BRINGING HIDDEN NARRATIVES TO LIGHT

2018 ANNUAL REPORT

CARL R. WOESE INSTITUTE FOR GENOMIC BIOLOGY

WHERE SCIENCE MEETS SOCIETY.

FROM GENOMIC TECHNOLOGY A STRONG, SUSTAINABLE

WE ARE NOW, CAN PROPEL US TO A POINT WHERE THE NEEDS OF

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11/28
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A MESSAGE FROM THE DIRECTOR

Gene E. Robinson
Director, Carl R. Woese Institute for Genomic Biology
Swanlund Professor of Entomology

Fundamental scientific research is a quest for foundational truths of the natural world. Applied research is an effort to shape that knowledge into new solutions to the many challenges we face as a species and as a global ecosystem. Underlying these intertwined endeavors is the impulse to imagine a future that is better than the present: one in which we know more about the world we inhabit and, as a result, enjoy longer, healthier, happier, and more sustainable lives.

For the last few decades, powerful new sequencing technologies have given us the opportunity to direct our scientific gaze toward the genome. At the Carl R. Woese Institute for Genomic Biology, piecing together ancient DNA sequence and comparing highly conserved genomic regions across taxa has allowed researchers to reconstruct an understanding of Earth's biological history, a profusion of ongoing genome sequencing projects are documenting life on our planet as it is today, and efforts like the proposed Earth BioGenome Project, co-led by myself and founding

Referenced Story

A digital library of life (p.16)

IGB Director Harris Lewin along with W. John Kress of the Smithsonian National Museum of Natural History, could give us greater control over whether and how we are able to preserve biodiversity in the future.

This year, our Annual Report shines a spotlight on a few of the current genomic phenomena that are positioned to have significant impact on the next few decades of innovation. Throughout the book, you will find pages that provide a window into our vision of the future and explain how our researchers aim to make it a reality. We hope that by including these glimpses of our goals, we will successfully invite you to share them.

As always, our report also contains briefer stories of research discoveries and developments in the many different areas that genomics has penetrated. In the last year we have tracked the delivery of cancer therapeutics to individual cells; used computer vision to document the round-the-clock social interactions within a honey bee colony; developed a visual method to map the location of a specific portion of the genome inside a living nucleus; and inferred the story of kidney stone formation from the appearances of their cross-sections. These and other stories from this year showcase our thriving research program.

Science Spotlight

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The ability to imagine a future world better and brighter than the present is perhaps the best aspect of human nature. Scientific exploration is one important way to pursue that goal; strengthening societal connections, creating opportunities to collaborate, is another. At IGB, it is our mission to embrace both.

We believe that the only way societal benefits of scientific innovation can be fully realized is through meaningful dialogue among researchers and other members of the public. This year, over 200 IGB members and over 9000 visitors came together at 68 different outreach events to exchange ideas about genomics and society. The largest of these events, IGB's World of Genomics hosted this year by the St. Louis Science Center, presented hands-on activities designed to appeal to attendees of all ages; this event helped to solidify the developing relationship between the IGB and Drs. Catherine and Don Kleinmuntz, two Illinois entrepreneurs with an interest in promoting genomic research and innovation.

The ability to imagine a future world better and brighter than the present is perhaps the best aspect of human nature. Scientific exploration is one important way to pursue that goal; strengthening societal connections, creating opportunities to collaborate, is another. At IGB, it is our mission to embrace both.

GENE E. ROBINSON

About the IGB

Above_*Darwin's Playground* at the Carl R. Woese Institute for Genomic Biology.

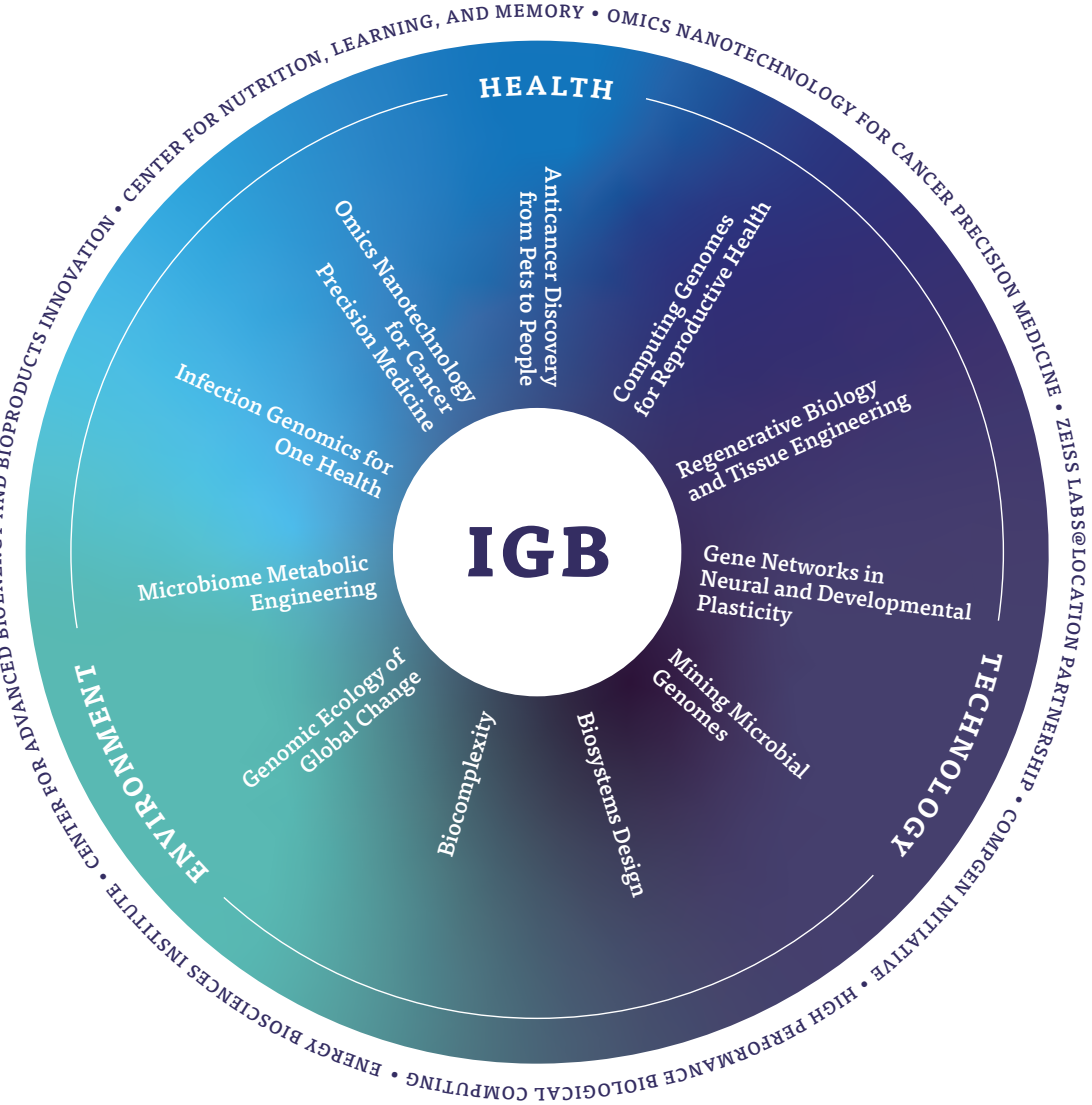
The Carl R. Woese Institute for Genomic Biology (IGB) was founded in 2007 with the intention of facilitating genomic research across the campus. IGB members are drawn from many schools and departments, including biology, chemistry, physics, engineering, sociology, and business. What unites them is a shared vision of what a genomics-based approach can achieve: a healthier global population, increased food and fuel security, a toolbox of genomic technologies to meet future societal challenges, and a deep knowledge of the diversity of life on our planet.

Our mission

To advance life science research at the University of Illinois at Urbana-Champaign and to stimulate bio-economic development in the state of Illinois

IGB Strategic Partnerships & Research Themes

IGB's research is organized into research themes, each of which comprises multiple laboratory groups brought together by shared scientific approaches and goals. Our research themes are connected through their overlap within three broad areas of fundamental and applied research: health challenges and solutions, genomic technologies, and environmental resources and conservation. Our scientists participate in a variety of strategic partnerships with academic, governmental and industry partners.



Strategic Partnerships

Energy Biosciences Institute
BP, Shell, UC Berkeley, Lawrence Berkeley National Laboratory

Center for Advanced Bioenergy and Bioproducts Innovation
Boston University, Brookhaven National Laboratory, Colorado State University, HudsonAlpha Institute for Biotechnology, Institute for Systems Biology, Iowa State University, Lawrence Berkeley National Laboratory, Mississippi State University, Princeton University, USDA-Agricultural Research Service, UC Berkeley, University of Florida, University of Idaho, University of Nebraska–Lincoln, University of Wisconsin-Madison, West Virginia University

Center for Nutrition, Learning, and Memory
Abbott Nutrition, Beckman Institute

Omics Nanotechnology for Cancer Precision Medicine
Macro and Nanotechnology Laboratory

ZEISS Labs@Location Partnership
ZEISS Microscopy

CompGen Initiative
Coordinated Science Laboratory, Abbott Molecular, Dow Agro Sciences, Eli Lily and Co., IBM Systems, Strand Life Sciences, Intel Corporation, Xilinix Inc., OSF Healthcare

High Performance Biological Computing
Carver Biotechnology Center

Research Themes

Anticancer Discovery from Pets to People (ACPP)
Develops cancer treatments in pet animals that translate to human disease

Biocomplexity (BCXT)
Explores the origin of life and the behavior of biological systems

Biosystems Design (BSD)
Applies engineering principles to real and artificial biological systems

Computing Genomes for Reproductive Health (CGRH)
Examines the interplay among genetic and environmental factors that influence disorders of reproduction

Genomic Ecology of Global Change (GEGC)
Studies the intersection of plant genomics and global climate change

Gene Networks in Neural and Developmental Plasticity (GNDP)
Examines the effects of coordinated gene activity on biological diversity

