavors of future neuroscience. Understanding how the brain works might be the more complicated part. And to really understand something, you have to build it.

While most current technical efforts are aimed at reverse-engineering the brain (figuring out how the brain works by taking it apart), future neuroscience will guide forward-engineering. Given our accumulated knowledge of how the brain works, we will be able to create machines that mimic or replace brain function.

At Harvard, David Cox's lab is working toward reverse-engineering the biological visual system by gathering neural data from experiments in rats, and then applying those lessons to forward-engineer better computer vision systems. Computer vision and facial recognition systems such as Facebook's, as well as neural prosthetics that replace faulty senses or add novel ones (like artist Neil Harbisson's "eyeborg"), are just a few examples of ground-breaking neural research already being put into practice.

In addition to advances in computation, understanding the brain as a machine could also provide solutions to mental illnesses faced by millions. Knowledge of the neural mechanisms behind common disorders like depression or anxiety could guide behavioral treatments that help afflicted people live happy, productive lives.

A recent study at MIT showed that old, deeply ingrained fear memories, typically difficult to forget, were easily extinguished with the help of a molecule that promotes malleability of neural circuits. When mice underwent fear-conditioning, their traumatic memories were malleable for a short period of time, during which neuronal chromatin — packets in which DNA is stored — was relatively plastic. If the memories were allowed to age, however, the associated chromatin lost its plasticity and the memories became hard to attenuate. Using a drug that promotes chromatin malleability, the researchers showed that the old fear memories became just as easy to extinguish as new ones. This research could one day be combined with PTSD therapy to help patients lose negative associations to known stressors.

We are still far from being able to reap the full benefits of neuroscience, but treating the brain like a machine will eventually allow us to fix or alter it to our liking. Humans have been striving to take control over nature since the dawn of time — by building fires and homes, by domesticating wild animals and cultivating the land, and by creating technology in all its forms. A deep understanding of the brain could give humans the ultimate control: control over the self.

And while this struggle for self-improvement is a familiar theme, the potential of neuroscience to make a positive contribution isn't well appreciated. We forget that our entire selves — our minds, personalities, and emotions — are a product of data-crunching neurons. Manipulating these neurons could not only relieve illness, but change what it means to be human.

Grigori Guitchounts is a first-year PhD candidate in the Division of Medical Sciences (neurobiology).

FLORENCE YONG

An Analytic Approach to Risk and Intervention

On a bright, sunny morning, the editor-in-chief of the scientific journal *Advances in Nanoparticles* was killed on her way to work by a reckless driver. The tragic crossing of their paths proves a common point: every day, we are exposed to various types of risk — from accident or disease, from crime or the environment. Our vulnerability to risk is ever-present in our increasingly volatile world.

Florence Yong

Do we simply wait for our fate to befall us? The increasing availability of "big data" — massive, complex volumes of data generated from genomics, from electronic medical records, and from social media, among other sources — has provided us with a golden opportunity to harvest useful information, reduce risk, and develop targeted treatment or intervention for undesirable outcomes. With the many resources spent in drug development, how can we identify the right group of patients for more effective treatment? With limited government resources, how can we efficiently help children at risk of abuse? With our modern transportation infrastructure, how can we reduce the number of people killed and injured in traffic crashes each year — a number that would fill Fenway Park 60 times over?

Led by Professor Lee-Jen Wei, my dissertation research aims at developing quantitative methods in personalized medicine. Combining advanced mathematical, statistical, and computational methods, we propose systematic procedures to build and evaluate risk-scoring systems according to how well they predict in an independent population.

We then optimally separate subjects into distinctive groups with a clinically meaningful risk difference between them. For example, four groups of patients with different characteristics may be identified with an average of six-month survival difference between neighboring risk groups. When employed in collaboration with subject-matter experts, such novel methods to stratify individuals can help practitioners develop a more personalized intervention strategy for people in each distinct risk group.

The data analytics team for the 2012 presidential election used uplift modeling to identify likely voters early on for fundraising and voter-mobilization efforts. In a similar spirit, early identification of sub-populations who are (or are not) likely to experience a treatment benefit can potentially save lives and resources, while alleviating adverse treatment effects. Our proposed concepts and procedures, now in active research, could be adapted in vast areas of application, ranging from identifying people with high risk of life-threatening disease to finding those who are at high risk of endangering themselves or other people. Intervention or therapeutic treatment programs can then be developed via multidisciplinary collaborations.

Imagine if that reckless driver had been identified earlier and had undergone anger management. Imagine if his smart phone or car had signaled his outrageous speed and controlled it. The scientist who died on that sunny morning — my beloved sister Virginia — might still be alive. The development of innovative analytic methods presents an exciting opportunity to avert crises across a range of areas. By harnessing the passion and prowess of subject-matter experts, and our ever-growing bank of available data, we can develop targeted and cost-effective strategies to deter harm and create a safer and healthier environment for all.

Florence Yong is a fourth-year PhD candidate in biostatistics.

KATIE BORONOW

A Tale of Two Lizards: How Behavior Can Buffer Against Climate Change

Katie Boronow

On a cold morning, 8,000 feet above sea level, the Caribbean island of Hispaniola looks and feels more like New England: Instead of palms, pine trees surround me, and I'm wearing a fleece and a rain jacket over my t-shirt to stay warm. I am here with fellow PhD student and head researcher Martha Muñoz and a team of undergraduates to study the lizards that live in this unusual environment. Unlike humans, these lizards can't just put on a sweater to stay warm. Genetic evidence indicates that these high-elevation lizards (*Anolis shrevei* and *A. armouri*) are descended from the same ancestor as another species that lives in the island's tropical lowlands (*A. cybotes*). By comparing the high-elevation species to their low-elevation relative, we hoped to identify differences between the species that could have resulted from adaptation to differing environments.

What we found surprised us: High- and low-elevation lizards are similar in fundamental ways. Crucially, Muñoz found no difference among the three species in either body temperatures recorded in the field or temperatures selected by lizards during a lab experiment that offered them a range of choices. How could high-elevation lizards living in a much colder environment still prefer the same temperatures as their tropical relatives?

We think the lizards have changed their behavior to compensate for the different temperatures in the two environments. At low elevation, lizards choose densely forested areas where they spend most of their day in the shade; at high elevation they spend almost all of their time in open areas in direct sunlight. But perhaps most important, the lizards switch from perching on tree trunks at low elevation to rocks at high elevation. Unlike tree trunks, rocks heat up rapidly, and it is only on rocks that high-elevation lizards can achieve body temperatures comparable to those of their tropical counterparts.

In this case, behavior appears to shield the high-elevation lizards from evolving a preference for cooler temperatures. This result challenges our assumptions of how animals will respond to global climate change. Scientists have often theorized that climate change will cause animals to migrate to areas matching their current environmental preferences, rather than stay put and adapt. This way of thinking forms the basis of models predicting how species' habitat availability will change under hypothetical climate scenarios. For many species, suitable habitat is predicted to shrink, sometimes to levels that threaten their survival.

But these models ignore how individuals can use behavior to construct their own microclimates. By burrowing deeper into the ground, retreating into the shade, or perching on a rock, an animal can manipulate its local environment and maintain its climatic preferences even in seemingly unsuitable habitat. Incorporating this understanding into models of habitat shifts will lead to more accurate predictions of the impact of climate change on animal communities — and perhaps lower the number of species predicted to become endangered. While global climate change threatens our environment, animals acting to buffer themselves from climatic shifts will be able to stand their ground.

Katie Boronow is a third-year PhD candidate in organismic and evolutionary biology.