# 2017–18 UCSANTACRUZ

## **Electric** avenues





### The spirit of inquiry@UC Santa Cruz

Welcome to the third edition of *inquiry@UC* Santa Cruz! This annual research magazine is jointly sponsored by the Office of Research and



University Relations, and provides updates on some of the exciting and innovative work being conducted by UC Santa Cruz researchers. It also highlights our campus's training in public outreach: the magazine showcases features written by graduates of UC Santa Cruz's internationally renowned Science Communication Program.

In this issue, the creativity that is part of the ethos of the UC Santa Cruz

campus, from engineering to the arts, is illustrated through topics that include the deployment of novel materials made from crustacea and cephalopods (shrimps and squids) as guides for applications that range from biosensors to environmentally friendly surfboards; UC Santa Cruz's spearheading research on the Victorian author and social critic Charles Dickens, via its ongoing Dickens Project; and the urban planning implications of self-driving cars, which are programmed to defer to pedestrians.

Our researchers also continue to be honored for the impact of their work: honors this year include the three-million-dollar Breakthrough Prize, endowed by Silicon Valley entrepreneurs, awarded to Harry Noller for his half-century of pioneering work on how ribosomes and RNA make cells work—and how they may have even been the keys to the first life-forms on Earth.

We hope that you enjoy the descriptions of the research enterprise at UC Santa Cruz that are highlighted in this 2017–18 edition of *inquiry*. As can be seen in the features, our researchers, staff, and students all contribute to making UC Santa Cruz research a bold, creative, and vibrant enterprise that pushes the frontiers of human knowledge in new and unexpected directions.

Scott A. Brandt Vice Chancellor for Research and Professor of Computer Science

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About the cover: Hawaiian bobtail squid, one of many ocean-dwelling creatures that have beaks made of chitin, a hard substance from which UC Santa Cruz engineers are developing more efficient biosensors and novel materials. PHOTO BY KLAUS STIEFEL, FLICKR, CREATIVE COMMONS

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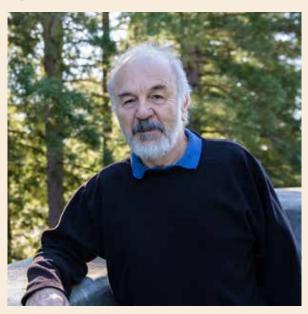
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#### **MOLECULAR BIOLOGY**

#### By ribosome rewarded



Harry Noller, the Sinsheimer Professor of Molecular Biology at UC Santa Cruz, won the 2017 Breakthrough Prize in Life Sciences for his decades of discoveries that revealed how RNA played a central role in ribosome function and, in turn, all of the building blocks of life.

For revealing the central role of ribosomes in creating life through RNA and proteins, Harry Noller, Sinsheimer Professor of Molecular Biology, won the 2017 Breakthrough Prize in Life Sciences. The \$3 million award is funded by Silicon Valley entrepreneurs to support the sciences.

"I can't think of a more meaningful way to spend one's career than working on the ribosome, one of the most amazing objects in all of the universe," said Noller.

Since 1972, when Noller first showed that RNA was essential for ribosomes to produce proteins, his studies have spotlighted the role of RNA-not DNA-in

the origin of life. In 1999, his lab produced the first high-resolution image of the molecular structure of a complete ribosome, a feat upon which they later improved.

"Our long-term goal is to create a threedimensional movie of the ribosome carrying out protein synthesis at the atomic level," said Noller, who plans to continue at the lab despite his emeritus status.

**Pinpointing structural** changes during protein production could provide clues to how complex life arose from simple combinations of atoms, heat, and water. "It's a tall order," said Noller, "but it's not crazy."

#### BIOMOLECULAR ENGINEERING

#### Cutting edge

In normal cells, mRNA splicing can edit a single sequence of genetic material in various ways, making transcripts for many different proteins.

Increasingly, studies have shown that aberrant splicing induces widespread transcript changes in associated cancers, noted Angela Brooks, UC Santa Cruz assistant professor of biomolecular engineering. For the first time, in a study published in Cancer Cell, Brooks and her colleagues linked one specific change in the splicing complex to a functional effect.

The SF3B1 mutation alters a single protein in the splicing complex. With Brooks' expertise in computational analysis of mRNA transcripts, researchers uncovered an SF3B1-induced change in the DVL2 gene, which, in turn, activated a cancer pathway previously known as a factor in chronic lymphocytic leukemia, but not known to be activated by SF3B1.

Now Brooks is developing highthroughput assays to simultaneously test the functional effects of hundreds of mutated RNA transcripts. She's also focused on better understanding the splicing mechanism.

PLUTO COURT

NOLLER

-0S:

"Even in normal tissue we get different splicing patterns and we don't really have a grasp of what's happening," she said.

#### **ECONOMICS**

#### **College chances**

Will lottery winners spend their windfall on college education?

Only if they win big, according to UC Santa Cruz economists George Bulman and Robert Fairlie, in a working paper published through the National Bureau of Economic Research.

"College is a big capital investment that drives government programs, tax exemptions, and life outcomes," said Bulman, whose research focuses on why people choose higher education-or not.

U.S. Census Bureau data shows that 63% of students from highincome families attend college compared with 36% from low-income families. This disparity is often attributed to college costs and constraints to getting loans, said Fairlie.

After analyzing federal tax records linked to federal financial aid awards for more than one million children whose parents won \$600 or more in the lottery from 2000 to 2013, they found wins less than \$100,000 had little effect on college enrollment. Surprisingly, payouts that exceeded the cost of college continued to increase the probability of enrollment; the effect of a \$1 million win was much larger than that of a \$500,000 win.

"Maybe it's not all about money," said Fairlie. "We may need to do more to show people the value of education."

#### COMPUTER SCIENCE

#### Linked up

Making sense of big data can be a big problem. Information comes from disparate sources with bias, collection and missing data issues, noted Lise Getoor, UC Santa Cruz professor of computer science. So how do you build methods that can integrate this data and make interesting (and valid) inferences?

PLANETARY SCIENCE



Surface images of Sputnik Planitia (an area on the heart-shaped feature of Pluto that was formerly known as Sputnik Planum), taken by NASA's New Horizons mission, bolstered the argument for a subsurface ocean on Pluto.

It's no coincidence that Sputnik Planitia has a special place in the heart-shaped surface feature on Pluto. The big basin, flooded with nitrogen ice, lies almost exactly underneath and opposite Pluto's largest moon. Holding that nearly-equatorial spot requires a lot of extra weight, noted Francis Nimmo, professor of Earth and planetary sciences at UC Santa Cruz. The question was, in a 1,000 kilometer-wide hole, where was that heft hiding?

"A subsurface ocean is the easiest way of getting extra density, since water is denser than ice," said Nimmo, making that case in a paper published in Nature.

A Fellow of the Association for the Advancement of Artificial Intelligence, Getoor founded a line of research called statistical relational learning. Her methods mix network information with statistical information, exploiting background knowledge and domain theory as well-mapping, for instance, the underlying power structures among corporate entities or

predicting outbreaks of social unrest.

For such work, Getoor and her collaborators developed an opensource, probabilistic soft logic (PSL) tool, that can represent structure and uncertainties in networks, and make inferences in a scalable way-at orders of magnitude faster than competing approaches. The latest PSL release occurred this year.

Returning with images of fractured surfaces all over Pluto, NASA's New Horizons mission helped resolve the hidden ocean question, a possibility Nimmo previously described in a 2011 paper. If a big impact dug out the basin, the ice removed would be replaced with denser water from an ocean below. The slow expansion of the freezing water closer to the surface would crackle the sphere's crust.

"We're finding more oceans in the outer solar system," said Nimmo. While they could indicate habitability, he's more intrigued by the fundamental science: "With the information we have, what can we learn about these icy bodies?"

#### BRIEF inquiries

"The key thing about my work," said Getoor, "is that it not only makes use of probabilistic information, it also makes use of relational information, uncovering links and ties among all kinds of data."

On the flipside, Getoor and her group also study privacy issues learning how to prevent unwanted linkages.

#### PHYSICS

#### **Proton power**

Proton radiation treatment can target solid tumors with less harm to surrounding tissue than X-ray radiation therapy.

Pretreatment planning requires a 3D map of "proton stopping power," or how fast the proton loses energy and slows down as it passes through tissues before hitting the tumor. Those values are now estimated from images taken by X-ray computed tomography (CT) scanners, but a proton CT (pCT) scanner would make direct and more accurate measurements.

Now, UC Santa Cruz researchers, working with Loma Linda University Medical Center scientists, have a prototype pCT capable of completing a full scan of a human headsized object in less than 10 minutes, said Robert Johnson, chair of the Physics Department and first author on a paper describing the machine, published in *IEEE Transactions on Nuclear Science.* 

Making a scan in a few minutes requires measuring a million individual protons per second, noted Johnson. With experience designing NASA's Fermi–Gamma ray Space Telescope–plus leftover silicon-strip detectors from that project—Johnson helped overcome those technical challenges.

"We are now comparing simulated treatment plans [with the prototype] against those obtained by a new X-ray technique," said Johnson. "If we're successful it could really improve cancer treatments, which is the ultimate goal."

#### LINGUISTICS

#### **Talking points**

Technology started talking back when Siri was introduced. But

#### CHEMISTRY AND BIOCHEMISTRY

#### Knot known

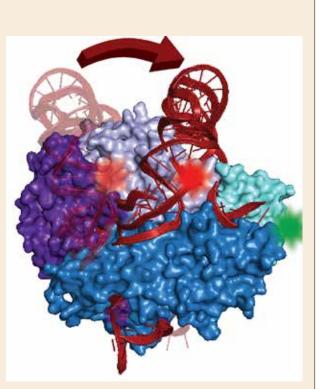
Rapid cell division relies on telomerase. an enzyme complex that makes DNA for protective caps on the ends of chromosomes. Despite decades of studies that link telomerase mutations with cancer, scientists don't vet have a structural model of the complex or know how it self-assembles in cells-a first step for developing drug targets or diagnostics.

Made of protein parts and RNA, the complex contains a distinctively folded section of RNA called a pseudoknot. Found in many organisms, similar kinds of knots in other cell structures play key roles in promoting proper function.

With expertise in an advanced form of fluorescence microscopy

that can measure structures one molecule at a time, UC Santa Cruz chemist Michael Stone and grad student Joseph Parks collaborated with computational modeling experts at Stanford to show a pseudoknot movement that occurred surprisingly far from telomerase's active site. "Whatever it's doing functionally, it must be acting indirectly," said Stone. The results are described in the journal RNA.

The bigger success of this study was combining single molecule measurements with computational modeling to find this pseudoknot movement, said Stone: "Telomerase is one of many protein-RNA complexes for which we don't know the structure. This is just the beginning."



The RNA pseudoknot on the top of this structural model is shown moving during telomerase enzyme function (red arrow). The colorful star shapes represent the fluorescence probes attached to the molecule to follow this movement.

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PHOTO:

"conversational agents" like Siri can't yet carry a conversation. While machine-learning systems can follow pre-scripted repertoires and adapt to user patterns, other elements of language—such as sarcasm—don't yet compute.

"To be effective, computers might need to acquire some social inferences," said Marilyn Walker, UC Santa Cruz computer science professor and leader of the Natural Language and Dialogue Systems Lab in the Baskin School of Engineering.

To create those capabilities, Walker

#### RACHEL CARSON COLLEGE

#### Peregrine proof



The peregrine falcon recovery is a case study in successfu conservation work, said Glenn Stewart, former director of SCPBRG, a group formed in 1975 when only two breeding pairs of the birds were known in California.

> tts" mines online social sites to develop statistical algorithms that capture the flow of natural conversations. A team of her graduate students, the SlugBots, were picked to compete in Amazon's \$2.5 million Alexa Prize Challenge to develop a "socialbot" that could turn the company's voicecontrolled devices into

> > chatterboxes.

Improving conversational algorithms also advances fundamental science, noted Pranav Anand, associate professor of linguistics. Working with Walker and UC Santa Cruz cognitive psychologists Jean Fox

n of algo s, Ana will lang to FEM Soi co Putu the a conal fool

Putumayo is located in the Andean-Amazonian foothills of southern Colombia. An extremely biodiverse region, it was also an epicenter of the U.S.-Colombia War on Drugs which, until recently, included aerial spraying of illicit coca crops.

Glenn Stewart's Santa Cruz Predatory Bird Research Group (SCPBRG) shepherded peregrine falcon recovery efforts from almost uncountably low populations in the '70s to removal from the federal list of endangered species in 1999 and—now—more than 50 breeding pairs in the Bay Area alone.

A network of conservation biologists and raptor enthusiasts boosted falcon numbers by collecting and hatching thinshelled wild eggs, then pioneering methods for captive breeding and releasing the young. Nest cameras brought the population recovery story to a public audience, including that of "Clara," who raised four generations, and counting, on San Jose City Hall.