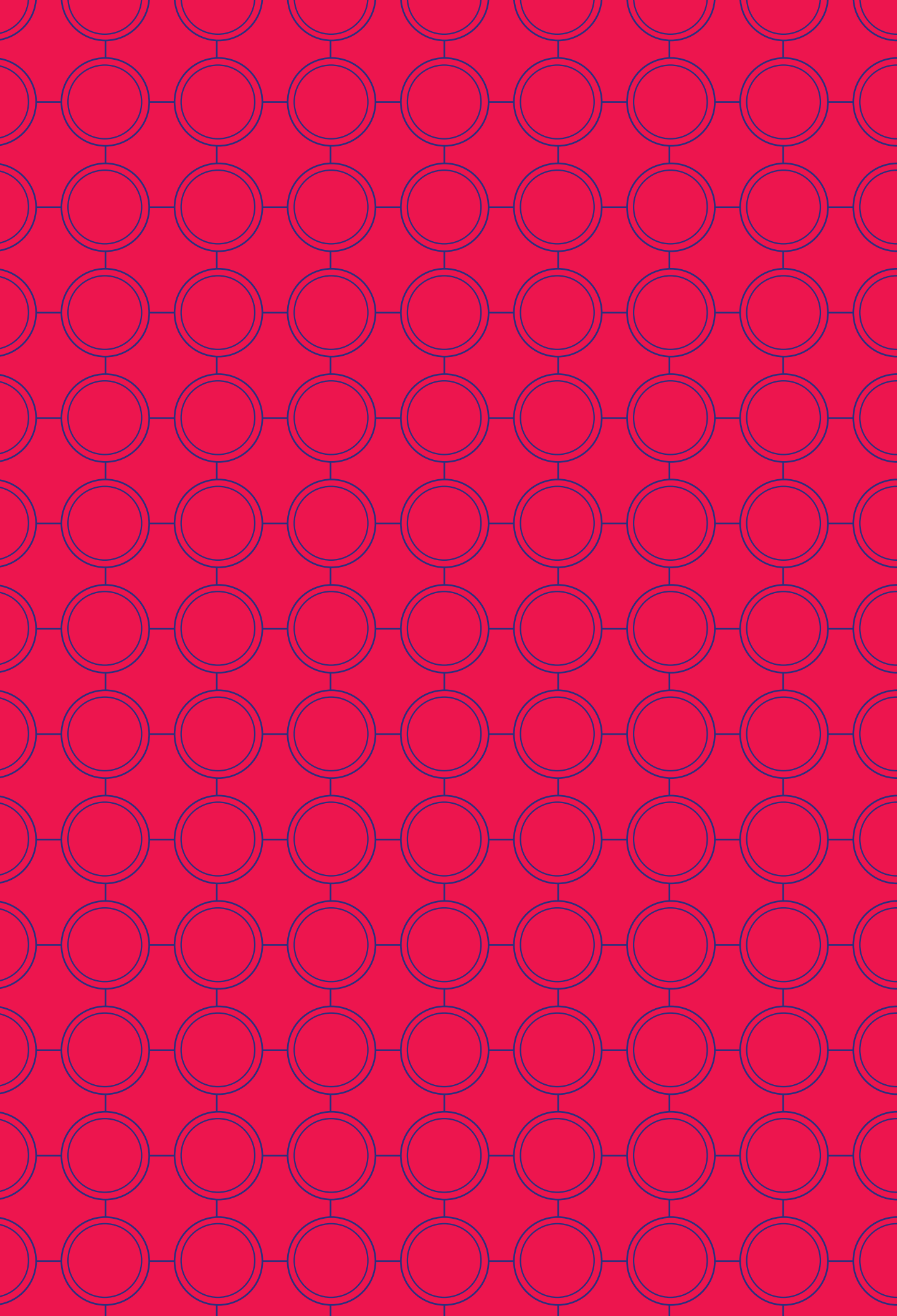
Infection Genomics for One Health (IGOH)
Examines how microbes in human-inhabited environments influence health and disease

Microbiome Metabolic Engineering (MME)
Explores the relationships between human microbiota, environment, and health

Mining Microbial Genomes (MMG)
Discovers small molecules that might provide new medical solutions

Omics Nanotechnology for Cancer Precision Medicine (ONC-PM)
Develops new technology to identify and manage cancerous tumors

Regenerative Biology and Tissue Engineering (RBTE)
Studies the replacement or regeneration of tissues and organs



STORIES FROM 2018

LOOK OUT FOR

SCIENCE SPOTLIGHT

Agricultural fungicide attracts honey bees

go.igb.illinois.edu/fungicide

When given the choice, honey bee foragers prefer to collect sugar syrup laced with the fungicide chlorothalonil over sugar syrup alone, researchers reported in *Scientific Reports*.

The puzzling finding comes on the heels of other studies linking fungicides to declines in honey bee and wild bee populations.

Swanlund Professor of Entomology May Berenbaum (GEGC/IGOH) led the study with postdoctoral researcher Ling-Hsiu Liao. They set up two feeding stations in an enclosure and allowed foraging honey bees to fly freely from one feeder to another, choosing to collect either sugar syrup laced with a test chemical or sugar syrup mixed with a solvent as a control. They tested responses to naturally occurring chemicals, fungicides and herbicides.

Above_Swanlund Professor of Entomology May Berenbaum, left, and postdoctoral researcher Ling-Hsiu Liao found that honey bees have a slight preference for food laced with the fungicide chlorothalonil at certain concentrations.

They found that honey bees prefer the naturally occurring chemical quercetin over controls at all concentrations tested. The bees also preferred sugar syrup laced with glyphosate—the active ingredient in Monsanto's Roundup herbicide—in certain amounts, along with the fungicide chlorothalonil.

The bees' preferences for some potentially toxic chemicals may be the result of their distinct evolutionary history, Berenbaum said. These findings are

Left_Fungicides are among the top contaminants of honey bee hives and can interfere with the bees' ability to metabolize other pesticides.

worrisome in light of research showing that exposure to fungicides affects honey bees' ability to metabolize acaricides, which are used by beekeepers to kill the parasitic varroa mites that can infest their hives.

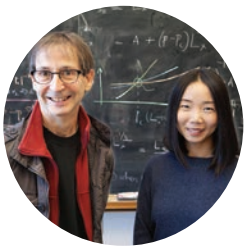
The USDA, the Interdisciplinary Environmental Toxicology Program at the University of Illinois, and the Almond Board of California supported this study.

Virus-bacteria coevolution solves diversity paradox

go.igb.illinois.edu/winner

When many species are competing for the same finite resource, a theory called competitive exclusion suggests one species will outperform the others and drive them to extinction, limiting biodiversity. But this isn't what we observe in nature. Theoretical models of population dynamics have not presented a fully satisfactory explanation for what has come to be known as the diversity paradox.

Researchers have shed new light on this fundamental question in ecology by improving a popular proposed explanation for diversity known as "Kill the Winner."



Swanlund Professor of Physics Nigel Goldenfeld (left) works with colleague Chi Xue (right).

Chi Xue and Swanlund Professor of Physics Nigel Goldenfeld (BCXT leader/CGRH/GNDP) approached the diversity paradox from the perspective of non-equilibrium statistical mechanics. Their findings were published in *Physical Review Letters*.

The researchers created a stochastic model that incorporates multiple factors observed in ecosystems, including competition among species and simultaneous predation on the competing species. Using bacteria and their host-specific viruses as an example, the researchers showed that as the bacteria evolve defenses against the virus, the virus population also evolves to combat the bacteria. This "arms race" leads to a diverse population of both, and to boom-bust cycles when a particular species dominates the ecosystem and then collapses—the so-called "Kill the Winner" phenomenon. This coevolutionary arms race is sufficient to provide a possible solution to the diversity paradox.

This research was supported by the IUB.

Automated system finds rapid honey bee networks

go.igb.illinois.edu/beenetwork

By developing a system that automatically monitors the social interactions of honey bees, researchers uncovered an unexpected property of the bee social network that may someday help us design more effective human and machine communication systems.

The research team published their findings in the *Proceedings of the National Academy of Sciences*.

Automated system finds rapid honey bee networks continued

Tim Gernat, a graduate student in the laboratories of IGB Director and Swanlund Professor of Entomology Gene Robinson (GNDP) and Leipzig University Professor Martin Middendorf, wanted to create an automated system that could spot trophallaxis, a behavior in which one bee requests food and her nestmate offers up a drop of regurgitated sugary liquid. This exchange may transmit chemical signals that the bee offering the food has produced or received from others.

Right_By tagging bees with custom barcodes, researchers were able to automatically track all members of a small honey bee colony.

The researchers created a system that photographed honey bees with custom-designed barcode tags glued to their backs. Taking one picture every second, the system created a near-complete record of the bees' interactions for more than a week.

The team created software that could flag likely exchanges of food between bees. They found that the honey bee social network shared a feature of human networks: sporadic bunches and gaps of interactions described as "bursty." But unlike bursty human networks, information in the bee networks spread rapidly.

Robinson said this work could help us understand the underlying principles of honey bee networks and how they could apply to human social networks.

The NSF, the Christopher Family Foundation, the National Academies Keck Futures Initiative, and the NIH supported this work.

Using an economic concept to understand microbial communities

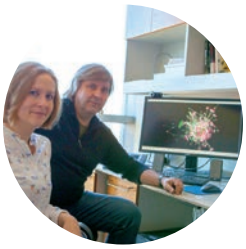
go.igb.illinois.edu/marriage

Researchers like Bliss Faculty Scholar and Professor of Bioengineering Sergei Maslov (BCXT) want to better understand microbial communities so they can learn how to manipulate them.

Microbial communities are complex, but are typically stable. To better understand how these stable states are formed and to predict what would make them unstable, Maslov collaborated with graduate student Veronika Dubinkina and Akshit Goyal, a visiting scholar from the Simons Centre for the Study of Living Machines.

Their research, published in *The ISME Journal*, describes their conceptual model that uses an economic concept called the stable marriage problem, which explains how stable states are formed in real life situations.

Solving the stable marriage problem involves a conceptual "game." Imagine an equal number of men and women that are seeking to be married. Each man



Above_PhD student Veronika Dubinkina, left, with Bliss Faculty Scholar and Professor of Bioengineering Sergei Maslov, applied the theoretical concept of the "stable marriage problem" to microbial communities.

proposes to a woman he wants to marry, and the woman can accept or reject. Eventually, every person will be married and every marriage will be stable—no person will prefer someone else over their current spouse.

The researchers said a similar process happens in microbial communities. Microbes actively look for the best nutrients they can find. Competition between microbes may prevent them from getting the best nutrients possible, but eventually, the microbes settle into a stable state.

This work helps us understand the competition for nutrients taking place in microbial communities, which could one day help scientists manipulate microbial communities to our advantage.

DOE grants $10.6 million to produce more biofuel

go.igb.illinois.edu/biojet

The DOE awarded the University of Illinois a $10.6 million, five-year grant to transform two of the most productive crops in America into sustainable sources of biodiesel and biojet fuel.

The new research project, Renewable Oil Generated with Ultra-productive Energycane (ROGUE), will engineer Miscanthus and energycane, a bioenergy crop derived from sugarcane, to produce the oil that is used to create biodiesel and biojet fuel.

Their work is guided by computer models that project that these crops can achieve 20 percent oil content in the plant—a dramatic increase from natural levels of less than a tenth of one percent.

Right_University of Illinois research project Renewable Oil Generated with Ultra-productive Energycane (ROGUE) will transform energycane and Miscanthus (pictured) into sustainable sources of biodiesel and biojet fuel with support from the DOE.