Unlike the 10,000 kilometer migrations of Arctic populations, Stewart's studies showed that Central California peregrines stick around. They follow the food, he said, nesting anywhere from Mt. Diablo to the smokestacks in Moss Landing.

Now retired from the SCPBRG, Stewart continues his research and bands 3-week olds each spring. And, as a Rachel Carson College lecturer, he passes on the peregrines' success story. "We figured out how to cover the Earth with peregrines again," said Stewart." They are proof that conservation works."

Tree and Steve Whittaker, he brings a "rich intuition about language" to develop these new algorithms. Ultimately Anand hopes their work will improve studies of language itself.

#### FEMINIST STUDIES

#### Soils, war, life

When UC Santa Cruz cultural anthropologist Kristina Lyons began her fieldwork in Putumayo, she intended to research the public health and environmental consequences of the herbicide, glyphosate, that rained down from the sky.

Instead, after almost twelve years working with small farmers, soil scientists, state officials, and others, Lyons ended up following the practices that make life possible in a criminalized and poisoned ecology. "The farmers I met pushed me to transform my research questions, and to think about how life is being

#### **BRIEF** inquiries

cultivated in the midst of war," she said.

#### Lyons' work,

"Decomposition as Life Politics: Soils, Selva, and Small Farmers under the Gun of the U.S.–Colombia War on Drugs," was published in Cultural Anthropology and garnered the Junior Scholar Award from the Anthropology and Environment Society of the American Anthropological Association.

In post-conflict Colombia, after a peace agreement between leftist guerrillas and the government, Lyons continues to examine the cells without the

complexities of science, nature, and justice.

#### SOCIOLOGY

#### Asymmetrical lines

Informed consent for medical research participants didn't exist in 1951 when researchers took the cancerous cervical cells of Henrietta Lacks, a poor African American woman, and developed "HeLa" cell cultures for worldwide study.

By 2013, when scientists sequenced-and published-Lacks' genome from those

family's permission, it spotlighted ethics, race, gender, and justice in biomedical research. Further, the National Institutes of Health director described Lacks as a matriarch for her contribution to science; an irony that didn't escape many, including James Doucet-Battle, a UC Santa Cruz medical anthropologist.

"Matriarchal societies are those in which women wield control over political and economic resources," said Doucet-Battle. "For Henrietta Lacks, and historically for African American women, that's not quite the case."

With Henrietta Lacks as a starting point, Doucet-Battle examined the social contract between society and government in his paper, "Bioethical Matriarchy: Race, Gender, and the Gift in Genomic Research," published in Catalyst.

whether there's a possibility of an ideal democratic form of citizenship, in which the obligations to give and receive are based not on sacrificial forms of exchange, but on egalitarian forms of exchange," he said.

#### MOLECULAR, CELL, AND **DEVELOPMENTAL BIOLOGY**

#### Supporting role

During development and learning, neurons in the brain grow small protrusions along branching dendritesthe dendritic spinesto boost cell-to-cell connectivity.

This process may be modulated by neuronal supporting cells, called astrocytes, more than previously thought according to new research by Yi Zuo, professor of molecular, cell, and developmental biology. The study was published in Biological Psvchiatrv.

Zuo discovered the astrocytes' contribution by first studying mice with Fragile X syndrome, in which a lack of Fragile X mental retardation protein (FMRP) leads

to too many dendritic spines and impaired motor skills.

While neurons and astrocytes both express the FMRP protein, the neurons have 10 times as much, noted Zuo. So, she was surprised to find that selectively eliminating FMRP in astrocvtes-while maintaining neurons' protein expression-still led to symptoms of Fragile X. "Even though astrocytes express very little of this protein, they seem to be contributing to the disease," said Zuo,

Next, Zuo's team seeks changes in astrocytes that may be important for synaptic transmission. She also wants to learn more about the role of



Healthy dendritic spines on the surface of nerve cells.

astrocytes in aging. "Neurons are still very important," said Zuo,

"It's about answering

SER/ FOREST U.S. Ь BEETLE COURTESY REINHARD; JOHAN LA DONCELA BY. EMBO: MACKENSEN, UTAI

HOTOS:

MUSIC

Most musicians don't

patent their work, but

David Dunn, assistant

professor of sound

art and design in the

UC Santa Cruz Music

own proverbial beat.

than I am in using it

for exploration and

discovery," he noted.

His patent (No. 9,480,248)

uses acoustics to deter

wood-infesting insects,

such as Ips confuses, a

"I'm less interested in

#### **ANTHROPOLOGY**

#### **DNA** directions

With modern genomic tools, UC Santa Cruz biological anthropologist Lars Fehren-Schmitz follows the molecular footprints of ancient people. By analyzing DNA from prehistoric and historic human remains, he studies where-and when-our ancestors went. This genetic data can also show how disease, environment, and lifestyles affect human adaptation.

For example, reconstructing the aenomes of 92 pre-Columbian individuals enabled Fehren-Schmitz and his colleagues to track the migration of people, once isolated on the Beringian land bridge for thousands of years, into the Americas starting around 16,000 years ago. That early

isolation period created a unique pattern of genetic diversity, traceable as those populations moved southward to Chile, explained Fehren-Schmitz, an author on the study published in Science Advances.

Among those ancient samples, Fehren-Schmitz also found DNA markers no longer seen in modern data sets, suggesting a high extinction rate of Native American people around the time of first European contact. "Our high-resolution data allowed us to verify the

historic record," he said. DNA markers in another study showed that adaptation to high altitudes existed before people got to the Andes, a trait that allowed populations to persist there.

# tiny beetle blamed for

eavesdrop under the bark of a tree, Dunn recorded a soundtrack which led to a collaboration with Northern Arizona University researchers and rigorous studies of beetles' behavioral responses to sound. After ciphering *lps'* natural communications-noises related to mating, building tunnels, or attacking

killing conifers across the western states. Provoked Sound solutions by the death of entire forests, Dunn wondered: "Is there any sound associated with that?" Devising an "ear" to Department, follows his music for self-expression

"but we should pay more

attention to astrocytes."



La Doncela is an Incan mummy that was found at Mount Llullaillaco in Argentina in 1999. Her DNA was included in the study of pre-Columbian individuals who lived 500 to 8,500 years ago, and helped archaeologists follow the movement of people to the Americas.

Now the UC Santa Cruz Paleogenomics Lab is expanding and, along with it, Fehren-Schmitz's research plans. "How far can the interactions between biology and culture shape diversity in populations?" he

wants to know; "not just in ancient peoples, but in contemporary populations and in how our future development will look."

rival species—Dunn synthesized a playlist that drove beetles to such distraction that they couldn't damage trees.

In a reverse tech transfer, from the arts to the sciences, UC Santa Cruz doctoral student David Kant digitally reproduced the complex "chaos circuits" Dunn had designed. This digital format enables miniaturization of the sound system, making acoustical protection feasible for many trees at once.

#### "Something

extraordinary happens when we apply human imagination to rational understanding," said Dunn. "Art can contribute to real world problem solving."



Bark beetle



Self-driving cars have gone from science fiction to fact in just a few decades, and could go mainstream within several more. Touted for freeing commuters from drudgery and stress, autonomous vehicles are likewise hailed as a boon to elderly and disabled people who are unable to drive. But this new technology may also have surprising consequences.

"Autonomous vehicles could provide the most dramatic transformation in urban transportation systems since the arrival of the motor car more than a century ago," said Adam Millard-Ball, UC Santa Cruz environmental studies assistant professor, who studies the intersections between transportation policy, urban planning, and climate change.

His recent work shows that self-driving cars could tip cities toward sprawl-or walkability. These shifts in urban form could either hasten or check the pace of climate change. And the way people react to autonomous vehicles will determine which of these wildly different futures becomes reality.

Millard-Ball's interest in research was sparked when he was a transportation planner and led a car-sharing study for the National Academies of Sciences' Transportation Research Board. "I realized research can be fun," he said.

His project with autonomous vehicles is a perfect example. While most self-driving car studies focus on the technical side, Millard-Ball investigated the impact of human behavior. "The assumption is that everyone will be nice and cooperative," he said. "But we know that's not how people always behave."

#### Street games

To explore the interplay between people's behavior and self-driving cars, he developed a model based on the game of chicken. In the classic version of this dangerous road contest, two drivers zoom straight towards each other and the loser swerves-or chickens out-to avoid collision, while the winner stavs on course. In a twist, Millard-Ball pitted an autonomous vehicle against a pedestrian at a crosswalk.

"U.S. law gives pedestrians priority at crosswalks but it's almost never enforced, and in most places you would be taking your life in your hands if you asserted that right," he said. So, people's behavior on roads depends as much on social norms as on the law. Take Manhattan, for example, where pedestrians often assert their legal right of way at crosswalks. New York City drivers tend to expect this and usually slow down for people on foot. In

many other places, however, the norm is for pedestrians to let drivers go first. After all, people on foot have far more to lose than those in cars.

"A pedestrian at a crosswalk is the most clear-cut example of where people's behavior differs from the rules of the road, and this is where you might expect to see the biggest changes," Millard-Ball said.

A big change is exactly what he saw. First, he modeled a game of "crosswalk chicken" between a conventionally-driven car and a pedestrian, and, as expected, the pedestrian yielded and lost. But when he substituted in a self-driving car, the pedestrian asserted the right to cross and won. "The pedestrian knows that the autonomous vehicle will not be drunk or distracted, and that it will follow the law," he explained, reporting his findings this year in the Journal of Planning Education and Research. "It's intriguing how autonomous vehicles could change norms because of how safe people feel."

Millard-Ball hasn't personally tested his theory, yet. "I want to step in front of an autonomous vehicle but always see them a bit too late," he said.

Building on his crosswalk chicken scenario, Millard-Ball envisions cities where pedestrians rule. In a city full of self-driving cars that always brake for people on foot, pedestrians could take over the streets. "They could cross with impunity even at midblock because they merely need to step into the street to force the risk-averse car to slow down," he said,

adding that from the car's perspective it would be like driving down a street full of five-year-old children who could run out into traffic at any moment.

This scenario rings true for David Fields, a transportation planner at San Francisco consulting firm Nelson\Nygaard. "In locations with lots of pedestrians, such as lower Manhattan and the French Quarter of New Orleans, a vehicle could end up completely stopped as people recognize it won't move when they are in the way," Fields said.

#### Sprawl

While it's fun to think about the supremacy of pedestrians at a personal level, the crosswalk chicken game also has much larger-scale

said.

implications. Millard-Ball believes that by empowering pedestrians, self-driving cars could shift the shape of entire cities.

> Urban patterns and the forces behind them are a major focus of Millard-Ball's research.

He's particularly interested in sprawlurban development riddled with so many cul-de-sacs, dead ends, and T-intersections that it's hard to get around without a car. The disconnected streets that characterize sprawl occur in much of the developed world, but are most pervasive in the United States. "In most of the 20th century, policy pushed American cities to be more suburban and car-centered," he said.

Streets were laid out on a grid in most U.S. cities in the early 1900s, and these well-connected roads persist today in urban cores. Beginning in 1936, though, the Federal Housing Administration recommended cul-de-sacs for new development. "The assumption was that car travel was the future, and places should be built for driving," Millard-Ball

Sprawl is also typified by multi-lane arterial roads, often lined with walls, which surround and isolate cul-desac neighborhoods. Arterials let cars go fast, but can be challenging to cross on foot. "They make walking unattractive if not downright infeasible," he continued.

In a 2015 study in the journal Proceedings of the National Academy of Sciences, Millard-Ball and Christopher Barrington-Leigh of McGill University in Montreal analyzed street patterns of new construction in U.S. cities over the last century.

To their surprise, they discovered that sprawl is on the wane: after peaking in the mid-1990s, the number of disconnected streets fell roughly 10 percent over the next decade.

"The long march toward sprawl in the 20th century seems to have come to an end," Millard-Ball said, pointing toward the recent emphasis on walkable cities as a likely driver of this turnaround.

Planning policies like "smart growth," which concentrate new development in the urban core, also encourage connected streets and walkability. "I would probably advocate banning anything

#### Driving change

but essentially gridded road networks for new residential developments," Barrington-Leigh said. "Or at least implementing a very large "cul-detax"-a tax on cul-de-sacs-disincentive on lowconnectivity road-building."

Virginia has statewide standards discouraging culde-sacs. Elsewhere, most urban planning policies are local. Municipalities that stand out for curbing sprawl in new neighborhoods include Dallas, which requires gridded streets, and Gainesville, Florida, which prohibits cul-de-sacs in some districts.

If empowered pedestrians do rule city streets in the future, as Millard-Ball's chicken crosswalk game



The cul-de-sacs and multi-lane arterial roads of this suburban development in Colorado Springs, Colorado, hinder walking and promote sprawl. "Almost any time you take a plane trip, you can look down from the air and see this pattern in just about every U.S. city," Millard-Ball said.

predicts, they could shunt self-driving cars to the periphery of the urban core. This would free space now allocated to parking-which can account for nearly one-third of urban land-and allow denser, people-centered development within cities. "Between less parking and potentially less space dedicated to vehicle movement, our cities will literally find new real estate," transportation planner Fields said.

And this could make urban areas more appealing. "Cities thrive when they're lively because people like to see other people walking around having a good time," Millard-Ball said. "Autonomous vehicles may reinforce the advantages of cities by making them safer and more attractive."

#### Urban form and climate change

Another possible advantage of walkable cities is lower carbon emissions. "One of the reasons the U.S. is a high greenhouse gas emitter is because of the way cities are laid out—but most of the climate change discussion is on technology, for example, how effectively biofuels and electric vehicles will reduce emissions," Millard-Ball said. "We saw a disconnect: City form is key to deciding whether we drive or walk."

In a study published in the journal Environmental *Research Letters,* he and Barrington-Leigh followed up on their sprawl work and investigated how road patterns influence carbon emissions. Previous studies have shown that street patterns affect whether people own cars and how much they drive. For example, less-connected streets (such as cul-de-sacs and T-intersections) mean more driving. In contrast, more connected streets (those on a grid) mean less driving.

Using existing databases on household car ownership and commute mode, Millard-Ball and his colleague estimated the number of vehicle miles traveled in urban areas across the U.S. Next they looked for correlations between street patterns and two proxies for emissions—car ownership and vehicle miles traveled.

Their analysis revealed that urban form had an unexpectedly large impact on carbon emissions. At current rates, the trend away from sprawl and toward connected streets could reduce carbon emissions about three percent by 2050. And increasing the rate of connectivity could triple that, cutting emissions nearly nine percent in the same time frame. "It's quite remarkable how much potential connected roads have from a climate perspective," Millard-Ball said.

Indeed, the impact of connected streets compares favorably with other strategies for mitigating climate change. For example, doubling the density of most new development could reduce vehicle travel and associated carbon emissions nearly eight percent by 2050, according to a 2009 Transportation Research Board report.

In addition, the impact of connected streets may last longer than this strategy. Developments can easily be torn down and rebuilt to be less dense. But once streets are laid down, their patterns can persist for centuries. After London's Great Fire in 1666 and San Francisco's Great Earthquake in 1906, both cities were rebuilt along the lines of the original

streets. "We cannot change what was already built in the past, so let's stop making more mistakes as quickly as we can," Barrington-Leigh said.



The connected streets laid out on a grid in Phoenix, Arizona, help reduce greenhouse gas emissions.

#### **Turning point**

Millard-Ball's work suggests that self-driving cars could accelerate the transition from sprawl to connected streets, boosting walkability in cities and cutting carbon emissions.

#### Or not.

Autonomous vehicles could also reverse the trend toward connected streets. In this alternate future, the ease of self-driving cars facilitates longer trips. As the website for Google's self-driving car program promises: "Time spent commuting could be time spent doing what you want to do." Enjoyable commutes could encourage people to live farther from work, promoting sprawl. Moreover, autonomous vehicles could increase driving by the elderly, blind, and disabled.

And more driving means more energy consumption, which means more carbon emissions. The range of possibilities is wide. Autonomous vehicles could cut energy use to a tenth of the current level—or double it, according to a 2015 Transportation Research Board report for the National Academies of Sciences.

"There's no set destiny toward which autonomous vehicles are taking us," Millard-Ball said. "Autonomous

vehicles are a turning point but we don't know how people will respond to the technology."

While autonomous vehicles are projected to be widely used as early as 2030, much of the public is not yet ready to accept them. Self-driving cars may be statistically safer than human drivers, but there's still something unsettling about ceding control to a machine.

"Designing the human out of the driving system altogether is probably untenable for the time being," said Michael Nees, psychology professor at Lafayette College in Pennsylvania, who studies acceptance of self-driving cars. He thinks people will want to monitor and even override self-driving cars. "This is a different design philosophy than one that assumes the automation will work perfectly at all times and thus ignores the human driver altogether," he added.

A 2017 American Automobile Association survey found that 78 percent of respondents were afraid to ride in an autonomous vehicle, and only 19 percent would trust the car to drive itself. It probably didn't help that an Uber self-driving car ran a red light on the first day of its short-lived pilot program last year in San Francisco. In addition, many people are uncomfortable with taking their eyes off the road even if they're not driving. In a 2017 poll by Morning Consult, a Washington, D.C.-based media and polling company, 55 percent of respondents said no emailing, 61 percent said no reading, and 75 percent said no sleeping in self-driving cars.

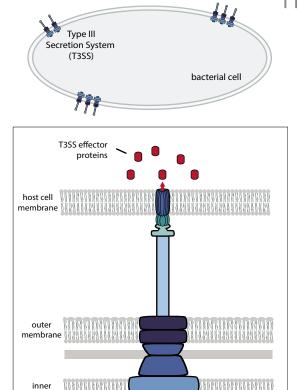
Another unknown in a future with autonomous vehicles is how city planners will respond. "If policy makers treat pedestrians as a nuisance, for example, forcing them to go into tunnels to cross streets, that could discourage walking," Millard-Ball said. Alternatively, if regulators do nothing, that could encourage walking by allowing pedestrians to play chicken with autonomous vehicles and win.

Does Millard-Ball want a self-driving car? He's not sure. But he does know he'd enjoy living in the kind of people-friendly city that could be ushered in by autonomous vehicles. "I'd like to be able to live without owning a car," he said. "I'd like to have that choice."

Paradoxically, as his own work shows, the rise of autonomous vehicles could give Millard-Ball-and many other people-the option of a car-free life.

# Disarming bacteria

Microbiologist searches for next-generation antibiotics



► When bacteria that cause maladies like typhoid fever, pneumonia, the plague, or even run-of-the-mill food poisoning get inside your body, they're quick to mount an offensive. The invading pathogens assemble minuscule syringe-like structures on their surfaces, filled with armies of toxic molecules ready to infiltrate. Then, when the bacteria sense that they're in the right place, these syringes—called type III secretion systems—poke directly into your cells, injecting their contents inside.

These microscopic "injections" are one of the first steps of infection for some species of bacteria, letting the bugs hijack your cells. Understanding how these injections work may hold the key to developing new antibiotics.

"Type III secretion systems are used by dozens of bacteria that cause a lot of morbidity and mortality in the world," said **Vicki Auerbuch Stone,** UC Santa Cruz associate professor of microbiology and environmental toxicology. "What we want to do is disarm the system."

Over the past few years, Auerbuch Stone has discovered a handful of compounds that shut off the type III secretion system. The drugs, she speculates, may be able to render disease-causing bacteria harmless to humans without killing the pathogens—or the body's beneficial bacteria—in the process, a distinction that could eliminate some of the problems with existing antibiotics.

"There's reason to think—at least, based on what we've seen in mouse models—that type III [secretion] inhibitors could be very effective against disease," said Auerbuch Stone, who recently published a series of papers on how one inhibitor works.

#### A need for new drugs

Classic antibiotics—most of which have been used clinically for many decades—work by stopping the growth of bacteria or killing bacterial cells outright. But bacteria can evolve resistance to these drugs; every year in the United States, more than two million people become infected with antibioticresistant strains of bacteria, according to the U.S. Centers for Disease Control and Prevention. The rising number of drug-resistant pathogens has been called a crisis by scientists and policy makers.

On top of that, these broad-acting antibiotics kill more than just the illness-causing germs that have gotten into a person's body. They also act on some of the trillions of other bacteria that are living in the body—the microbiota or microbiome. "We're just in the last five or so years realizing how bad it is to disrupt our healthy microbiota," said Auerbuch Stone. "And classic antibiotics do just that; they at least temporarily disrupt the microbiota."

With those challenges in mind, scientists like Auerbuch Stone are hunting for a new kind of antibiotic, dubbed "antivirulence" drugs. These new drugs block the ability to cause disease without killing bacteria. That's important because when bacteria are killed outright by drugs, any infectious culprits that develop a mutation to avoid that fate can very quickly spread; these living bacteria can reproduce while the ones killed by drugs can't. So, letting bacteria continue to live and grow, while taking away their ability to cause disease, gives bacteria with resistance mutations less of a competitive edge, scientists hypothesize. And targeting the virulence mechanisms—which are only used by pathogenic bacteria—could also spare the healthy bugs in the microbiome.

"I think there's really a need for new antimicrobials, and so-called antivirulence compounds make a lot of sense biologically," said James Bliska, a molecular biologist at Stony Brook University in New York, who also studies the type III secretion system.

Earlier this year, the World Health Organization published a list of "priority pathogens" that pose the greatest threats to human health. The top three are all Gram-negative bacteria that cause some of the hardest infections to treat—and are also those most prone to developing antibiotic resistance.

Named for their appearance under the microscope, these bacteria have an extra membrane surrounding them, making them especially good at keeping out existing antibiotics. That's one reason Auerbuch Stone's work with the type III secretion system is so important—the tiny syringe system is found

The type III secretion system (blue) is anchored in the two membranes of Gram-negative bacteria and can poke through human cells to inject toxins (red).

bacterial cytoso

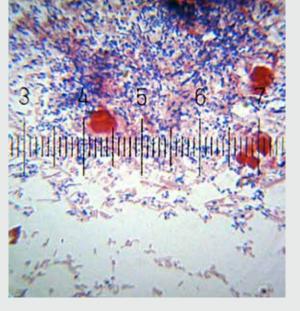
Supre-secretory

protein

membrane

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The Gram stain, named after microbiologist Hans Christian Gram, differentiates bacteria based on their uptake of a violet-colored dye. Gram-positive bacteria have a cell wall component that retains the dye, so they appear violet, while Gram-negative cells don't, but can be counterstained with red. In this microscopic image of dental plaque, the Grampositive bacteria are purple and Gram-negative appear red.

Examples of Gram-negative bacteria that deploy the type III secretion system to cause disease in people:

*Escherichia coli (E. coli)* is usually harmless but some strains cause food poisoning which can be severe enough to cause death.

*Chlamydia,* which causes the sexually transmitted disease of the same name.

*Pseudomonas aeruginosa* can cause serious infection in people with cystic fibrosis, severe burns, or weakened immune systems. Commonly blamed for hospital-acquired infections, it often lives on the surfaces of medical equipment.

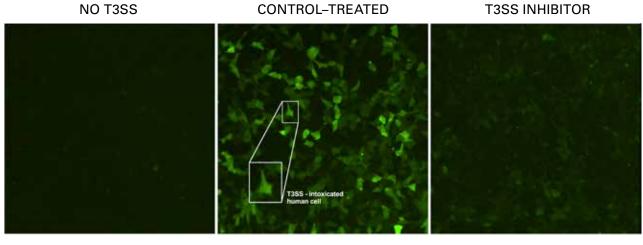
*Salmonella* can lead to typhoid fever, paratyphoid fever, and food poisoning.

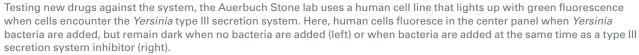
*Shigella,* which causes shigellosis, or bacillary dysentery, is one of the leading bacterial causes of diarrhea worldwide.

*Yersinia pestis* causes bubonic plague, responsible for multiple pandemics throughout history.

Other Yersinia strains including Yersinia pseudotuberculosis.

#### **Disarming bacteria**





specifically on Gram-negative bacteria, including the well-known bugs E. coli, Chlamydia, and Salmonella.

"There are a lot of challenges surrounding these particular bacteria and there hasn't been a new antibiotic for Gram-negative bacteria in a very long time," said Auerbuch Stone. Although penicillin was commercialized in 1938 and a flurry of other antibiotics hit pharmacy shelves in the decades following, no new classes of antibiotics that work on Gram-negative bacteria have been introduced since 1968.

#### Stopping the syringe

Since launching her lab at UC Santa Cruz in 2009, Auerbuch Stone has focused on unearthing compounds to block the type III secretion system. She's worked mostly with Yersinia pseudotuberculosis, a Gram-negative bacteria which causes food-borne illness. Her hope is that Y. *pseudotuberculosis* is a good model for all bacteria that rely on the injection system to infect humans.

"Ideally, some inhibitors will work in all bacteria that require the type III secretion system," said **Hanh Lam**, a UC Santa Cruz postdoctoral researcher in Auerbuch Stone's lab who's currently leading the project. "But we expect some will only inhibit certain bacteria."

Auerbuch Stone and Lam developed and finetuned a method to quickly screen large collections of molecules to find ones that block one aspect of the type III secretion system. Their approach tests whether *Y. pseudotuberculosis* produces and expels YopE (Yersinia outer protein E), one of the so-called "effector molecules" that the bacteria normally injects through the type III secretion system syringe.

The researchers put Y. pseudotuberculosis in a liquid that mimics the inside of the human body and then test whether-in the presence of new drugsthe bacteria can secrete YopE into the liquid. If the bacteria can still do this, the type III secretion system is functioning as normal. But if not, a drug they've added must be blocking some step of the system. They then run a series of experiments to see whether the effects still hold true when the bacteria are interacting with mammalian cells.