"If fully successful, these crops could produce as much as 15 times more biodiesel per unit of land compared to soybeans, a food crop that currently produces half of our nation's biodiesel," said ROGUE Director Stephen Long, Ikenberry Endowed Chair of Plant Biology and Crop Sciences (BSD/CABBI/GEGC).

ROGUE aims to improve the crops' ability to turn the sun's energy into plant energy to fuel their biological oil production. Improving these crops'

DOE grants $10.6 million to produce more biofuel continued

photosynthetic efficiency will ensure that the production of energy-dense oil will not lower yields or suppress plant defenses. This will also help the plant conserve limited resources such as water and nitrogen, particularly under stress.

The project will translate its discoveries into energycane and Miscanthus using synthetic biology. ROGUE will also develop energycane to be more cold-tolerant to expand its growing region and extend its growing season, and ensure the efficacy of crop technologies through techno-economic analyses and replicated field trials.

Engineering crops to conserve water, resist drought

go.igb.illinois.edu/psbs

Above_Realizing Increased Photosynthetic Efficiency (RIPE) researchers work together to plant crops for field testing.

Agriculture already monopolizes 90 percent of global freshwater, yet production still needs to dramatically increase to feed and fuel this century's growing population. For the first time, scientists have improved how a crop uses water by 25 percent without compromising yield by altering the expression of one gene that is found in all plants, as reported in *Nature Communications*.

The study is a part of Realizing Increased Photosynthetic Efficiency (RIPE), an international research project supported by the Bill & Melinda Gates Foundation, the Foundation for Food and Agriculture Research, and the U.K. Department for International Development.

"This is a major breakthrough," said RIPE Director Stephen Long, Ikenberry Endowed Chair of Plant Biology and Crop Sciences (BSD/CABBI/GEGC). "Crop yields have steadily improved over the past 60 years, but the amount of water required to produce one ton of grain remains unchanged—which led most to assume that this factor could not change. **Proving that our theory works in practice should open the door to much more research and development to achieve this all-important goal for the future."**

The team increased the levels of a photosynthetic protein to conserve water by tricking plants into partially closing their stomata, the microscopic pores in the leaf that allow water to escape. This improved the plant's water-use-efficiency, the ratio of carbon dioxide entering the plant to water escaping, by 25 percent without significantly reducing photosynthesis or yield in real-world field trials.

Million-plus new compounds hold pharmaceutical potential

go.igb.illinois.edu/millionplus

Researchers say they can now produce a vast library of unique cyclic compounds, some with the capacity to interrupt specific protein-protein interactions that play a role in disease. The new compounds have cyclic structures that give them stability and enhance their ability to bind to their targets.

The study, reported in *Nature Chemical Biology*, also revealed that one of the newly generated compounds interferes with the binding of an HIV protein to a human protein, an interaction vital to the virus's life cycle.

Above_HHMI Professor of Chemistry Wilfred van der Donk and his colleagues developed a new method for generating large libraries of unique cyclic compounds.

Using an enzyme they discovered from a bacterium that lives in the ocean, HHMI Professor of Chemistry Wilfred van der Donk (MMG) and his colleagues were able to generate a library of more than a million unique multicyclic proteins.

The researchers screened this library for proteins that could interrupt the binding of the HIV protein to its human host cell target. They found three potential therapeutic agents, one of which worked best. In a test tube and in cells, the compound bound to the human protein, stopping the HIV protein from interacting with it.

This agent likely will not be used therapeutically, but the researchers said the real advance is "the ability to generate libraries of millions of potentially therapeutic agents."

The NIH, the HHMI, and the United Kingdom Engineering and Physical Sciences Research Council supported this research.

Improving prostate cancer outcomes

go.igb.illinois.edu/prostate

Researchers received a $1.8 million grant from the NIH to develop a new assay technology that could determine the effectiveness of cancer drug treatments and aid in disease prognosis. Led by Associate Professor of Bioengineering Andrew Smith (ONC-PM), the team is focusing on detecting nucleic acid-based biomarkers in a single drop of a cancer patient's blood.

Above_Bioengineering Associate Professor Andrew Smith and fellow researchers are bringing their expertise in light-emitting quantum dots to the development of a new assay technology that could enhance prostate cancer outcomes, thanks to a new $1.8 million NIH grant.

Detecting most types of cancer involves invasive biopsies or imaging tests, Smith said. These conventional methods are unable to distinguish between slow-growing tumors and more aggressive forms of the disease. As a result, some patients opt for radical treatments that may be unnecessary and could compromise their quality of life.

Smith and his team, which includes researchers from the Medical College of Wisconsin and Mayo Clinic, are taking an entirely different approach. By frequently measuring the concentrations of microRNA biomarkers in a patient's blood during their cancer treatments, they believe they can determine precise therapeutic regimens for each patient.

Improving prostate cancer outcomes continued

The technology they are developing will be the first to read out nucleic acids in a single drop of blood. The team will test its assay in a trial involving 100 patients with metastatic prostate cancer at Mayo Clinic. Patients will use the developed tool to draw a single drop of their own blood at home. The researchers will then use these samples to predict how individual patients will respond to prescribed cancer treatments.

A digital library of life

go.igb.illinois.edu/EBP

An international consortium of scientists announced the Earth BioGenome Project, a massive initiative to sequence, catalog and analyze the genomes of all known eukaryotic species on the planet. It's an undertaking that could take 10 years, cost $4.7 billion and require more than 200 petabytes of digital storage capacity.

Eukaryotes include all multicellular organisms and the small percentage of single-celled organisms that are not bacteria or archaea. There are an estimated 10-15 million eukaryotic species on Earth. Of those, the team proposes sequencing 1.5 million known species.

Above_Swanlund Professor of Entomology and IGB Director Gene Robinson and his colleagues are calling for an international effort to sequence the genomes of all eukaryotic species.

The proposed initiative, described in the *Proceedings of the National Academy of Sciences*, would require the cooperation of governments, scientists, citizen scientists and students from around the globe. The authors compare it to the Human Genome Project, an international scientific research project that cost roughly $4.8 billion in today's dollars.

"Genomics has helped scientists develop new medicines and new sources of renewable energy, feed a growing population, protect the environment and support human survival and well-being," said IGB Director and Swanlund Professor of Entomology Gene Robinson (GNDP), a leader of the project. "The Earth BioGenome Project will give us insight into the history and diversity of life and help us better understand how to conserve it."

The project will take advantage of the low cost of genome sequencing and other new technologies to speed the process of data collection and analysis.

"The greatest legacy of the Earth BioGenome Project will be a complete digital library of life that will guide future discoveries for generations," Robinson said.

Protect forest elephants to conserve ecosystems, not DNA

go.igb.illinois.edu/elephants

Right_Forest elephant nuclear DNA is genetically diverse, and this diversity is consistent across populations throughout Central Africa, which should be conserved to protect their habitats rather than their DNA.

Although it is erroneously treated as a subspecies, the dwindling African forest elephant is a genetically distinct species. Research published in *Ecology and Evolution* found that forest elephant populations across Central Africa are genetically quite similar to one another.

Conserving this critically endangered species across its range is crucial to preserving local plant diversity in Central and West African Afrotropical forests, meaning conservationists could save many species by protecting one.

"Forest elephants are the heart of these ecosystems," said Professor of Animal Sciences Alfred Roca (CGRH/GNDP), the study's principal investigator. "Without them, the system falls apart, and many other species are jeopardized."

The study found that the forest elephant's nuclear DNA is genetically diverse, yet this diversity is consistent across populations throughout Central Africa—any differences are too small to warrant treating them as distinct subspecies.

This nuclear DNA lacks the geographic patterns preserved in forest elephants' mitochondrial DNA, the small proportion of the genome that is passed down only from mothers to their offspring. The mitochondrial DNA suggests that five genetically distinct populations existed in the past, most likely due to the Ice Age when their habitat was greatly restricted.

"However, all of this precious DNA may soon be eradicated as forest elephants face extinction due to poaching and habitat loss," Roca said. "We must act swiftly to preserve them, and by extension, their habitats."

This work was supported by a U.S. Fish and Wildlife Service African Elephant Conservation Fund Grant.

SCIENCE SPOTLIGHT

CRISPR IS A TECHNOLOGY THAT ALLOWS SCIENTISTS TO MAKE VERY PRECISE CHANGES TO THE SEQUENCE OF DNA. CROP SCIENTISTS HAVE RECOGNIZED

WHAT CRISPR CAN DO

FOR GENOMIC ENGINEERING: BY MAKING SPECIFIC EDITS TO A PLANT'S DNA, THEY CAN PRODUCE A MORE RESILIENT AND PRODUCTIVE CROP.

DIGGING DEEPER INTO CRISPR

CRISPR systems were discovered in and borrowed from bacteria. CRISPR molecules cut DNA strands at specific locations. When the DNA is repaired, custom-made sequences can be inserted at the cut site, allowing researchers to cut and paste genomic content as if it were digital text.

WHAT CRISPR CAN DO

Stable food and biofuel crops that are being

engineered to produce higher yields and withstand the conditions of a changing climate

will help us achieve food and energy security for future generations.

Walnuts impact gut microbiome and improve health

go.igb.illinois.edu/walnuts

Diets rich in nuts such as walnuts have been shown to play a role in heart health and in reducing colorectal cancer. According to a study published in *The Journal of Nutrition*, the way walnuts impact the gut microbiome—the collection of trillions of microbes or bacteria in the gastrointestinal tract—may be behind some of those health benefits.

Walnuts are just one in a group of foods containing dietary fiber that have interested scientists for their impact on the microbiome and health. Dietary fiber is a food source for gut microbiota and helps the microbes do their jobs: breaking down complex foods, providing us with nutrients, and helping us feel full. Eating a variety of foods rich in dietary fiber helps promote a diverse gut microbiota, which in turn helps to support health.

The study found that consuming walnuts not only impacted the gut microbiota and microbial derived secondary bile acids, but also reduced LDL-cholesterol levels in the adults participating in the study—good news for cardio, metabolic, and gastrointestinal health.

Above_Assistant Professor of Food Science and Human Nutrition Hannah Holscher.

"We found that when you consume walnuts, it increases microbes that produce butyrate, a beneficial metabolite for colonic health. So the interaction of walnuts with the microbiome is helping to produce some of those health effects," said Assistant Professor of Food Science and Human Nutrition Hannah Holscher (MME), the lead author of the study.

This study was funded by USDA-ARS and California Walnut Commission.

Scholars urge engagement with Indigenous communities

go.igb.illinois.edu/indigenous

Right_The Summer internship for INdigenous peoples in Genomics allows students, professors and scholars of Indigenous ancestry to obtain skills to aid their exploration of their own ancestry and history.