#### **Promising candidates**

Armed with their screening method, Auerbuch Stone's group collaborates with three chemists who each have libraries of molecules that can be mined for drug discovery: at UC Santa Cruz, **Scott Lokey** synthesizes brand new molecules based on existing natural products and Phillip Crews isolates compounds from marine sponges, while Roger Linington, formerly at UC Santa Cruz and now at Simon Fraser University in Canada, collects molecules from marine bacteria during scuba dives.

In 2014, the researchers published their first success story; their high-throughput screen flagged two related molecules called piericidins, originating from marine bacteria, as type III secretion system inhibitors. When either of the piericidins were added to a culture of Y. pseudotuberculosis, the

bacteria continued to grow but didn't eject the toxic compounds—including YopE—that it normally uses to hijack human cells. Since then, they've identified a handful of other molecules that have similar effects, and even found a drug that works in multiple species of bacteria. Those results are currently awaiting publication.

"I think one of the reasons we've had success is that these are libraries no one has screened for type III [secretion] inhibition before," said Auerbuch Stone. "Other people have screened standard commercial libraries."

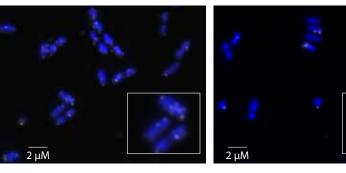
The team has gone on to develop a set of assays to help pinpoint how molecules like piercidins affect the secretion system. Using special stains and microscopy techniques, they can visualize the syringes that are formed on the outside of Y. *pseudotuberculosis.* That's how they discovered that piericidin A1, one of the marine bacterial molecules they homed in on earlier, works by blocking the assembly of the needle, reducing the number of type III secretion needles on any given bacterial cell.

Other inhibitors, though, could block other steps, allowing the needle to form but preventing it from injecting human cells, for instance. The finding on piericidin A1 was published this year, in the journal mSphere, and helps pave the way for more work on how to develop it as a potential antibiotic.

#### Next steps

Some of the remaining questions on type III secretion underscore just how little is known about the system. "We really don't fully understand how the type three secretion system works," pointed out Lam. "We don't know all the steps it uses to

CONTROL



Type III secretion system needles (white dots) stud the surface of Yersinia bacteria (blue rods). When the bacteria are incubated with the inhibitor piercidin (right), the number of needles decreases.

orchestrate all these proteins and then secrete these toxins in the order it wants."

But Auerbuch Stone thinks her inhibitors—even in advance of any clinical implications-might shed light on the basic science of type III secretion. An inhibitor can help reveal which bacterial cells in the body are using the system at any given time, and when during the course of an infection the secretion system is key.

"Our lofty goal is that we'd like a whole suite of inhibitors that each block different stages of secretion," said Auerbuch Stone.

As for moving the inhibitors to the clinic, that's still years away. So far, inhibitors of the type III secretion system have only been shown to be effective in isolated cells or mice, not in people.

"Ultimately, the next step is the harder step, which is testing out the activities of these inhibitors in a more complicated assay or preclinical model," said Stony Brook's Bliska, referring to the inhibitors described in published research papers by Auerbuch Stone's group.

Auerbuch Stone admitted there are still major questions about the feasibility of using type III secretion inhibitors to actually treat infections. For instance, the effector molecules or virulence factors that are churned out by the system may only be needed for a bacteria to initially infect someone's body, not to keep an infection going. "So it might be that giving this kind of inhibitor during an established infection won't treat it," said Auerbuch Stone, "but it could work as a preventive."

As the number of antibiotic-resistant infections around the globe continues to grow, though, increased pressure will be put on the pharmaceutical industry to develop new types of antibiotics. This, speculated Auerbuch Stone, might make more scientists take an interest in type III inhibitors.

#### **T3SS INHIBITOR**



"A lot of the diseases we're talking about have really only affected the developing world, which has made them not get the attention they might have otherwise," she said. "As they become more of a global threat, I think people are going to have to start caring."

## Art in a climate revolution Environmental crises call for creative solutions

Evidence for sea level rise, drought, or collapsing ice sheets may come from scientific studies, but solutions to these problems could arise from another realmthe arts.

That premise inspired T. J. Demos, professor in the History of Art and Visual Culture Department. to found the Center for Creative Ecologies at UC Santa Cruz. "Art can transform values through sights and feelings in a way that an argument based solely on scientific information might not succeed," explained Demos

Weaving in ideas from politics, ethics, and other the center fields. takes on tough environmental issues using visual art as a catalyst for change. "The climate change crisis doesn't exist in isolation." Demos said. "It is deeply connected to these other areas. We need a range of approaches to bring about meaningful and widespread cultural transition."

In a recent project entitled "Extraction," Demos partnered with UC Santa Cruz art professor Laurie Palmer to explore how developed countries and corporations extract resourcesmaterials, energy, labor, and time-from both people and the environment. They drew inspiration from the struggle against injustices toward

indigenous communities at Standing Rock

Indian Reservation and elsewhere around the world, said Palmer. "The aim of the project is to not only look at how extraction is happening and criticize it, but also to imagine other ways to live in the world," she added.

Demos and Palmer encouraged community members to participate in "Extraction" events such as field trips to the Amah Mutsun Relearning Program at the UC Santa Cruz Arboretum and fracking sites in Monterey County; a two-day international conference put on, in part, with the Resource Center for

Nonviolence in Santa Cruz; and invited artist lectures.

> Among these events, the center hosted award-winning American photographer

Subhankar Baneriee. His

photographs of caribou migrating across Alaska's Arctic National Wildlife Refuge circulated among the nation's policy makers and may have helped convince the Obama administration to forgo oil drilling in this region, Palmer said.

This visual approach to environmental activism and emphasis on community involvement drew Chessa Adsit-Morris, author of *Restorying* Environmental Education, to pursue her doctoral degree with Demos. "The potential of the center is to draw together scholars and activists and artists to productively talk about other ways of addressing these issues," she said.

Demos hopes that community participation and graduate student involvement will increase as the center expands its efforts to re-imagine human relationships with the environment, saying: "We need a multiplicity of paths to carry that out."

Caribou Migration I, 2002; from the series "Oil and the Caribou" by photographer Subhankar Banerjee shows Alaska's Arctic National Wildlife Refuge as a vast, fragile ecosystem.

# **Electric** avenues

Sea creature studies improve human biosensors

About the last thing one would expect to find on the laboratory website of an engineer is a recipe for calamaretti saltati piccanti, an Italian entrée of sautéed baby squid. But it makes perfect sense when the lab is run by Marco Rolandi, associate professor in UC Santa Cruz's Baskin School of Engineering: it's a dish Rolandi watched his mother make when he was a boy in Savona, a seaport town in northern Italy. Now, Rolandi and his lab group swap recipes for squid-centric cuisine, in tribute to the mollusks that provide a key ingredient for their research: chitin, the compound that gives cephalopod beaks and pens their toughness.

Rolandi and his collaborators create novel transistors that employ chitin-derived substrates to modulate the flow of protons, rather than electrons as conventional transistors do. "What we have developed, with these transistors that move protons, is a means of communicating a current of H<sup>+</sup>, which is the hydrogen ion, to the body rather than electrons," said Rolandi. These "bioprotonic" devices are a critical step toward enabling electronic technology to communicate seamlessly with living systems—using nature's own language. Such devices can be used to study physiological processes or, perhaps, even alter them.



Hawaiian bobtail squid

#### **Electric avenues**

In addition to being a good proton conductor, chitosan, the water-soluble chitin-derived compound that Rolandi's group works with, is nontoxic, biodegradable, and can be processed sustainably. His team develops innovative ways of creating chitin composites with desirable mechanical properties such as strength or flexibility. Potential applications include producing an environmentfriendly alternative to synthetic polymers, such as the polystyrene foam used for things like packing material—or surfboards.

#### The body electric

Transistors are what enable circuits to perform calculations and are the sine qua non of all the gadgets—mobile phones, smart watches, digital cameras, computers, game consoles—that figure largely in our lives. In a conventional transistor, special materials called semiconductors can be triggered to switch modes from conductor to insulator, manipulating the flow of electrons and electron "holes" (spaces that could be occupied by electrons but aren't). Integrated circuits microchips—have millions of transistors, each of which can be either "on," meaning current is flowing, which corresponds to the binary "1," or off, meaning no current is flowing, which corresponds to the binary "0."

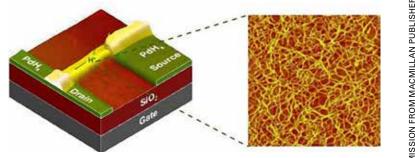
Electric current is also a major mode of communication among living cells. But water, which makes up as much as two-thirds of the human body and is a major constituent of all organisms, is not a good electron conductor. Charged atoms, however, such as sodium and potassium, which carry a positive charge, and chloride, which carries a negative one, move reasonably well in water. Thus, ions are the lingua franca of cellular communication in most living systems.

The challenge of interfacing electronic technology with the human body, then, is that subtleties in the information encoded in the current can be lost in the translation from electrons to ions. The situation is analogous to a traveler in a foreign country who doesn't speak the local language using broad gestures in hopes of getting his or her general point across; whereas someone conversant in the language can communicate in a much more nuanced way. Pacemakers, for example, work by monitoring the heartbeat and then delivering periodic pulses of electricity to normalize its rhythm. However, at the interface between the probes of the pacemaker and the heart tissue the flow of electrons is translated into ions moving in the bloodstream in a nonspecific manner. "Basically it's just giving a jolt; it's not specific to any ion. And every ion in the body serves a specific function," Rolandi pointed out.

XO

The hydrogen ion in particular plays a pivotal role in regulating a number of biological functions, Rolandi said. For one, the concentration of H<sup>+</sup> in solution corresponds to pH: the greater the concentration, the lower the pH, and the higher the acidity. And pH is one of the factors that influence the excitability of neurons, he noted; an alkaline environment lowers neurons' threshold for firing while an acidic environment raises it.

This can cause problems. In epilepsy, for example, the heightened excitability of neurons causes waves of disordered neuronal activity to sweep through the brain, resulting in a seizure. Rolandi speculated that a bioprotonic device that could control the flow of protons, and therefore pH, could be used therapeutically in epilepsy or other disorders. "Right now we are at the stage where we should be able to understand better certain neurological disorders. And we're looking into whether we can monitor, and then perhaps affect, the excitability of neurons," he said.



ABOVE: Diagram of the bioprotonic device:

The basic architecture of Rolandi's bioprotonic devices is similar to that of conventional field effect transistors. A gate contact, where external voltage can be applied to modulate current, is separated by an insulating layer of silicon dioxide  $(SiO_2)$  from palladium hydride (PdHx) source and drain contacts, which inject and collect, respectively, protons from a conducting channel. The channel is composed of one of two varieties of chitosan (a derivative of chitin): maleic chitosan, which transports H<sup>+</sup>, or proline chitosan, which transports OH<sup>-</sup> (the equivalent of a proton "hole"). The entire apparatus is only a few microns wide, about one-twentieth the width of a human hair. On the right is a magnified image of the chitosan fibers. In one study published in *Nature Scientific Reports*, members of Rolandi's UC Santa Cruz lab, led by postdoctoral researcher **Takeo Miyake**, and collaborators at the University of Washington (UW), demonstrated that such devices can be used to control pH-tunable biochemical reactions, such as the enzyme-triggered glow of fireflies. And in another, published in *Nature Communications*, a team led by UC Santa Cruz postdoctoral scholar **Zahra Hemmatian** created a hybrid device with a model cell membrane—complete with ion channels—that can precisely measure and control the flow of protons and, by extension, pH.

"Although we have mastered the art of electronic communication fairly well, the vast universe of chemical signaling remains virtually untapped," said Aleksandr Noy, a senior scientist focusing on bioelectronics and nanofluidics at Lawrence Livermore National Laboratory, in California. "Protons play a very prominent role in this signaling universe, and Marco's work on bioprotonic devices really paves the foundation for our efforts to harness this particular biological signaling language," Noy said.

#### Flukes and skates

Rolandi traces the evolution of using chitin derivatives to construct bioprotonic devices to a stroke of serendipity.

In the early 2000s, the quest to put more computing power into smaller devices by packing larger numbers of transistors into integrated circuits hit a plateau. "You needed to reduce the size of the transistor in order to pack more on a chip; they call it Moore's Law," Rolandi explained. And many people were worried that traditional semiconductor transistors would soon hit a "red brick wall" where further miniaturization was no longer feasible.

Interest in the potential of single molecule transistors was on the upswing, when, in 2002, a major fraud scandal undermined the credibility of the field. In a series of papers—published in preeminent journals—a researcher at Bell Labs falsified data to make it appear as though he had successfully coaxed organic molecules, which don't normally conduct electricity, to behave as semiconductors.