An article in *Science* provides guidance for those intending to study ancient human remains in the Americas. The paper, written by Indigenous scholars and scientists and those who collaborate with Indigenous communities on ancient DNA studies, offers a clear directive to others contemplating such research: First, do no harm.

Scientists studying ancestral remains have similar obligations to those that bind researchers working with living human subjects. The descendants or other people affiliated with those who lived hundreds or thousands of years ago deserve to be consulted before their ancestors are disturbed. Even in cases where the remains were collected long ago and moved far from their original burial place, and even when the surviving lineages are in doubt, scientists ought to consult Indigenous groups living on the land or claiming ancestral ties to the region where the ancestors were found, the authors said.

Above_Anthropology professor Ripan Malhi works with Indigenous communities, scientists and scholars to analyze their DNA and that of their ancestors.

Professor of Anthropology Ripan Malhi (CGRH/RBTE), a co-author of the report, said there are "inconsistent or no regulations for working with ancient ancestors," and the same goes for working with descendant or affiliated communities.

Malhi partners with Indigenous communities to study ancient DNA from individuals found on lands where their descendants still live. Malhi, along with Indigenous scientists, scholars and other scientists who work with Native American and First Nations communities, worked to create the Summer internship for INdigenous peoples in Genomics (SING), which trains Indigenous scientists in genomics techniques and explores ethical concerns.

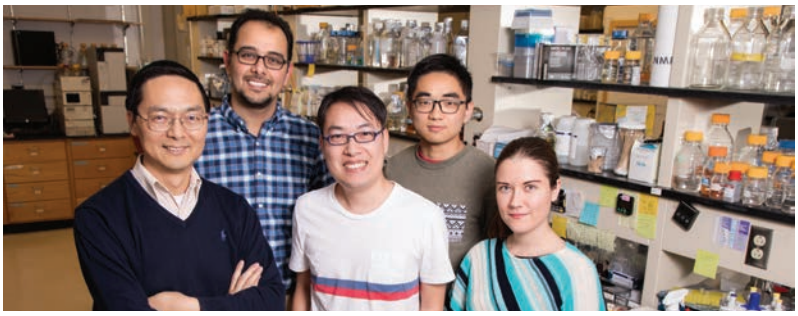
The NIH and the NSF support this work.

Knocking out yeast genes with single-point precision

go.igb.illinois.edu/knockoutyeast

The CRISPR-Cas9 system has given researchers the power to precisely edit selected genes. Now, researchers have used it to develop a technology that can target any gene in the yeast *Saccharomyces cerevisiae* and turn it off by deleting single letters from its DNA sequence, as reported in *Nature Biotechnology.*

Knocking out yeast genes with single-point precision continued



Right_Researchers created a system using CRISPR technology to selectively turn off any gene in *Saccharomyces* yeast. Pictured, from left: Steven L. Miller Chair Professor of Chemical and Biomolecular Engineering Huimin Zhao, graduate students Mohammad Hamedi Rad, Zehua Bao, Pu Xue and Ipek Tasan.

Such genome-scale engineering—in contrast to traditional strategies that only target a single gene or a limited number of genes—allows researchers to study the role of each gene individually, as well as in combination with other genes. It also could be useful for industry, where *S. cerevisiae* is widely used to produce ethanol, industrial chemicals, lubricants, pharmaceuticals and more.

Understanding and optimizing the genome could create yeast strains with increased productivity, said study leader and Steven L. Miller Chair Professor of Chemical and Biomolecular Engineering Huimin Zhao (BSD leader/CABBI/MMG).

Researchers produce "knockout" yeast in which one gene has been deleted, or "knocked out," to study each gene's contribution to the function of the cell. When a beneficial mutation is found, they can selectively breed yeast with that characteristic. Leading methods to produce knockout yeast excise the entirety of the targeted gene, creating unintended problems and making it difficult to isolate the effects of a single gene.

Zhao's group harnessed the CRISPR-Cas9 system's precision to create a quick, precise, and low-cost way to delete just one base in a gene's DNA sequence.

The IGB and the DOE supported this work.

Two Ancient populations diverged in the Americas later 'reconverged'

go.igb.illinois.edu/reconverge

A genetic study of ancient individuals in the Americas and their descendants found that two populations that diverged 18,000 to 15,000 years ago remained apart for millennia before mixing again. This historic "reconvergence" occurred before or during their expansion to the southern continent.

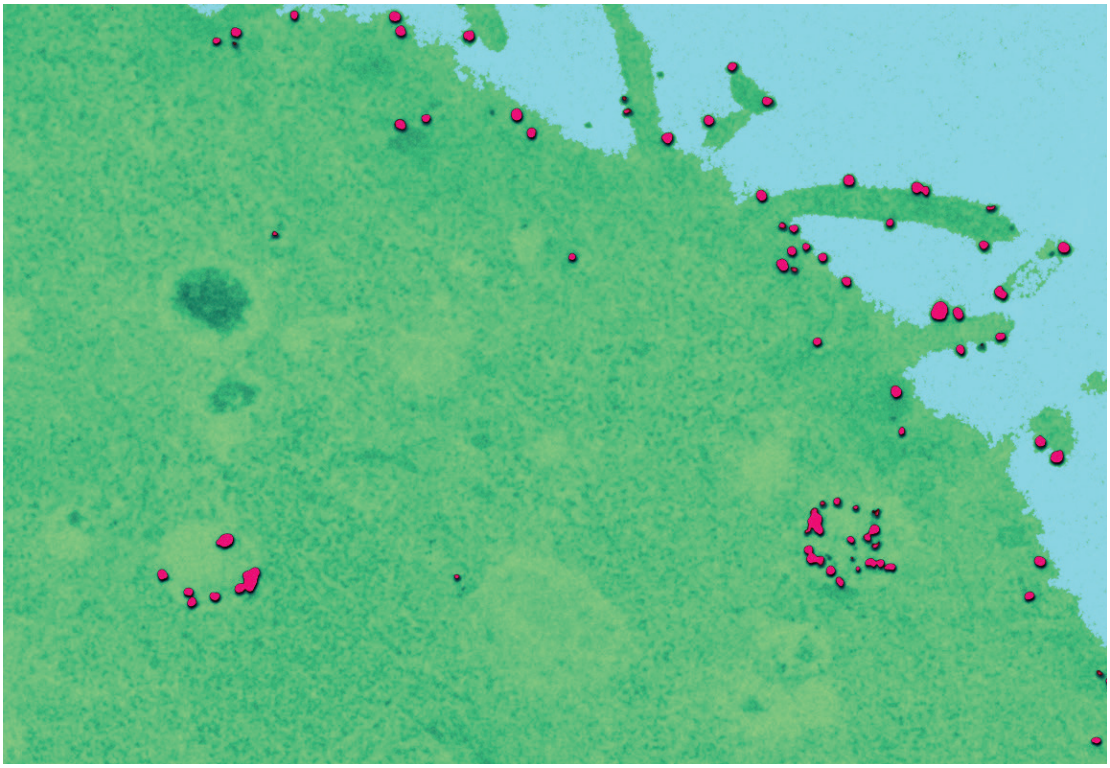
The study, reported in *Science*, challenges previous research suggesting that the first people in the Americas split into northern and southern branches and that the southern branch alone gave rise to all ancient populations in Central and South America.

This research shows many Indigenous people in the southern continent retain at least some DNA from the "northerners" who are the direct ancestors of many Native communities living today in the Canadian east.

The analysis, co-led by Professor of Anthropology Ripan Malhi (CGRH/RBTE) and Cambridge University professor Toomas Kivisild, adds to the evidence that two populations diverged 18,000 to 15,000 years ago. This would have been during or after their migration from Siberia along what is now coastal Alaska.

Ancient genomes from southwest Ontario show Indigenous ancestors representing the northern branch migrated to the Great Lakes region. Populations representing the southern branch likely continued down the Pacific coast, inhabiting islands along the way.

Technique tracks drug and gene therapy delivery to cells



go.igb.illinois.edu/agents

Above_A new technique allows researchers to count, map and track delivery agents, shown in red, as they enter and move through a cell.

With targeted drug and gene therapies, finding the target cells is only half the battle. Once these agents reach a cell's surface, they still have to get inside and do their job.

Researchers reported in *Nature Communications* that they have developed a method to track and map drug and gene delivery vehicles to evaluate which are most effective at infiltrating cells and getting to their targets, insight that could guide development of new pharmaceutical agents.

Led by Associate Professor of Bioengineering Andrew Smith (ONC-PM), the researchers combined two imaging tools to track and measure how different delivery agents entered human and mouse cancer cells. Using single-molecule imaging, they were able to see, count and track all of the delivery agents that entered the cell.

They found that molecules that are lightly charged are capable of getting inside cells but fail to reach their intended targets once inside. However,

Technique tracks drug and gene therapy delivery to cells
continued

molecules that are completely balanced in charge diffuse throughout the cell and can gain access to all of its machinery. These findings provide ideas for better methods of delivery, Smith said.

The study used "empty" delivery agents—those without therapeutic cargo attached—so the next step is to track the agents actually delivering therapies and observe the mechanisms along each step of the drug delivery pathway.

The NIH supported this work.

Boosting crop production by speeding up photorespiration

go.igb.illinois.edu/photorespiration

Right, top_ Patricia Lopez-Calcagno (left) and Kenny Brown (right) evaluate a field trial that helped prove that increasing a protein in the leaves of crops can increase production by nearly 50 percent.

Right, bottom_ Aerial view of the 2017 field trial that showed fine-tuning the increased expression of a protein can boost production by nearly 50 percent.

Soybeans and wheat waste between 20 and 50 percent of their energy recycling toxic chemicals created when the enzyme Rubisco grabs oxygen molecules instead of carbon dioxide molecules. Increasing production of a common, naturally occurring protein in plant leaves could boost the yields of major food crops by almost 50 percent, according to a study in *Plant Biotechnology Journal* and co-authored by USDA-ARS postdoctoral researcher Paul South (GEGC).

This work is part of Realizing Increased Photosynthetic Efficiency (RIPE), an international research project supported by Bill & Melinda Gates Foundation, the Foundation for Food and Agriculture Research, and U.K. Department for International Development.

In this study, the team engineered a model crop to overexpress H-protein, which is involved in the recycling process called photorespiration. Increasing the H-protein in the plants' leaves increased production by 27 to 47 percent. However, increasing this protein throughout the plant stunts growth and

metabolism, resulting in four-week-old plants that are half the size of their unaltered counterparts. This is the first time that the H-protein has been evaluated in a crop in real-world growing conditions.

The team plans to increase the levels of this naturally occurring protein in soybeans, cowpeas (black-eyed peas), and cassava, a tropical root crop that is a staple for more than a billion people around the world. **Their goal is to increase the yields and opportunities for farmers worldwide, particularly smallholder farmers in sub-Saharan Africa and Southeast Asia.**

Neighborhood, breast cancer rates in African American women linked

go.igb.illinois.edu/neighborhood

Neighborhood characteristics such as racial composition and poverty rates are associated with increased risks of late-stage breast cancer diagnoses and higher mortality rates among urban black women, according to an analysis published in *Hormones and Cancer.*

Even African American women living in low-income neighborhoods that are undergoing gentrification and economic improvement may be at significantly greater risk of having distant metastases at the time they are diagnosed with breast cancer, said lead author Brandi Patrice Smith, a graduate student in food science and human nutrition.

Right_ Racial disparities in breast cancer diagnosis and survival rates may have more to do with women's living environments than their racial backgrounds, suggests a new meta-analysis of recent research on the topic by, from left, graduate student Brandi Patrice Smith and Assistant Professor Zeynep Madak-Erdogan, both in the department of food science and human nutrition.

Smith and co-author Assistant Professor of Food Science and Human Nutrition Zeynep Madak-Erdogan (ONC-PM) conducted a systematic review of recent breast cancer research to explore possible associations between characteristics of urban neighborhoods and breast cancer rates among African American women.

Residential segregation significantly increased African American women's rates of late-stage diagnosis and doubled their chances of dying from breast cancer, the analysis showed. Comparable mortality rates were found among white women who also lived in predominantly African American neighborhoods.

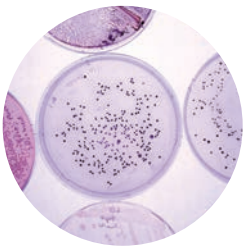
"This suggests that the environmental conditions associated with low-income neighborhoods—rather than race itself—increase women's risks of dying from breast cancer," Smith said.

The way microbes eat could explain their diverse yet stable communities

go.igb.illinois.edu/stable

A mathematical model of interactions among single-celled organisms could help scientists better understand an intriguing characteristic of microbial communities: their ability to achieve stability despite being so diverse.

Although microbial communities are complex, they are able to form stable ecosystems: communities that can resist a change in the nutrient supply or an invasion of a new species. Sergei Maslov (BCXT/CABBI), a Bliss Faculty Scholar and professor of bioengineering, and Akshit Goyal, a visiting scholar from the Simons Centre for the Study of Living Machines at NCBS in Bengaluru, India, created a mathematical model to further understand how microbial communities function and maintain stability.



Above_Researchers are interested in harnessing the metabolic capabilities of microbial communities.

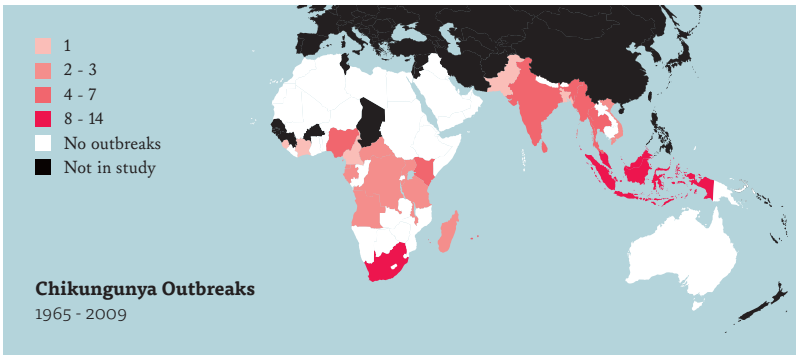
Their work, published in *Physical Review Letters*, addresses three signature aspects of microbial communities: diversity, stability, and reproducibility, which is how often a particular species is present in a community. The work was supported by the Simons Foundation and the Infosys Foundation.

The goal of their model was to understand which species are universally shared in microbial communities and which species are unique. A key ingredient in their model was a process known as cross-feeding. Microbes consume nutrients and then excrete metabolic byproducts, which return to the shared space of the microbial community and are consumed by other microbes. The group focused in on these levels of consumption and the ecosystem's maturity, which are both crucial in microbial communities' ability to function.

Certain risk factors linked to chikungunya, dengue outbreaks

go.igb.illinois.edu/outbreaks

Above_A team including, from left, pathobiologist Rebecca Lee Smith, GIS lab manager William Marshall Brown and pathobiologist Marilyn O'Hara Ruiz identified the factors most closely associated with a country's risk of experiencing a chikungunya outbreak. *Ruiz passed away in September 2018.*



In one of the largest studies of its kind, researchers analyzed chikungunya and dengue outbreak data from 76 countries over a period of 50 years, focusing on regions across the Indian Ocean that are hard hit by these and other mosquito-borne infectious diseases.

The study, led by pathobiologists Rebecca Lee Smith (IGOH) and Marilyn O'Hara Ruiz, revealed that population density and proximity to a country already experiencing an outbreak were the factors most closely associated with a country's own likelihood of experiencing an outbreak.

Chikungunya and dengue are mosquito-borne viral diseases with overlapping distribution globally. Dengue can be a more serious infection, with a mortality rate of about 20 percent for severe infections that go untreated. According to the World Health Organization, dengue infections are on the rise globally. Both diseases are more likely to occur in tropical or subtropical regions.

In contrast to the strong effects of proximity and population density, the new study found no significant association between local temperature or precipitation and outbreak risk, a somewhat unexpected finding since heat, rain and fluctuations in mosquito populations are often linked, the researchers said. The study was reported in the journal *Spatial and Spatio-temporal Epidemiology*.

We note with regret that Dr. O'Hara Ruiz passed away in September 2018.

Researchers first to sequence rare bacteria cause of rampant tooth decay

go.igb.illinois.edu/toothgenome

The most prevalent chronic disease in both children and adults, tooth decay, occurs when populations of beneficial and harmful bacteria in our mouth become imbalanced. These harmful bacteria are exemplified by *Streptococcus mutans*, which contributes to biofilm (aka tartar) formation and produces acid that decalcifies teeth and causes cavities.

A team of bioengineers led by Assistant Professor of Bioengineering Paul Jensen (MMG) has now successfully sequenced the complete genomes of three strains of *Streptococcus sobrinus*, a related harmful bacterium about which less is known. *S. sobrinus* is difficult to work with in the lab and it is not present in all people, so researchers have instead focused their efforts over the years on understanding the more stable and prevalent *S. mutans*, which was sequenced in 2002.

"Although it is rare, *S. sobrinus* produces acid more quickly and is associated with the poorest clinical outcomes, especially among children," said Jensen. "If *S. sobrinus* is present along with *S. mutans*, you're at risk for rampant tooth decay, which means there's some level of communication or synergy between the two that we don't understand yet."

Now that the *S. sobrinus* sequencing is complete, Jensen and his students are building computational models to better understand how the two bacteria interact and why *S. sobrinus* can cause such potent tooth decay when combined with *S. mutans*. Their work was published in the journal *Microbial Resource Announcements* and funded by the NIH and the University of Illinois.

SCIENCE SPOTLIGHT

MICROBES LIVE IN ALMOST EVERY ENVIRONMENT FOUND ON THE FACE OF THE EARTH, INCLUDING THE SURFACES AND TISSUES OF THE HUMAN BODY. COMMUNITIES OF MICROBES, CALLED MICROBIOTA, ENCOMPASS A NETWORK OF COMPETITIVE AND COOPERATIVE RELATIONSHIPS. IT IS

THE COLLECTIVE POWER OF MICROBES

THAT SCIENTISTS HOPE TO HARNESS AND ENHANCE TO PROMOTE HEALTH, PRODUCE USEFUL MOLECULES, AND PROTECT THE ENVIRONMENT.

ZOOMING IN ON MICROBES

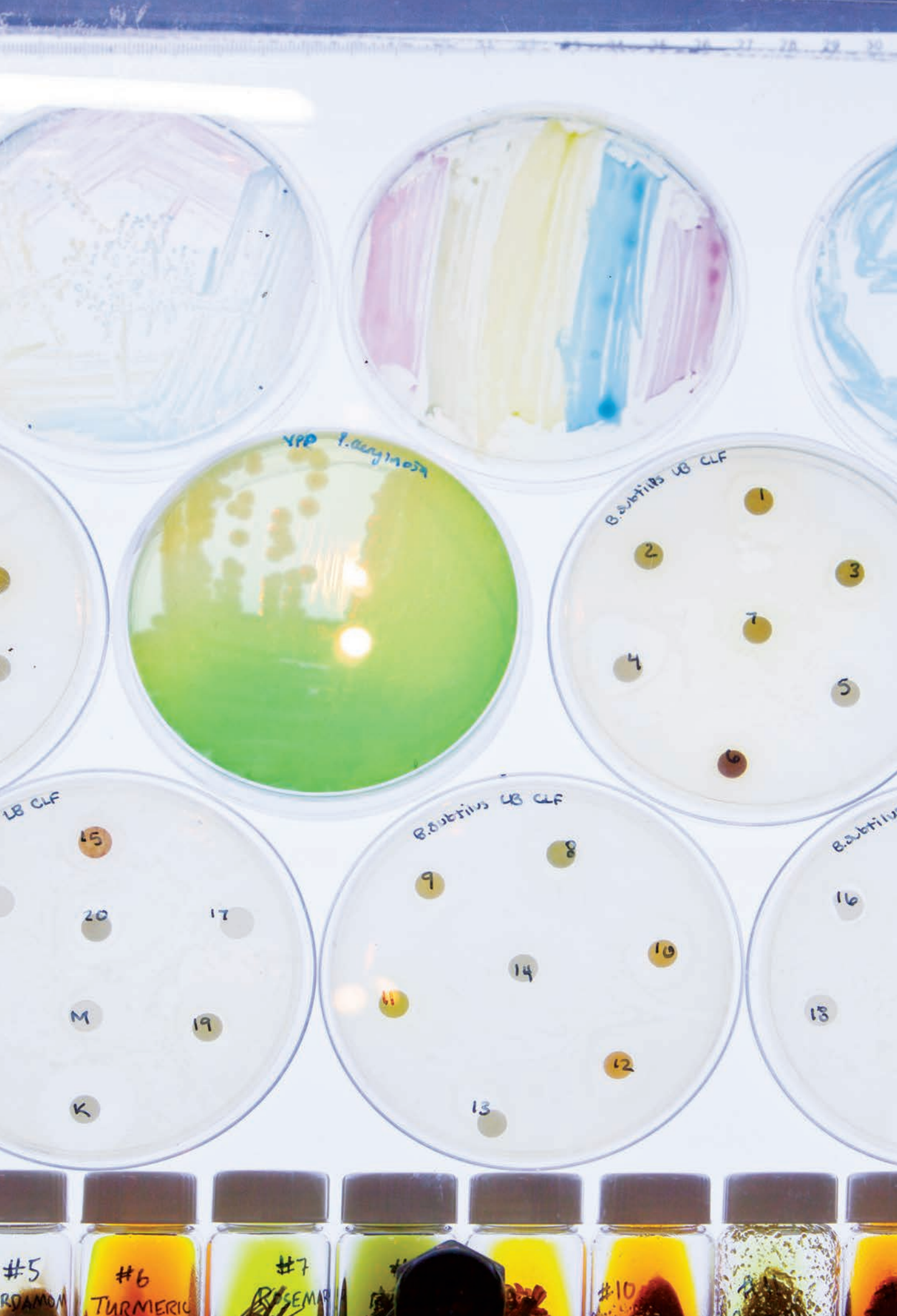
Microbial communities are made up of hundreds of cooperating and competing species. Researchers census these communities in Petri dishes in the lab and in the environment by extracting and reading their genomic DNA; collectively, all these genomes are referred to as a microbiome.