In the wake of the revelations, many researchers sought to distance themselves from that particular area of investigation. Rolandi decided to turn his focus to biological conductors when he established his first lab as an independent researcher at UW in 2008. "My curiosity was caught by this idea of proton conduction," he said. Prot thou beh of ti biole and a rig with mov I'm asp A se curi der rese bas mai whe Sar idea he'

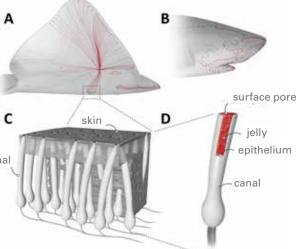
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ABOVE: (A and B) Skates and sharks locate their prey by detecting the weak electric fields naturally generated by biomechanical activity. (C) A network of electrosensory organs called the ampullae of Lorenzini is responsible for this sense. (D) An individual ampulla consists of a surface pore connected to a set of electrosensory cells by a long jelly-filled canal. Sharks and skates can sense fields as small as 5 nV/cm.

These organs may be the most sensitive electrosensors in the animal kingdom. They give sharks, rays, and skates the ability to pinpoint minute fluctuations in electrical fields—as small as five nanovolts per centimeter—generated by the muscle twitches and other physiological processes of

Protons are special in that they're only a couple thousand times larger than an electron, so they behave in a manner that's somewhere between that of tiny particles and large ions. Their conductivity in biological systems, for example, involves the breaking and reforming of bonds—like square dancers doing a right-and-left-grand, clasping and releasing hands with each dancer in turn. "So it's kind of a concerted movement while most ions move only by diffusion. I'm a physicist by training so from the fundamental aspects this was very interesting to me," said Rolandi.

A series of synergistic collaborations led to the lab's current focus on using ion-conducting polymers derived from marine life. First, a postdoctoral researcher with expertise in synthesizing chitin-based materials joined Rolandi's lab at UW. Then a marine biologist at Harvard University, **Joel Sohn**—who has since become a senior member of his UC Santa Cruz group—approached Rolandi with the idea of measuring the H<sup>+</sup> conductivity of a hydrogel he'd encountered in an odd sensory organ found in certain cartilaginous fish: the ampullae of Lorenzini.



#### Electric avenues

creatures in the vicinity. This enables sharks and their ilk to locate prey in murky water or when their guarry is concealed.

The organ is actually an array of structures underneath the skin. Each ampulla is shaped like a Florence flask, with a round bottom containing cells that respond to electrical stimuli, a long neck filled with a transparent, viscous jelly, and an opening to the external environment through a pore in the skin. Externally, they appear as clusters of small dark spots, concentrated around the snout; an individual animal typically has several thousand pores.

Erik Josberger, a former doctoral student in Rolandi's UW lab, tested the jelly and to everyone's surprise it turned out to be a good proton conductor. Extremely good, in fact. This so-called "shark snot" has the highest known H<sup>+</sup> conductivity in a biological material: three times higher than the maleic chitosan in the lab's bioprotonic transistors and just 40-fold lower than the state-of-the-art manmade polymer



used in fuel cells. The exceptional proton conducting power of the jelly raises the question whether it's an incidental property of the substance, or integral to the way the electrosensing cells transduce

the electric field

Nafion, which is

ABOVE: Pressing along the canals on the ventral side of an adult skate causes jelly to extrude from the pores of the ampullae of Lorenzini.

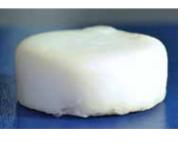
change signal, Rolandi mused. But that's a question for biologists. The discovery relates to the lab's core bioprotonics work insomuch as it utilized the strategies they've developed to measure proton conductivity of biomaterials (for example, using palladium hydride contacts that can inject and collect protons).

#### A better board and beyond

Chitin is the second most abundant natural polymer (after cellulose) on the planet. In addition to strengthening the beaks and pens of cephalopods such as squid, octopuses, and cuttlefish, chitin comprises a major component of the exoskeletons of insects such as grasshoppers and cockroaches, and crustaceans such as crabs, shrimp, and lobsters. Globally, the food industry produces

between six and eight million metric tons of crustacean carapaces annually, with a chitin content that ranges from 15 to 40 percent.

BELOW: Small sample of a foam blank that is being tested for properties that may make surfboards more ecologically sustainable.



Led by graduate student Xiaolin Zhang, members of Rolandi's lab devised methods for tweaking the mechanical properties of chitosan composites-to make them either rigid or flexible, for instance for a variety of

applications, described in a paper for Journal of Materials Chemistry B. The team's initial idea for a consumer product is to make the unshaped "blanks" for surfboards, which are typically made from polystyrene or polyurethane. The manufacturing process for those synthetic polymers pollutes the environment, and the discarded boards take up space in landfills, releasing toxic chemicals when they decompose. "And obviously most people who surf love the ocean," Rolandi asserted. "So the last thing that they want to do is actually further increase pollution with their sport."

Graduate student **John Felts**, who recently won a UC Santa Cruz "elevator pitch" competition with the idea, is spearheading the surfboard project. So far he has collected some proof-of-concept data that Rolandi said demonstrates that their shrimp chitin foam can match the mechanical properties and performance of the blanks currently on the market.

But the longer-term plan is to produce any kind of foam from chitin, for products ranging from packing "peanuts" to disposable coolers. The upward trend in online consumer spending means more goods are being packaged and delivered to homes and businesses. "The amount of foam waste this generates is really a problem," Rolandi lamented. "If we can eventually make stuff like that out of shrimp shells, you can see how the environmental impact is much smaller."

Or, perhaps, lobster shells? In point of fact, the chitin that Rolandi's team uses is not extracted in the lab, but that hasn't kept him from considering the gastronomic possibilities of expanding his research—or collecting recipes for surf and turf.

# Genes to go

Genome sequencing leaves the lab with handheld device



Advances in genome sequencing technologies have led to an explosion of genetic data—collected from fruit flies to woolly mammoth fossils—at an increasingly affordable cost. Over the next ten years, several companies plan to sequence human genomes by the millions. Buried inside the genetic information of any organism, its genome, are clues to health, inter-species relatedness, and, in some cases, susceptibility to disease. One misplaced building block, or portions of genes that have been deleted or relocated in the genome, could trigger drug resistance, cancerous changes, or disease.

Typically, specially trained scientists operate sequencing machines, each about the size of dorm room refrigerators, at dedicated centers. Now, a candy bar-sized commercial device called MinION, which incorporates a novel method of DNA sequencing developed at UC Santa Cruz, is making the process more rapid, portable, affordable, and accessible than ever before.

FOAM

HOTOS:

DXFORD

A handheld DNA sequencer can sequence the human genome in a few days, a task which once took a decade.

Inside a MinION, the controlled movement of DNA through a protein pore generates electrical signals that can be interpreted into genetic information within minutes of starting sequencing. With the fast results from this nanopore sequencing, scientists can guickly identify infectious bacteria or follow the spread of viral outbreaks. Dozens of MinIONS have hit the road, tucked into scientists' backpacks to identify frogs in Tanzanian jungles, or packed along with medical gear to study malaria in India; they've even been used to identify microbes on Arctic glaciers and the International Space Station.

Although nanopore sequencing is accumulating a record of success, during its development the UC Santa Cruz researchers faced skepticism from their colleagues. "Not long ago, people still didn't believe that it worked," said Mark Akeson, professor of biomolecular engineering at UC Santa Cruz.



One protein (light green) feeds a single DNA strand through a protein pore (teal). Each of the four DNA building blocks has a different structure, which each alter ion flow through the pore in ways that cause unique electrical signals for each building block (right).

#### Reading a genetic code

In the world of DNA sequencing technologies, the MinION is unique because it uses nanopores to directly detect a DNA sequence. More commonly, sequencers re-create the genetic coding by building a new strand of DNA on top of an existing strand.

The first method of DNA sequencing, developed by Frederick Sanger in the 1970s, mimicked how cells naturally copy DNA. During this process, proteins unzip a DNA helix, revealing the sequence of building blocks—the bases A, T, G, and C—on each strand. Another protein slides along one strand, identifying each base and pairing it with its partner, A with T, and G with C. Every so often, the protein adds a base carrying a molecular identification tag, which stops that strand from growing longer. Then researchers separate the newly synthesized strands by length, and determine the sequence by reading the tagged bases at the end of the strands in order from shortest strand to longest.

Two large teams of researchers, including UC Santa Cruz scientists, used the most advanced Sanger sequencing machines to generate the first publicly available draft of the human genome, part of a decade-long effort that produced a finished sequence in 2003. During that time, computer scientists at UC Santa Cruz also developed the web-based Genome Browser as a tool to visualize and explore the three billion bases of the human genome. Today, the Genome Browser also contains genomes of animals, fish, and common research organisms such as mice, rats, worms, and yeast. Over the past decade, improvements in technologies have led to machines that can sequence the human genome in a few days. These machines process 100 to 1000 times more DNA in each run than the best Sanger sequencers. The increased throughput means the machines need only a few days to sequence a genome up to 30 times to ensure that the order is accurate.

In addition to processing large amounts of DNA at the same time, the MinION has an added speed advantage: It delivers a complete viral genome sequence within minutes of a strand slipping through a nanopore.

"There's no field in science right now that's accelerating in terms of throughput and cost reduction anything like DNA sequencing," Akeson said, noting that one company offers to sequence entire human genomes for \$1000. "Companies are competing with each other aggressively, and the public gets benefit out of that."

#### Through the nanopore

**David Deamer,** biomolecular engineering research professor at UC Santa Cruz, first imagined nanopore sequencing in the middle of a road trip, pulling off the highway to scribble down his ideas. At the time, he was at UC Davis making pores in cell membranes trying, with his then-postdoctoral associate Mark Akeson, to create openings that would allow the building blocks of DNA, and its chemical cousin RNA, to slip inside.

If a pore could let the building blocks of DNA slip through, Deamer reasoned it might allow an entire DNA strand to pass through as well. Applying a positive charge to the inside of the membrane would attract negatively-charged DNA, drawing it through the pore along with additional ions. He imagined that structural differences of each base in DNA would impact the ionic flow in ways that caused a unique electrical signal for each base as it moved through the pore. Deamer started testing the idea in the lab, continuing experiments with nanopore sequencing when he moved to UC Santa Cruz in 1994. Akeson joined him on the faculty a few years later.

One challenge in developing nanopore sequencing was controlling the speed of the DNA as it moved through the pore. Akeson and his students wanted to guide DNA through the pore one base at a time using a ratchet-like protein attached to the top of the pore. However, the first few proteins they tried only briefly grabbed DNA before letting it pass through the pore. Then the researchers tried an enzyme called phi29 DNA polymerase. It held on 40,000 times longer than the others—enough time to detect signals from single bases inside the pore. For Akeson, that result remains a highlight in his 20 years of improving nanopore sequencing.

#### Anyone, anything, anywhere

In 2007, the executives of a company called Oxford Nanopore, based in the UK, visited Deamer and Akeson with a mockup of a handheld nanopore sequencer. Akeson and Deamer were surprised: "We thought that it would work, but we didn't think it could be that small," Akeson said.

With their tiny device, the founders of Oxford Nanopore—nanopore scientist Hagan Bayley and biotech executives Gordon Sanghera and Spike Willcocks—chased a large goal: to produce DNA sequencers that anyone could use, anywhere, to sequence genetic information from anything. In 2014, the company released the MinION, produced in part using technology licensed from UC Santa Cruz, to a select group of researchers at a cost of \$1000, at least 50 times less costly than many common sequencers.

The name of the device, pronounced min-ion, combines mini and ion, though it reminds many of the cartoon Minions, yellow pill-shaped henchmen who comically struggle to serve an evil villain. The protein components inside the MinION are different than those developed at UC Santa Cruz, but the sequencing concept is the same: one protein, a helicase, controls the movement of DNA through a protein pore embedded in a membrane.

Rather than tailor the device for particular applications before its release, Oxford Nanopore borrowed a strategy from the tech industry. They enlisted a few hundred researchers, eager to use a MinION, to play with early versions of the device. The researchers tweeted pictures of their MinION experiments and shared troubleshooting tips with their colleagues in the company's online forums. Three years later, the MinION research community still gathers at twice-yearly conferences, hosted by the company in London and New York.

"There's lots of playfulness in the research community," said Christiaan Henkel, a biologist at Leiden University in the Netherlands, who was among the first researchers to use the MinION. "We all enjoy ourselves while doing important work," he said.

Henkel studies the genomes of unusual animals, like the European eel. There is less funding available to gather genome sequences from these animals, compared to common laboratory animals such as mice and zebrafish, he said. So, the MinION's affordability enables him to access the technology for his research, which can help eel biology,

#### **Extraterrestrial nanopores**

Nanopores could be part of unmanned space expeditions one day. David Deamer, who first invented nanopore sequencing thirty years ago, and **Holger Schmidt**, an engineer at UC Santa Cruz, are working on a device that will look for signs of microbial life around Enceladus, a moon of Saturn. As the Cassini spacecraft flew past the moon, it detected ice and organic compounds in an atmospheric plume of water. Those ingredients indicated a hydrothermal vent spewed salty ocean water into the moon's atmosphere, conditions that astrobiologists consider could host microbial life.