2
4

THE COLLECTIVE POWER OF MICROBES

For decades,
individual strains of engineered microbes
have produced vitamins, medications,
and a host of other products.

Engineered communities of microbes hold the promise to achieve the next level of bioproduction and to support the health of human and other animal hosts.


YPD P.aeruginosa
B.subtilis LB CLF
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LB CLF
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B.subtilis LB CLF
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In responding to predation risk, secondhand experience can be as good as new

go.igb.illinois.edu/predation

Throughout the living world, parents have many ways of gifting their offspring with information they will need to help them survive. A new study in *Nature Ecology and Evolution* examining the effects of exposure to predators across two generations of stickleback fish yielded a surprising insight into how such transgenerational information is used.

The NIH- and NSF-funded study was led by Laura Stein, who began the work as a doctoral student in the laboratory of Professor of Animal Biology Alison Bell (GNDP). Stein, Bell, and doctoral student Abbas Bukhari found that when either a stickleback father or his offspring experienced the threat of predation, the offspring responded with the same adaptive strategy—developing to be smaller and more timid. Even if both generations experienced the threat, the developmental differences in size and behavior remained the same.

Above_A new animal biology study of stickleback fish by Illinois animal biologist Alison Bell (left) and former Illinois doctoral student Laura Stein (right) shows that individuals display the same molecular and developmental responses to their own versus their parent's exposure to predators.

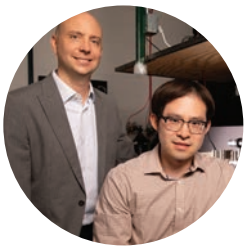
"The results were not what we had predicted, because models assume that information from different sources is additive," said Bell. "If, say, the developmentally plastic response is to be smaller in response to predation risk and if the generational response is to be smaller in response to predation risk, the models all assume that if those two things are combined together, they should be doubly small ... that's not what we found at all."

By comparing levels of brain gene expression across their experimental groups, the researchers determined that paternal experience and personal experience predominantly activated a shared set of molecular responses, perhaps helping to explain on a mechanistic level why either or both were able to produce the same developmental outcomes.

How polymers relax after stressful processing

go.igb.illinois.edu/polymers

Below_Chemical and Biomolecular Engineering Professor Charles Schroeder, left, and graduate student Peter Zhou have found that single polymers acting as individuals work together to give synthetic materials macroscopic properties like viscosity and strength.



A new study has found that entangled, long-chain polymers in solutions relax at two different rates, marking an advancement in fundamental polymer physics. The findings will provide a better understanding of the physical properties of polymeric materials and critical new insight into how individual polymer molecules respond to high-stress processing conditions.

The study, published in the journal *Physical Review Letters*, could help improve synthetic materials manufacturing and has applications in biology, mechanical and materials sciences as well as condensed matter physics.

"Our single-molecule experiments show that polymers like to show off their individualistic behavior, which has revealed unexpected and striking heterogeneous dynamics in entangled polymer solutions," said co-author Charles Schroeder (BSD), Professor of Chemical and Biomolecular Engineering.

"A main goal of our research is to understand how single polymers acting as individuals work together to give materials macroscopic properties such as viscosity and toughness."

The team is excited to bring new insight to the understanding of how complex fluids flow and how they are processed and manufactured, especially with polymers that are subjected to intense stress, such as the fluids that are used for 3D printing.

The work was supported by the NSF and PPG Industries.

New informatics tool makes the most of genomic data

go.igb.illinois.edu/informatics

The rise of genomics, the shift from considering genes singly to collectively, is adding a new dimension to medical care; biomedical researchers hope to use the information contained in human genomes to make better predictions

New informatics tool makes the most of genomic data continued

about individual health, including responses to therapeutic drugs. A new computational tool developed through a collaboration between the University of Illinois and Mayo Clinic combines multiple types of genomic information that could help biomedical researchers predict what drugs will most safely and effectively treat individual patients.

The tool was described in *Genome Research* after its development by members of KnowEnG, a Center of Excellence housed within the IGB and established by an NIH Big Data to Knowledge (BD2K) Initiative award to the University of Illinois in partnership with Mayo Clinic. KnowEnG stands for Knowledge Engine for Genomics, representing the center's mission to develop analytical resources for biomedical work with genomic data.

"There was no tool that would exploit all of these [data types] together," said Professor of Computer Science and Willett Faculty Scholar Saurabh Sinha (BSD/GNDP), who co-directs the BD2K Center. "Our end result was testable predictions" about how different genomic features would influence the effectiveness of different drugs, he said.

Sinha and graduate student Casey Hanson created and tested an algorithm that takes in data on gene expression, genomic factors that help control gene expression, and resulting traits (such as drug response) and uses these to predict which genes are most important in determining the latter.

Endocannabinoids may have anticancer effects

go.igb.illinois.edu/omega3

A class of molecules formed when the body metabolizes omega-3 fatty acids could inhibit cancer's growth and spread, a new study in mice indicated. The molecules, called endocannabinoids, are made naturally by the body and have similar properties to cannabinoids found in marijuana, but without the psychotropic effects.

In mice with tumors of osteosarcoma—a bone cancer that is notoriously painful and difficult to treat—endocannabinoids slowed the growth of tumors and blood vessels, prevented the cancer cells from migrating and caused cancer cell death. The work, which was supported by the NIH and the American Heart Association, was published in the *Journal of Medicinal Chemistry.*

Above_Comparative Biosciences Assistant Professor Aditi Das and Veterinary Clinical Medicine Professor Timothy Fan found that a class of molecules that form when the body metabolizes omega-3 fatty acids may prevent cancer from migrating.

The researchers, led by Assistant Professor of Comparative Biosciences Aditi Das, found that the endocannabinoids they focused on did kill cancer cells, but not as effectively as other chemotherapeutic drugs on the market. However, the compounds also combated osteosarcoma in other ways: they slowed tumor growth by inhibiting new blood vessels from forming to supply the tumor with nutrients, they prevented interactions between the cells, and most significantly, they appeared to stop cancerous cells from migrating.

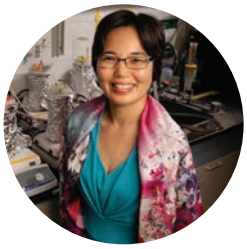
"The major cause of death from cancer is driven by the spread of tumor cells, which requires migration of cells," said study co-author Timothy Fan (ACPP/ONC-PM), a professor of veterinary clinical medicine and veterinary oncology. "As such, therapies that have the potential to impede cell migration also could be useful for slowing down or inhibiting metastases."

Chemicals that keep drinking water flowing may also cause fouling

go.igb.illinois.edu/fouling

Many city drinking water systems add softening agents to keep plumbing free of pipe-clogging mineral buildup. According to new research published in *Biofilms and Microbiomes*, these additives may amplify the risk of pathogen release into drinking water by weakening the grip that bacteria like those responsible for Legionnaires' disease have on pipe interiors.

Biofilms, which are similar to the films that grow on the glass of fish tanks, are present in almost all plumbing systems and anchor themselves to mineral scale build-ups in pipes. They are teeming with harmless microbial life and incidents of waterborne illness are rare. But civil and environmental engineers Helen Nguyen (CGRH/IGOH) and Wen-Tso Liu (BCXT/IGOH/MME) and colleagues found that when water treatment plants use chemicals to combat such mineral accumulation, biofilms grow thicker and become softer.



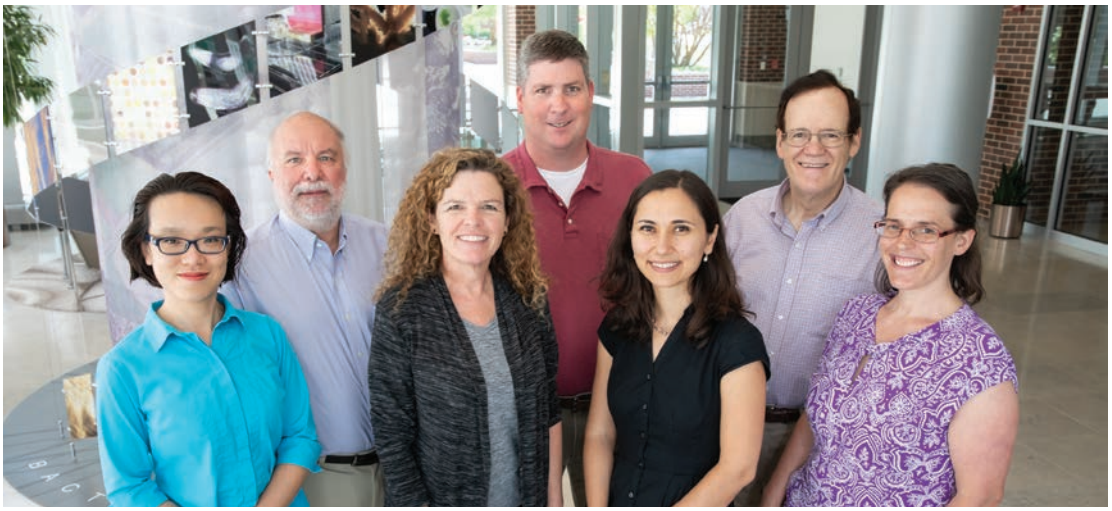
Above_Civil and Environmental Engineering Professor Helen Nguyen has found that water-softening additives may increase the risk of pathogen release into drinking water by weakening the grip that bacteria have on pipe interiors.

The team used a method developed by electrical and computer engineer Stephen Boppart (RBTE) to measure the thickness and stiffness of lab-grown biofilms. They set up multiple scenarios with and without added polyphosphates, a class of chemicals commonly used to combat mineral build-up. All scenarios produced biofilms, but the system that used polyphosphates grew much thicker and softer biofilms than the others.

The team is moving ahead with related studies that look at ways to help physically remove biofilms while pipes remain in place and others that look at the effects of anti-corrosive chemicals on biofilms and water quality. The U.S. EPA, the National Institute for Biomedical Imaging and Bioengineering and the NIH supported this study.