To detect viruses using a nanopore, Deamer wants to use solid-state pores developed by Daniel Branton, biology professor emeritus at Harvard University, and one of the coinventors on the first nanopore sequencing patent. As Deamer continued experimenting with protein pores, Branton switched to studying nanopores carved into thin sheets of silicon nitride. These solid-state pores have not yet been used for sequencing because it's hard to control the pore dimension with enough precision to give reproducible signals, Branton said. Also, the tiny signals from DNA passing through solidstate pores are harder to detect compared to those from protein pores.

But solid-state pores can withstand larger temperature and pressure variations than protein pores, making them ideal for the harsh conditions of outer space. Deamer and Schmidt plan to build a device with a solid-state nanopore large enough to allow viruses through. Viruses passing through the pore would trigger additional laser-based analyses of the salts, minerals, and organic compounds on the outside of the virus, providing researchers more information about its surroundings. "I think nanopores may have new life in solid-state systems for detecting life," Deamer said.

Urinary tract infections could be treated more quickly and efficiently using a DNA sequencing device the size of a USB stick-according to research from the University of East Anglia. Researchers used MinION to perform nanopore sequencing to characterize bacteria from urine samples four times more quickly than traditional methods of culturing bacteria. The new method can also detect antibiotic resistance-allowing patients to be treated more effectively and improving stewardship of available antibiotics.

breeding, and conservation efforts. Eels are critically endangered, yet farming eels depends on catching young eels in the wild. Deciphering the eel's genome has improved scientists' understanding about its health, physical development, and population structure, information that can help biologists and ecologists coordinate fishing to maintain healthy wild eel populations.

Nanopore sequencing could also help tulip farmers in the Netherlands who lose up to 10 percent of their crop to fungi every year, said Henkel. The flower's lengthy life cycle means that new varieties can take 25 years to develop. Decoding the tulip's genome could provide information about which genes help resist disease, so that breeders can develop hardier varieties faster.

#### Identifying infectious microbes

Genome sequences provide important health information for humans, too. In August 2016, an astronaut aboard the International Space Station used a MinION to sequence samples of mouse, virus, and bacterial DNA in microgravity. Identifying microbes by their genetic sequences could help astronauts detect health threats. Back on Earth, researchers are testing the MinION for applications in medical diagnostics and infectious disease monitoring.

For serious infections like sepsis, severe pneumonia, and complicated urinary tract infections, rapid treatment with an effective antibiotic is key. MinION sequencing could identify infection-causing bacteria faster than, yet as effectively as, current culturing methods, said Justin O'Grady, a medical

microbiologist at the University of East Anglia, UK. The genome also contains information about antibiotic resistance, providing doctors with clues about which drugs would not effectively treat an infection.

O'Grady and his colleagues have already used a MinION to identify bacteria, along with antibiotic resistance profiles, within four hours of receiving a urine sample in the lab. Since patients typically receive antibiotics every eight hours, rapid identification using genetic sequencing could help doctors prescribe a more effective drug before a patient receives a second dose of antibiotics, he said. "We can develop a diagnostic pipeline [that's rapid enough] to make a difference in the clinic," he said.

In February, the World Health Organization announced that the most common bacteria to cause urinary tract infections are becoming resistant to some antibiotics. Though genome sequencing for clinical microbiology is still in the research phases, O'Grady hopes it could eventually help patients receive appropriate drugs guickly, and ensure that doctors reserve the antibiotics effective against multi-drug resistant pathogens for when they are absolutely needed.

Other microbes, such as viruses and some parasites, can cause infections that spread quickly, sickening hundreds to thousands of people. For Jane Carlton, a biologist at New York University, the genome of the parasite that causes malaria is a basic tool to understanding its biology, ability to cause disease, and sensitivity to drugs. She, too, was part of the first group of researchers to use the MinION, and



The MinION DNA sequencer sits atop a state-of-the-art nextgeneration sequencer. The MinION is significantly smaller than typical laboratory sequencers, which are about the size of a personal refrigerator, and not so easy to travel with.

she thought the device's portability could change how she does research in rural India. Genomic information can be limited when infectious disease outbreaks happen in countries without access to the latest DNA sequencing technology. Developing the capacity for local scientists to sequence the genomes of infectious diseases such as malaria means that precious samples do not need to be sent to foreign labs, which can be expensive, logistically difficult, and take time.

Last year, Carlton and her colleagues brought MinIONs to India to sequence the genome of the malaria parasite from clinical samples. When their field station experienced frequent electrical shortages, the researchers took the MinION devices back to their hotel and continued sequencing overnight. A portable sequencer like the MinION means a lab can go to where it's needed, enabling local researchers to study the diseases that most affect their people, rather than relying on visits by foreign researchers, Carlton said.

Genomic information from clinical samples can help scientists document the spread of outbreak after it's occurred. But Nick Loman, a genomicist at the University of Birmingham, UK, thinks genomic information could also be used to stop an outbreak, provided researchers can guickly sequence clinical samples. Mutations in the genome of a virus or parasite help researchers track the microbe as it spreads to different communities, counties, or countries.

In December 2013, the largest Ebola outbreak in history began in West Africa, resulting in more than 28,000 cases and 11,000 deaths. The first viral genome sequences collected from infected patients in Guinea publicly appeared in April 2014. In July, Ebola genomes sequenced from 99 patients in Sierra Leone confirmed that the outbreak had spread to another country. The next new sequences weren't available until mid-November, timing that left a genomic data gap during two months of rapid growth in the number of Ebola cases.

By March 2015, Loman, and his student Joshua Quick, had been working with the MinION for about a year as some of the early adopters. They realized bringing

#### Back to the beginning

As the MinION provides current genetic information at remote sites around the world, Akeson and Deamer are using nanopore sequencing to dive further into the past.

Akeson and his students, along with others in the MinION research community, are sequencing RNA, the chemical cousin of DNA. One type of RNA, found in ribosomes, accumulates mutations so slowly that tracking sequence changes between different organisms can reveal millions of years of evolution.

Deamer, meanwhile, is returning to questions about the origins of life that first inspired his idea for nanopore sequencing: He's using the MinION to decode DNA produced by primitive cells, hoping to show they are producing molecules that resemble genetic information.

The evolution of nanopore sequencing started with an idea sparked on a road trip, grew out of early experiments inspired by attending talks at conferences, and developed into a technology now used around the world. For Deamer, the story of nanopore sequencing reveals the serendipitous path of science: "You have to have your brain wide open to all these patterns. There are a whole bunch of balls out there, and if you pick the right bunch, you can juggle them and do some tricks." Additional reporting contributed by Laurel Hamers, SciCom '16

PEXELS

SMOOTHIE COURTESY

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SEQUENCER

MINION

the sequencers to field research stations in West Africa could speed access to viral genomes, so they teamed up with European researchers operating a mobile laboratory in Guinea. In April, Quick carried suitcases of equipment for a portable MinION-based genomics lab to Guinea where he sequenced samples at the field station for two weeks and then trained other researchers to continue the process. The team sequenced Ebola from 142 patient samples collected from March to October 2015, generating results within 24 hours of collecting samples. Two local researchers continued the MinION sequencing at least through February 2016.



#### **Sequencing for** students

The portability and affordability of nanopore sequencing enables classrooms around the world to access genetic information before class ends. Students at the University of Cambridge, UK, extracted DNA from a smoothie and sequenced it using a MinION to identify its fruit ingredients. For this experiment, the group read ten million DNA bases, which, more than a decade ago, would have cost \$100,000 using machines in a dedicated sequencing center, said Kerstin Göpfrich, a graduate student at the university, who donated her strawberry-banana smoothie to science.

By Cameron Walker

# Camp Dickens Victorian author unites modern scholars

Some writers have thousands of Twitter followers; others have dedicated book clubs. At UC Santa Cruz, one 19th-century author has his very own summer camp.

The Dickens Project, a UC Santa Cruz–based multicampus research unit that promotes research and teaching on Charles Dickens, runs the Dickens Universe conference, drawing enthusiasts from around the world to discuss the author's novels.



#### TOP: Dickens's letters.

ABOVE: The Victorian dance. John Jordan accompanied by longtime Dickens Universe attendee, Martha Stead.

RIGHT: The box contains a silver toddy ladle used by Charles Dickens, now in the Dickens Project collection at McHenry Library's Special Collections, UC Santa Cruz. Each summer, scholars present research, professors and graduate students teach courses—and everyone from experts to high school students and Road Scholars share dining-hall meals and dormitories for a full week of talks, festivities, and even Victorian dancing. "It's a combination of a scholarly conference, a festival, and summer camp," said **John Jordan,** professor emeritus of literature and co-founder of the Dickens Project, started in 1981.

Dozens of scholarly articles and 25-plus books have sprung from the event, which initially consisted of UC researchers and students



but now involves more than 40 member universities. The *Dickens Studies Annual*, published by AMS Press in New York, has the right of first invitation for papers presented here.

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"It's a research powerhouse," said Sharon Weltman, a Louisiana State University English professor and longtime attendee. Two of Weltman's keynote addresses are part of her forthcoming book on Broadway musicals and Victorian literature. Each of Dickens's novels deals with societal problems, whether class division or electoral corruption, so "it's impossible to write about Dickens without touching on contemporary issues," she said.

That's part of the author's widespread appeal, said **Murray Baumgarten**, professor emeritus of literature and a Dickens Project co-founder.

Past keynotes have included everything from a modern take on motherhood in *Dombey and Son* to ways that digital versions of Dickens's work can aid research. Even public transportation, filtered through a Dickensian lens, is grist for discussion; the shift from stagecoaches to railroads altered the author's world, just as automobiles shape society today.

The 2017 event will focus on *Middlemarch*, written by Dickens's contemporary George Eliot (the pen name of Mary Anne Evans). Along with discussing her novel, participants will consider how Dickens, who corresponded with Eliot, was aware she could offer a new perspective on the world.

Novel perspectives seem essential to the Dickens Project, connecting diverse scholars and readers to create new ways of looking at the author and his work. And to enjoy it, too. "His writing sparkles," said Baumgarten. And readers from the 19th century to today share the same sentiment about Dickens, he noted: "People love him."

# OS: DICKENS LETTERS COURTESY THE DICKENS PROJECT; LADLE COURTESY UC SANTA CRUZ SPECIAL ECTIONS; DANCE BY ELIZABETH WALKER; ALEWIVES © HEATHER PERRY / HEATHERPERRYPHOTO.COM

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# Forcing evolution's hand

When humans build, nature remodels

▶ When early settlers landed on America's eastern shores in the 1600s, most new communities did two things: they built a church and a dam. The consequences of those dams persist today.

While blocking the flow of rivers and streams made it possible for pioneers to power up their mills, the dams also shut off the natural journey of the anadromous alewife—a river herring that spends most of its life in the ocean but must return to rivers to spawn. In response to this new lifestyle, the alewife consigned to inland waters underwent dramatic physical changes.

As the fish developed new traits to survive in their altered surroundings they, in turn, transformed their ecosystem, a phenomenon that lures **Eric Palkovacs**, associate professor of ecology and evolutionary biology at UC Santa Cruz. He investigates the ways that human impacts on the natural world affect the rate at which a species evolves, a process known as eco-evolutionary dynamics.

Palkovacs' research shows that when anthropogenic activities force organisms to modify their physical traits to survive, those small evolutionary steps can also alter the environment creating unintended consequences for people, too.

RIGHT: Alewives encounter a dam along their anadromous migration in Winslow, Maine, in the Sebasticook River—a tributary of the Kennebec River. Dams blocking upstream passage isolate inland lakes, and force landlocked populations to evolve. The dam has since been removed. By Amy West



#### Forcing evolution's hand

#### **Isolating alewife**

In the case of the alewife, several hundred years of segregating lake-locked alewife from their ocean-migrating brethren led to smaller body sizes, smaller mouth gape, and different spacing of their gill rakers—all traits designed to capture smaller food. Why? Because to survive, they had to evolve to forage on the tinier stuff; their lake-bound behavior had disrupted the ecosystem in which their anadromous ancestors had evolved.

Normally, when alewife migrate to lakes or rivers to spawn, they feed on the larger animal plankton. Eventually, the fish swim for open seas and the large zooplankton populations bounce back. But alewife trapped behind dams couldn't leave, so the larger plankton populations never rebounded. That change in feeding behavior had a cascading effect: not only did the fish need to find smaller plankton, but with few large animal plankton remaining, the microscopic algae bloomed out of control.

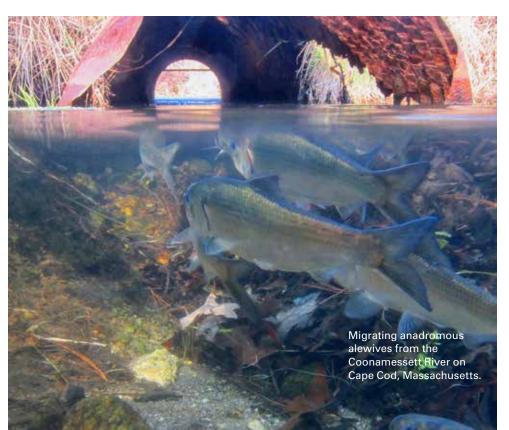
Alewife disrupted the ecology of lakes elsewhere, too. While growing up, Palkovacs witnessed massive die-offs of alewife in the '80s; fish littered the shores of Lake Michigan after they invaded the upper Great Lakes. There, zooplankton populations —decimated by the surge of alewife—weren't large enough to keep the smaller plant plankton in check, a situation that likely exacerbated the algal blooms already overwhelming the Great Lakes. Alewife also reduced native whitefish populations that competed for the same food.

#### **Evolving questions**

Now, years later, Palkovacs investigates how those fish made it from the ocean to the Great Lakes by tapping into the genetics expertise and cuttingedge equipment at the National Oceanic and Atmospheric Administration (NOAA) Southwest Fisheries Science Center based in Santa Cruz —UC Santa Cruz's next-door neighbor. Not only does he collaborate with NOAA scientists, which helped to expand the diversity of his genetics work, but Palkovacs is also the director of the NOAA Cooperative Institute that supports NOAA and UC Santa Cruz partnerships.

With all these resources, Palkovacs also studies mosquitofish, trout, stickleback, salmon, and green sturgeon. Each of these species has been altered by human activities: from blocked waterways to warming water temperatures. In every field setting he poses the same eco-evolutionary questions: How are humans forcing these organisms to change, and how do those changes affect their survival?

While evolution likely conjures a timescale of thousands of years, it can also happen fast, "on the order of years and decades," said Palkovacs. These trait changes, or rapid evolution, can occur from a behavioral change in response to an altered

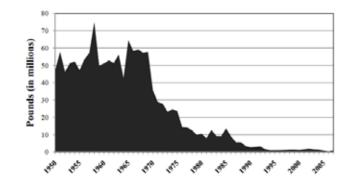


ecosystem, or from hunting and fishing. When people place selective pressure on animal populations, like killing bigger fish or larger-horned sheep, within a few generations the animals can evolve new traits. They may start to mature at a younger age, shrink in size, or shift their migration behavior. "This happens whenever we kill stuff," said Palkovacs. "We often select against the traits that we actually value."

#### **Damming evidence**

The anadromous populations of alewife have steadily declined since the 1970s. A variety of culprits were put on the table: dams, pollution, freshwater harvests, predators, and now people are suggesting effects from climate change, explained Palkovacs. "And then there's marine bycatch," he added.

Palkovacs' background in population genetics drove him to search for reasons why alewife numbers continued to dramatically drop along stretches of the Eastern Seaboard, despite years of improving pathways for fish, protecting water quality, and setting limits on freshwater harvests. He surmised the only thing left relatively unchecked was their vulnerability as bycatch; trawl nets targeting oceanic Atlantic herring accidentally scoop up blueback herring and alewife swimming among them.



The decline of the herring. Total commercial landings of river herring from the U.S. Atlantic Coast, 1950–2007

To test his hypothesis, Palkovacs and his partners at NOAA turned to a database they built with nearly 8,000 specimens of alewife and blueback herring collected in rivers from Florida to Canada. Using non-lethal snips of fish fins, they catalogued the river herring's genetic fingerprints and linked each fish to a region of rivers. The scientists could then match the genetic fingerprint of each bycatch-caught alewife and blueback herring to their spawning rivers.

The results of this work showed that the threatened East Coast alewife populations are from rivers in southern New England and the Mid-Atlantic—areas that Palkovacs said "really do overlap strongly with areas where they find the greatest magnitude of bycatch."

This DNA detective work also revealed to Palkovacs the extent to which these foot-long fish travel up and down the coast, and their susceptibility to ending up as bycatch. "We can't say with 100 percent certainty that it [bycatch] caused past declines, but I can say it's contributing to their lack of recovery," he said.

Alewife return to their original spawning streams less frequently than Pacific salmon. Migrating between several rivers means alewife aren't as genetically differentiated as salmon, explained **John** Carlos Garza, an ocean sciences adjunct professor at UC Santa Cruz and NOAA geneticist who works closely with Palkovacs on river herring. Without data showing distinct alewife populations (stocks) for each river, the fish don't fit into neat biological categories that fisheries managers need. This makes managing alewife complex if they fare better in some rivers and not others. "When you see populations declining over your own career, it's disconcerting," said Palkovacs, who once saw tens of thousands of these fish during his doctoral studies in 2005, but now sees only hundreds.

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NOAA's John Carlos Garza shows what's needed for the genetic analyses of alewives: a non-lethal snip of an adipose fin.

Palkovacs' alewife bycatch research garnered attention at the last Mid-Atlantic fishery management council meeting when members voted on whether to federally protect the river herring. Although he presented strong evidence for alewife decline along a large swath of the coast, the council focused on lesscertain evidence of alewife populations improving in Maine, he noted. In the end, the council opted not to grant federal status to river herring under the Magnuson-Stevens Act, which requires a thorough population assessment that reveals how much river herring can be sustainably fished.

That designation would have provided legal teeth to prevent overfishing, explained Palkovacs, which alewife don't currently have because they aren't directly harvested. "They are in fisheries management limbo," he said.

#### **Fishy encounters**

Now, many of those dams from the 1600s have been dismantled, giving fish the upstream access they once had. Connecticut's Rogers Lake, for instance,

#### Forcing evolution's hand

has a new fish ladder, and Palkovacs and his team have a unique opportunity to monitor a natural evolutionary experiment from the outset: What happens when ocean-migrating fish finally reconnect with their lake-bound family nearly 350 years later?

By taking fin clips as the fish enter the lake and from those already in residence, scientists can determine if the two groups interbreed or whether one group dominates. They can also follow how the lakes respond ecologically; for instance, ocean-migrating fish bring marine nutrients to a lake system. "Is the process of reconnecting these populations going to provide overall benefit, or might it be the opposite?" said Garza.

While many people may overlook alewife, they are a keystone species for lakes, said Andrew Hendry,

professor of evolutionary biology at McGill University in Montreal and a noted author on eco-evolutionary dynamics. He believes alewife demonstrate the importance and consequences of evolutionary dynamics. In addition to being a contemporary and reproducible study, Palkovacs' alewife research occurs in a natural setting, said Hendry, which is an advantage over studies in controlled lab settings that can't always show the magnitude of evolutionary change.

#### Altered lives

On the West Coast, steelhead trout have an ecological story similar to that of alewife. They,

too, battle for clean water, spawning habitat, and unobstructed river access. Though steelhead trout migrate between the ocean and rivers, they can also become a permanent freshwater resident in the form of a rainbow trout-the same species, Oncorhynchus mykiss, with a different lifestyle.

Scientists recently discovered that genetics and body size trigger whether a rainbow trout becomes a lake resident or decides to migrate as a steelhead. "We've found that when steelhead are isolated above barriers we can see on a molecular level that they undergo selection against migratory behavior,' said Garza.

By constructing dams across a river, "humans can tip the balance in what they prefer," said Palkovacs.

Additionally, the human propensity to harvest the biggest fish has, over time, led to a smaller body size and younger spawning age in wild salmonthe steelhead's cousin. Selecting bigger fish is commonplace in fisheries. "But that can reduce the productivity of a fishery, decrease its resilience to environmental change, and have negative impacts for people that rely on those fisheries," said evolutionary biologist Hendry.

The effects of culling bigger predators reverberate down the food chain. For instance, there are fewer eggs to develop into more salmon, less fish to control their prey, and less marine nutrients to enter

a river system. To learn how consistent that decline is across Alaska's rivers and salmon species, Palkovacs is leading a group of scientists to comb through 50 years of historical data to tease out how harvesting, food availability, and warming ocean temperatures may work collectively to cause Alaskan salmon to shrink.

Good documentation has been lacking, said Palkovacs, to show that fish are changing size, that those changes are evolutionary, and that humans feel the impacts. So, by wading deeper into this Alaskan salmon issue, Palkovacs wants to know: How do these humaninduced changes circle back to humans?

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For example, subsistence Native Alaskans feel the economic and cultural impacts. "Now it takes two or three modern fish to make up the biomass of a historically sized Chinook in the Yukon River," said Palkovacs. It requires more effort to catch enough fish to fill their freezer for the winter.

While it's easy to understand how mass extinctions can drastically alter ecosystems and species, human activity can also trigger ecological shifts that force species to adapt in small, but continuous, increments. Palkovacs' research shows how our actions can also come back to damn us.

A mathematical quest

TALA14 .

Images of a falling cat captured by a chronophotographic gun appeared in the journal Nature in 1894. Almost a hundred years later Richard Montgomery's solution, "Gauge Theory of the Falling Cat" was published in the Journal of the American Mathematical Society in 1993, and led to his pursuit of a solution to the three-body problem.

Ever since Newton precisely predicted the orbits of two celestial bodies governed by gravity, the guest began for a solution to a three-body problem. It wasn't something that UC Santa Cruz mathematician Richard **Montgomery** ever planned to tackle, once saying: "Celestial mechanics is the land of old, famous, longdead men; a world of very hard problems."

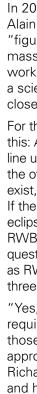
This "N-body problem" arose after Newton posed a system of differential equations whose solutions described how some arbitrary number, "N," of gravitating masses can move. His solution for the two-body problem forms the foundation for much of physics and astronomy. Yet a solution for three bodies in orbit eluded even Newton.

In the ensuing centuries only five families of explicit formulae (applicable only under specific sets of conditions) have been found. Furthermore, French polymath Poincaré proved the three-body problem can never be "solved" with a single closed-form formula that describes all solutions. But the quest didn't end there.

"As is almost always the case in mathematics, impossibility proofs open up much vaster fields of study than those which they close," said Montgomery, noting that Poincaré's proof led to "chaotic dynamics" and other modern mathematics.

By 1993, Montgomery solved the classic "falling cat problem," showing how cats could change their shape to land on their feet despite the fact that their angular momentum must remain zero throughout the fall. His closed-form solution simplified the cat's body to three points of mass-echoing the three-body problem. With that, Montgomery entered the fray.

Two forms of the same species from Scott Creek in Santa Cruz, California: a freshwater resident rainbow trout, and the anadromous steelhead adult, which swims between the ocean and river.





In 2000, collaborating with French mathematician Alain Chenciner, Montgomery rediscovered the "figure-eight" solution, in which three equal masses chase each other around an 8-shape. Their work inspired numerous other choreographies (and a science fiction novel), but none offered explicit closed-form formulae.

For the next 17 years, Montgomery grappled with this: As the three masses move, they occasionally line up, all three on a single line with one between the other two; an eclipse. Three kinds of eclipses exist, depending on which mass is in the middle. If the bodies are "Red," "White," and "Blue," the eclipses can be "R," "W," or "B." (In the figure-8, RWBRWB repeats infinitely.) But the overarching question was: Given any sequence of eclipses, such as RWBRWBRRWWWRBR, is there a solution to the three-body problem which realizes this sequence?

"Yes," said Montgomery, but getting that answer required different mathematical methods from those that revealed the figure-8 solution. That new approach came from working with mathematician Richard Moeckel, at the University of Minnesota, and his chaotic dynamics theories. Their solution, derived in 2014, also allowed for resting points in each orbit-though real stars never stop moving. But their answer requires close to equally sized masses and a small angular momentum.

What happens when the angular momentum, like that of the falling cat, is actually zero? No one yet knows. "But, in pursuing really good problems we develop new methods," said Montgomery, "and mathematics becomes as much art as science."

# Lessons from teen activists

Youth organizations empower students



Teenagers involved with the California Endowment's #Health4All advocate at a 2015 rally in Sacramento.

In the fall of 2012, returning Oakland High School students met with more than new teachers. They also encountered routine police patrols on campus and a new stop-and-frisk policy, enacted after several incidents of violence and weapons possession in the previous year. Students felt these new policies, along with teachers' established authority to hand out suspensions for "willful defiance," were unfairly targeting students of color. During the first quarter, school records showed that 32 percent of all student suspensions stemmed from willful defiance, which could cover anything from disrupting class to simply chewing gum or forgetting homework. Instead of just complaining, the students got organized.

Assisted by an Oakland-based grass-roots youth group, Californians for Justice (CFJ), the high schoolers surveyed their peers about the situation, compiled the results, and presented their report to the school principal. Other social advocacy groups used the students' report to pressure the Oakland Unified School District Board of Education to join Los Angeles, San Francisco, and other school boards to eliminate willful defiance as a reason for high school suspensions.

Reflecting on the students' involvement, UC Santa Cruz sociology associate professor **Veronica Terriquez** explained that "in [the] teenagers' minds, they don't necessarily think about their work as [being] political, especially when they start to get involved. It's about helping their communities."

#### Politicizing moments

Terriquez works in an emerging area of sociology, studying citizen-based organizations in low-income and historically marginalized communities. She's focused on civic youth groups, like CFJ, that work toward equality and racial justice. From statistically validated surveys and descriptive interviews, Terriquez catalogs the various ways youth can affect their schools and communities through these organizations. Her research also reveals the benefits these groups provide to students, such as the skills and mindset they develop, which can persist far past a student's initial involvement.