Football fans have a ball at Gameday Genomics

Right_Illini fans enjoyed a new addition to Grange Grove this year: Gameday Genomics offered a photobooth and a series of genomics-flavored tailgate games, including a tree of life-inspired ladder toss.



Long-term estrogen therapy changes microbial activity in the gut

go.igb.illinois.edu/estrogentherapy

Above_Estrogen supplements change the bacterial composition in the intestinal tract, affecting how estrogen is metabolized, according to a new study in mice. From left (front row): postdoctoral research associate Xiaoji (Christine) Liu; National Center for Supercomputing Applications senior research scientist Colleen Bushell (CGRH/GNDP); Food Science and Human Nutrition Assistant Professor Zeynep Madak-Erdogan (ONC-PM); Pathobiology Assistant Professor Rebecca Smith (IGOH). Back row, from left: NCSA senior data analytics advisor Michael Welge (RBTE/CGRH); Food Microbiology Associate Professor Michael Miller (MME/IGOH); and Swanlund Professor of Chemistry John Katzenellenbogen.

Long-term therapy with estrogen and bazedoxifene alters the microbial composition and activity in the gut, affecting how estrogen is metabolized, a study in mice found.

According to the study, published in *Scientific Reports* and led by Professor of Food Science and Human Nutrition Zeynep Madak-Erdogan (ONC-PM), the enzyme B-glucuronidase plays a pivotal role in metabolizing synthetic estrogens in the intestinal tract.

The study's findings suggest that changing the chemistry in the gut could be a way to improve the effectiveness and long-term safety of estrogen supplements for postmenopausal women and breast cancer patients.

"Our findings indicate that clinicians might be able to manipulate the gut biome through probiotics to change the half-life and properties of estrogens so that long-term users obtain the therapeutic benefits of estrogen-replacement therapy without increasing their risks of reproductive cancers," Madak-Erdogan said.

While the findings need to be replicated in humans, the research offers insight into estrogen-replacement therapy's impact on the expression of microbial genes, and may help explain why individual patients' responses to hormone therapy can vary.

This research was supported by the University of Illinois, the NIH, the USDA, and Pfizer Inc.

A starring role for chaperone protein in gene regulation

go.igb.illinois.edu/chaperone

The more we learn about how cells respond and adapt to their external environments, the more we appreciate the flexibility of their inner molecular partnerships. In a study published in *Nucleic Acids Research*, graduate student

Muhammad Azam and Professor of Microbiology Cari Vanderpool (MME) have demonstrated that a protein that was typically assumed to support the functions of other molecules is actually able to assume a primary role itself.

Their work, supported by the NIH, is part of the Vanderpool laboratory's efforts to understand how bacterial cells balance uptake of sugars with their metabolic needs. They study a genetic regulatory system that helps bacteria keep this balance.

In this study, the focus was the regulation of a gene called *manX*, which codes for a protein that transports a sugar into the cell. The researchers studied how a molecule called SgrS helps control how much manX protein is made.

They analyzed how SgrS slows down sugar uptake to allow metabolism to catch up, and how it might be supported by a protein called Hfq.

Surprisingly, they found that SgrS doesn't appear to cling to the part of the manX mRNA where a ribosome needs to attach. Instead, Hfq grabs onto this area, reversing roles that researchers have consistently observed before.

Below_Professor of Microbiology Cari Vanderpool.

This discovery of a reversed relationship may lead to further documentation of similar mechanisms in bacteria. A better understanding of gene regulation in bacteria may enable scientists to reprogram bacterial behavior by affecting gene activity.

Tiny jumping roundworm undergoes unusual sexual development

go.igb.illinois.edu/roundworm

Above_A newly hatched *Steinernema carpocapsae* juvenile is only about 0.25 mm (less than 1/100 of an inch) long with a gonad only 0.013 mm in length. During development, the worm will increase over 10 times in length (in comparison, the average human only increases about 4 fold in height from birth to adulthood) and its gonad increases almost 500 times in length.

Nematodes may be among the simplest animals, but scientists can't get enough of these microscopic roundworms. They've mapped the genome of *C. elegans*, the "lab rat" of nematodes, and have characterized nearly every aspect of its biology, with a particular focus on neurons. For years, it was assumed other nematodes' neurons were similar to those of *C. elegans*, until a study in the *Journal of Nematology* demonstrated the vast diversity in neuronal anatomy across species.

Assistant Professor of Crop Sciences Nathan Schroeder (GNDP), who led the study, showed that gonad development also varies in other nematodes relative to *C. elegans*. He and graduate student Hung Xuan Bui focused on *Steinernema carpocapsae*, a nematode used in insect biocontrol applications in lawns and gardens.

The gonads in all nematodes develop within a structure called the gonad arm, a tube through which multiple reproductive organs migrate into place throughout the animal's postembryonic development. This happens in a predictable manner in *C. elegans*, but not so much with *Steinernema*.

Tiny jumping roundworm undergoes unusual sexual development continued

Finding and understanding variability within and among species can help scientists understand how diversity arises, an open question with relevance to evolution and genetic processes.

This study also represents an advancement in studying organisms that develop almost entirely inside another organism, as *Steinernema* does by infecting and feeding on another insect. Bui developed a technique to study the nematode's reproductive development without being inside the insect, allowing further study of the anatomy and behavior of bug-eating nematodes.

The Lee Foundation Fellowship program supported this research.

Engineering bacteria to exhibit stochastic Turing patterns

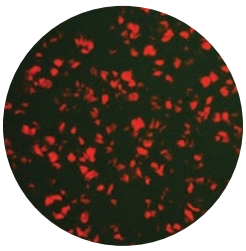
go.igb.illinois.edu/Turing

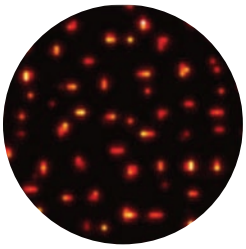
How did the zebra get its stripes or the leopards its spots? Scientists have long tried to understand the origin of pattern formation in living systems, which could help develop engineered tissues with countless medical applications.

A study published in the *Proceedings of the National Academy of Sciences* has brought us one step closer to a molecular-level understanding of how patterns form in living tissues. Researchers engineered bacteria that displayed stochastic Turing patterns—a "lawn" of synthesized bacteria in a petri dish fluoresced an irregular pattern of red polka dots on a field of green.

Below, top_Representative fluorescent image of a stochastic Turing pattern of signalling molecules in a biofilm of forward-engineered *E. coli* cells. The field of view is about 300 microns across.

Below, bottom_Computer simulation of a stochastic Turing pattern with parameters corresponding to the experimental conditions. The simulation region is smaller than that of the experiment, but the statistical properties of the patterns are in agreement with those of the experiment.





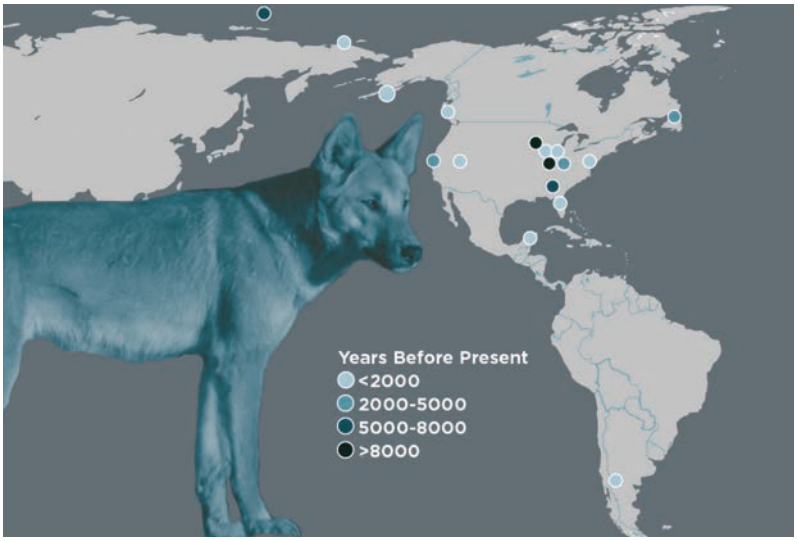
Turing patterns, first introduced by mathematician Alan Turing, can be stripes, spots or spirals that arise naturally out of a uniform state. In this study, co-authored by Swanlund Professor of Physics Nigel Goldenfeld (BCXT leader), researchers demonstrated that Turing patterns do in fact occur in living tissues, but with a twist. It's actually randomness that generates what Goldenfeld has coined a stochastic Turing pattern.

The research was supported by both the NIH and NSF.

"Ultimately, bioengineers would like to use this type of technology to make novel tissues and new functional biological systems," Goldenfeld said.

The origins and fate of first dogs in Americas

go.igb.illinois.edu/firstdogs



A study reported in *Science* by anthropology professor Ripan Malhi (CGRH/RBTE), his then-graduate student Kelsey Witt, and colleagues offers an enhanced view of the origins and ultimate fate of the first dogs in the Americas. The dogs were not domesticated North American wolves, as some have speculated, but likely followed their human counterparts over a land bridge that once connected North Asia and the Americas.

This was the first comprehensive genomic study of ancient dogs in the Americas to analyze nuclear DNA, which is inherited from both parents, along with mitochondrial DNA, which is passed down only from mothers to their offspring. By comparing genomic signatures from 71 mitochondrial and seven nuclear genomes of ancient North American and Siberian dogs spanning a period of 9,000 years, the research team revealed that these canines arrived in the Americas many thousands of years after people began migrating over a land bridge connecting present-day Siberia and Alaska. These ancient dogs followed a similar path to disperse to every part of the Americas, migrating with human counterparts, but almost completely vanished after European contact, suggesting a catastrophic event likely associated with European colonization.

Above_As a graduate student at Illinois, Kelsey Witt led the mitochondrial DNA genome work on a newly published study of ancient dogs. Witt is now a postdoctoral researcher at the University of California, Merced.

"By looking at genomic data along with mitochondrial data, we were able to confirm that dogs came to the Americas with humans, and that nearly all of that diversity was lost—most likely as a result of European colonization," said Witt, who is now a postdoctoral researcher at the University of California, Merced.

This research was funded by the American Kennel Club, the European Research Council, the Illinois State Museum Society, the Leverhulme Trust, the Max Planck Society, Millennia Research, Muséum National d'Histoire Naturelle, the Natural Environmental Research Council, NIH, NSF, the Russian Science Foundation, the Santa Barbara Museum of Natural History, the Social Sciences and Humanities Research Council, the University of Oxford, Wellcome Trust, and the Wenner-Gren Foundation.

SCIENCE SPOTLIGHT

A BIOMARKER IS ANY MOLECULE THAT IS NATURALLY AND RELIABLY PRODUCED BY A DISEASE OR CONDITION. BECAUSE THESE MOLECULES ARE SELECTED FOR THEIR EASE OF DETECTION AND MEASUREMENT,

STRONG BIOMARKERS REVEAL THE UNSEEN

PROCESSES OF DISEASE WITHOUT THE NEED FOR AN INVASIVE PROCEDURE.