"There's a longer-term commitment by young people who have been civically engaged in their community—they tend to give back," said Terriquez, who observed this firsthand during work with an Oakland grass-roots organization after earning her bachelor's degree. Terriquez's own politicizing moment came during the fight against passage of California Proposition 187, in the mid-1990s, which would have barred undocumented individuals from access to public services like non-emergency health care and public schools—to devastating effect in her community, she said. Ensuing work with community organizations guided her career toward "understanding how people could have a voice in their communities."



Terriquez collected nearly 4,000 surveys from the 132 BHC-affiliated youthserving organizations in 2016. The number of BHC-affiliated organizations serving youth has grown since the initiative's inception. This report draws on data from 132 separate organizations, which run a total of 151 programs operating within the 14 BHC sites.

#### Individual impact

To identify the experiences and benefits students acquired from their involvement with CFJ and other youth organizing groups, Terriquez and her students surveyed youth in 98 civic groups associated with the Building Healthy Communities (BHC) program. This 10-year initiative was launched in 2010 by The California Endowment, a private health-oriented foundation based in Los Angeles, to analyze how funding community-based organizations can affect the overall health of 14 low-income urban and rural California communities. It's not easy to elicit replies from high school students, but Terriquez's persistent approach resulted in a 92 percent overall response rate—a total of 1,396 surveys-that she keeps in an impressive collection of grey, orange, and turquoise file boxes around her office.



#### Lessons from teen activists



California students protest school discipline tactics such as expulsion in favor of practices that keep students in schools as part of the #SchoolsNotPrisons campaign.

She credits her high survey return rate to partnering her students with interns from the organizations she studied. The interns also collaborated on the analysis of the surveys they helped gather resulting in 14 reports crediting a total of 25 student and intern coauthors.

#### **Active benefits**

In her surveys, over half of the students reported participating in college preparation activities, improving their chances of enrolling in a two- or four-year college. But Terriquez also found that at least half the respondents said their grass-roots efforts helped them "a lot" in communicating, speaking in public, and understanding how government policies affect their own community.

Those kinds of soft skills can boost graduation rates because they equip students with strategies to help them stay in school, said Terriquez. Additionally, students' engagement with school boards and local governments helps them see their academic struggles as a result of systemic inequality, and not necessarily their personal failings.

Far from just shifting the blame away from themselves, this realization helps college students resolve their problems, Terriquez explained. For example, she found that students disproportionately took advantage of tutoring programs and Educational Opportunity Programs designed to assist students with their backgrounds.

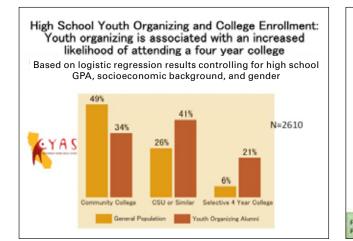
#### Legacy lessons

Terriquez found that the effects of youth activism are lasting. Former members continue to be active

in grass-roots groups at their colleges and within their community. Many of the students involved in changing their school's discipline policies went on to take active roles in the immigrant rights movement. "They weren't just participating," said Terriquez, "they were actually leading."

In a 2015 paper published in *Sociological Perspectives,* Terriquez compared the civic engagement of former youth organization members with the general population, based on records by the California State Fullerton Social Science Research Center in 2011. While former youth organization members were nearly twice as likely to come from low-income households—88 percent versus 46 percent of the general California population they were statistically more likely to volunteer, be involved in community organizations, attend a protest, and vote. Terriquez credits this long-term effect to practical experiences gained at grass-roots organizations.

One example of these experiences, noted Geordee Mae Corpuz, lead organizer for the Oakland CFJ, occurred after the elimination of willful defiance suspensions in Oakland High. Students wanted increases in staff trained in restorative justice to lead students and teachers in conflict resolution. To fund this training, students joined their district's Local Control Funding Formula Advisory Committee. Established in 2013, this California program provides extra funds to low-income school districts based on accountability plans drafted by students, parents, and community members. The process of submitting the plans is very bureaucratic, and the Oakland students relied on CFJ's expertise to navigate the system. Corpuz said the participating



teenagers met with parents across the district, people in the restorative justice movement, the school superintendent, and the budgeting office to draw up plans and secure the funds.

Additional qualitative data—revealed though analyses of Terriquez's trove of recorded interviews—show students from grass-roots organizations also develop strong social networks within their community. These students become knowledgeable about who their government representatives are, and often personally know the staff, she said.

Mining these interviews, which can be more than three hours long, offers an inside look at how students apply activism in their everyday lives. For instance, to learn how youth organization members engage with their parents about politics, Terriquez found incidences of youths reading through California's voting guides with their parents. She also found behaviors specific to each family's background; children of political refugees would assure their parents that political involvement in California was not dangerous in the way it had been in their home country, while children of undocumented immigrants would sometimes teach their parents about their rights in this country.

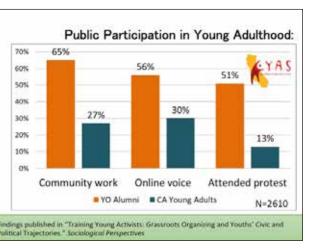
In her "control" interviews with random teenagers, Terriquez found that parents' interests and involvement in politics usually predicted their children's interest. This was not the case, however, with teenagers involved in civic youth organizations. "When children are very civically engaged, they politicize their parents," said Terriquez.

#### After school

Activist g role in co Numerou school e graduatio more like increase health of Terriquez educatio invest in California youth pro other fur efficacy. "We're I spark an makers," organizin aggressi

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Activist groups like CFJ also play a positive role in community health, believes Terriquez. Numerous studies show that decreasing high school expulsions and suspensions leads to higher graduation rates. Students who graduate are also more likely to pursue further education that, in turn, increases their earning potential and the overall health of their community.

Terriquez's research is being used to persuade educational and youth development funders to invest in similar programs. It's an area in which the California Endowment has heavily invested, said the youth program manager, Albert Maldonado Jr., but other funding organizations remain uncertain of its efficacy.

"We're learning that young people, with their spark and energy and passion, are critical change makers," said Maldonado "When assisted by youth organizing groups and adult allies, they can drive aggressive agendas," he said

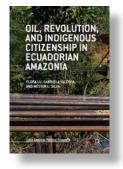
### Areas of California youth organization impact:

Los Angeles School Police Department: military weapons return–including grenade launchers–from U.S. Department of Defense weapon surplus program.

San Diego Unified School District: interpreters in Karen, Kizigua, Somali, and Swahili for immigrant families.

Kern High School District, Arvin High School: filter installation in drinking fountains to lower arsenic levels.

## PEN&INO



#### **Oil Change**

When Ecuador's President Rafael Correa took office in 2007, he restructured and expanded natural resource extraction. Income from those industries, mostly oil, helped fund Correa's developmentalist vision-a "Citizens Revolution"with purportedly positive social and environmental outcomes.

Yet living conditions in the country's Amazonian region-where oil is extracted-have not experienced the grandiose changes promised by his administration, said Flora Lu, associate professor of environmental studies and UC Santa Cruz provost of Colleges

Nine and Ten. Lu takes a critical look at the Correa administration's "21st century socialism" in her book Oil, Revolution, and Indigenous Citizenship in Ecuadorian Amazonia,

coauthored with Gabriela Valdivia, and UC Santa Cruz alum Néstor Silva. Based on decades of fieldwork in Ecuador, much among the indigenous Waorani, Lu explores the complexity of "oil entanglements" as they manifest in the nation's seat of power, Quito, and in three Amazonian communities along different oil roads.



#### Chance **Encounters**

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"Science may be a methodical progression of work," said James Estes, adjunct professor of ecology and evolutionary biology, "but a lot of learning happens in a different That premise

underlies his book Serendipity: An **Ecologist's Quest to Understand Nature.** Blending natural

history, principles of ecology, and his own research, Estes recounts the unexpected events that began with a contract job in the Aleutian Islands and continued throughout his career studying sea otters and the impact of

top predators on ecosystems. In a moment underwater, Estes saw that kelp didn't grow where sea otters were absent. Many studies later, he confirmed the connections: sea otters ate sea urchins. keeping urchins from overeating kelp. Although his work started in the Pacific Northwest. the importance of apex predators is worldwide. Whether it's otters, whales, wolves, or elephants: "Big animals matter to ecosystems," he said.

Estes hopes his book encourages students to keep their minds and eyes open to opportunity.



#### Payment in Kind

After the collapse of the Soviet Union, many low-income Russians turned to church-run food banks and soup kitchens because the "new" capitalism eliminated most assistance programs. This survival network grew to include NGOs and government agencies, creating a powerful alternative welfare system of people who believed that doing good creates more good.

In her third book, Living Faithfully in an Unjust World: **Compassionate Care** in Russia, UC Santa Cruz anthropology professor Melissa Caldwell explores the rise of this "compassion

Caldwell chronicled the expanding scope of churches, and the bureaucratic structures they used to manage people, money, and distribution of goods and care. 'lt's a true market with goods-food, medicine, construction equipment-through which ideas of assistance and compassion circulate," she noted It's a self-boosting

economy."

economy, too. Over and over, people told Caldwell they believed putting kindness into the world creates more kindness.



#### **Perfect Tense**

In her most recent book, What Becomes Us, UC Santa Cruz literature professor Micah Perks uses unborn twins' point of view to tell their mother's story; a woman who escapes her controlling husband in Santa Cruz and flees to rural New York to teach in the local high school. There, a controversial book assignment impacts the pregnant teacher, her students, and the community.

The landscapes are familiar to Perks-she was raised in upstate New York and now lives in Santa Cruz. However, contrary to the "write what you know" adage, Perks writes to know.

"My overarching interest is exploring the tensions between individual and community, the I and we," said Perks who lives in an extended, blended family. Writing the novel helped her probe "that central tension between longing to be close with others and being claustrophobic," she said.

UC Santa Cruz students benefit from Perks' real and fictional experiences. Said Perks: "I definitely bring all that back to the classroom."

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**X Factor** 

"Where are the women?" came the shouts when an allmale panel closed the NGO Forum Against Racism In South Africa on the eve of the 2001 World Conference Against Racism. Racial Discrimination, Xenophobia, and Related Intolerance.

That lack of inclusion impelled Sylvanna Falcón, associate professor of Latin American and Latino studies at UC Santa Cruz, to add her voice to the outcry: it also inspired her awardwinning book, Power **Interrupted: Antiracist** and Feminist Activism Inside the United Nations.

Sifting through the United Nations' archives, Falcón found the UN routinely addressed concerns raised by women as "women's issues." detached from the broader dynamics of racism

She also discovered that two of the four women signatories to the UN charter, from Latin America, successfully lobbied for a gender equity clause in the charter. "My book reminds us that it doesn't take many people to make a meaningful change,' said Falcón.

Progress is fragile, though. "It's one thing to put words on paper and another to actually live it," she noted.





Elizabeth Devitt ('13)

Melissae Fellet ('11) Greta Lorge ('03)



Laura Poppick ('13) Kim Smuga-Otto ('15)

With the expertise of scientists-turned-journalists, nine graduates of the UC Santa Cruz Science Communication Program reported these stories about scientific research that span the university's departments. While the UC Santa Cruz scientists may keep offices and laboratories on the redwood tree-studded campus, the impact of their work reaches around the world-and beyond.

At a time when the credibility of science and the news media is under scrutiny, the Science Communication Program is more important than ever, said Erika Check Hayden, the program's new director. "Through our students, alums, and instructors, we have a huge role to play in promoting well-informed dialogue on science," she said.

The "SciCom" graduate certificate program was established in 1981 by alum John Wilkes (B.A., M.A., and Ph.D.), a scholar in English literature with a plan to teach scientists how to skillfully extract and create readable stories from the realms of scientific study. His successor, a freelance science writer and former Wilkes' student himself.

and international media outlets to deliver science discoveries in print, radio, video, television, and formats we haven't yet imagined. Despite concerns about the current media climate, Check Hayden is optimistic about the future. Although there's a perception that so-called fake news, with its sensationalism and click-ability, will overshadow real news, Check Hayden said: "If we're doing our jobs as communicators, we'll be able to tell our stories in ways that resonate with readers, listeners, or viewers in ways that make true news far more compelling." We hope you find compelling reading among the

inguiry@UC Santa Cruz

## INQUIRING**MINDS**

Robin Meadows ('87)



Cameron Walker ('02) Amy West ('12)

Sarah C. P. Williams ('07)

**Robert Irion** (SciCom '88) expanded the program's resources and influence during his decade of directorship. Now, Check Hayden is leveraging her international investigative reporting credentials and seven years of experience as a SciCom instructor in social media to oversee the next generations of UC Santa Cruz's science-savvy writers.

Like the 300-plus SciCommies before them, the next graduates will fill posts at regional, national,

articles in this edition of inquiry@UC Santa Cruz.

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