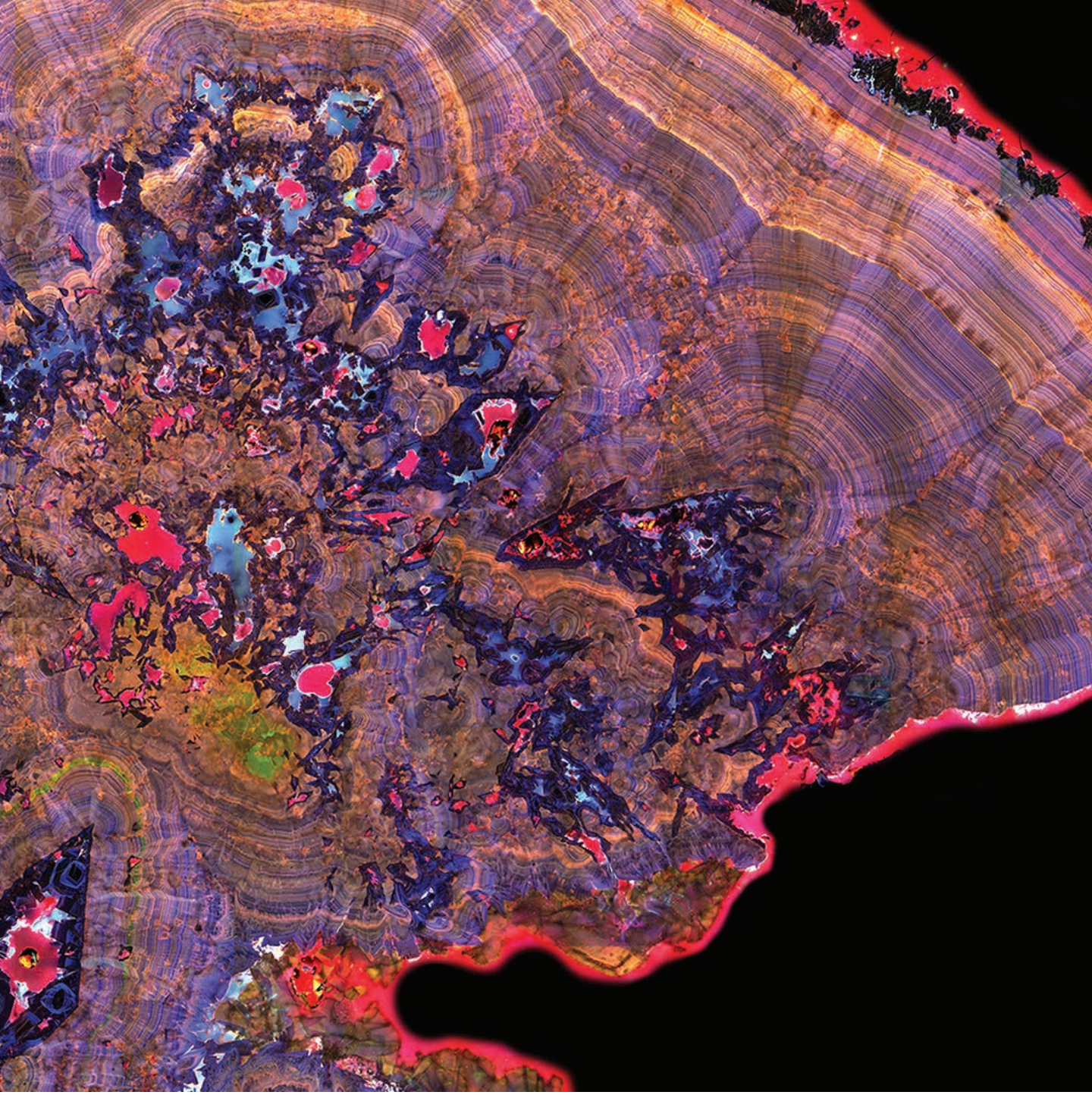
BOOKMARKING BIOMARKERS

Biomarkers are detected and measured in blood or peripheral tissue. Antibodies and hormones are well-known biomarkers; gene products, including proteins and RNA molecules, are also being identified as reliable biomarkers for health conditions.

STRONG BIOMARKERS REVEAL THE UNSEEN

The identification of reliable biomarkers for a multitude of disorders is leading to earlier disease detection, more effective treatment,

and the possibility of tailoring health care to the biology of the individual—pathways to healthier populations of pets and people.



Kidney stones have distinct geological histories

go.igb.illinois.edu/geohistory

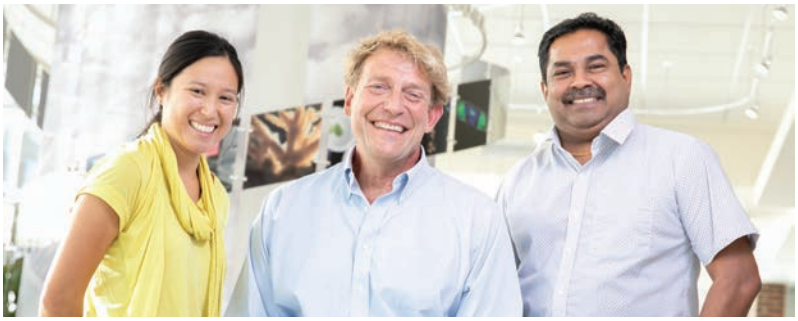
Above_Fluorescence micrograph of a human kidney stone from Mayo Clinic.

A geologist, a microscopist and a doctor walk into a lab and, with their colleagues from across the nation, make a discovery that overturns centuries of thought about the nature and composition of kidney stones. The team's key insight, reported in the journal *Scientific Reports*, is that kidney stones are built up in calcium-rich layers that resemble other mineralizations in nature, such as those forming coral reefs or arising in hot springs, Roman aqueducts or subsurface oil fields.

Most importantly for human health, the researchers found, kidney stones partially dissolve and regrow again and again as they form.

This contradicts the widely held notion that kidney stones are homogenous rocks that never dissolve and are different from all other rocks in nature, said

geologist Bruce Fouke (BCXT), who led the new research with Jessica Saw, an M.D. student at the Mayo Clinic School of Medicine and Ph.D. student at Illinois; and Mayandi Sivaguru, associate director of the Core Facilities microscopy suite at the IGB.



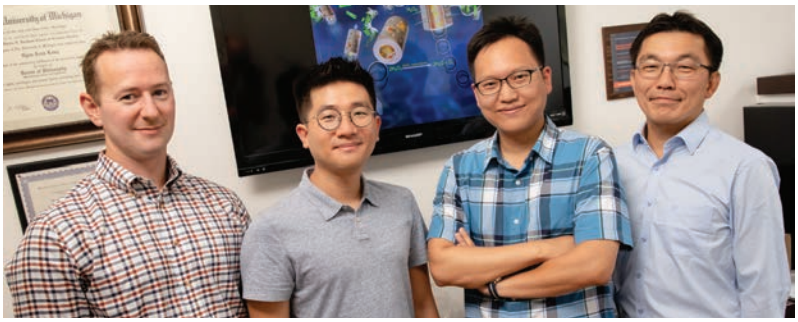
Right_Using a suite of techniques both common and new to geology and biology, researchers, from left, M.D./Ph.D. student Jessica Saw, geologist and microbiologist Bruce Fouke, microscopy expert Mayandi Sivaguru and their colleagues made new discoveries about how kidney stones repeatedly grow and dissolve as they form inside the kidney.

"Contrary to what doctors learn in their medical training, we found that kidney stones undergo a dynamic process of growing and dissolving, growing and dissolving," Fouke said. "This means that one day we may be able to intervene to fully dissolve the stones right in the patient's kidney, something most doctors today would say is impossible."

The Mayo Clinic and University of Illinois Strategic Alliance for Technology-Based Healthcare, the Mayo Clinic O'Brien Urology Research Center and the NASA Astrobiology Institute supported this research.

Microbubble scrubber destroys dangerous biofilms

go.igb.illinois.edu/scrubber



Right_Professor of Chemical and Biomolecular Engineering Simon Rogers, left, postdoctoral researchers Jun Pong Park and Yongbeom Seo and Professor of Chemical and Biomolecular Engineering Hyunjoon Kong led an international team that developed hydrogen peroxide-bubbling microparticles that may help eradicate dangerous biofilms.

Stiff microbial films often coat medical devices, household items and infrastructure such as the inside of water supply pipes, where they can lead to dangerous infections. Researchers have developed a system that harnesses the power of bubbles to propel tiny particles through the surfaces of these tough films and deliver an antiseptic deathblow to the microbes living inside.

In the journal *ACS Applied Materials and Interface*, a team led by Professor of Chemical and Biomolecular Engineering Hyunjoon Kong (RBTE) described how they loaded diatoms, the tiny skeletons of algae, with an oxygen-generating chemical to destroy microbes. The NIH, the NSF and the Korea Institute of Industrial Technology supported their work.

Microbubble scrubber destroys dangerous biofilms continued

Above_3% H_2O_2 + MnO_2 diatom bubbler treated biofilm on microgrooved PDMS (x40 magnification).

"Most of us get those black or yellow spots in our showers at home," said co-author Kong, also a Carle Illinois College of Medicine affiliate.

"Those spots are biofilms and most of us know it takes a lot of energy to scrub them away. Imagine trying to do this inside the confined space of the tubing of a medical device or implant. It would be very difficult."

Biofilms are slimy colonies of microbes held together by internal scaffolds, clinging to anything they touch. About 80 percent of all medical infections originate from biofilms that invade the inner workings of hospital devices and implants inside patients. The researchers developed a system that uses naturally abundant diatoms along with hydrogen peroxide and tiny oxygen-generating sheets of the compound manganese oxide. They believe that their success is a result of a decision to focus on the mechanical aspects of biofilm destruction.

Scientists search for coral's new home

go.igb.illinois.edu/reefs

Right_Researchers hope that a partnership of material science and biology can provide novel ways to support regeneration of corals, which are key players in ocean ecosystems.

Coral reefs have long faced problems like overfishing, global warming and pollution—but they're also threatened by how slowly they regenerate.

To reproduce, coral release sperm and eggs and form larvae, which then swim around and attach to a surface, where they begin to develop into coral polyps and grow. They face a variety of competitors, and most don't survive. If they do survive, it takes years for the coral to be able to reproduce and even longer for entire reefs to form.

Researchers at the IGB want to increase the rate of coral regeneration by creating a new home for coral larvae: artificial structures that encourage larvae settlement and discourage the growth of competitor species. The team is funded by a three-year NSF Growing Convergence Research Grant, which encourages collaboration between scientists who don't typically work together.

The research will be led by Amy Wagoner Johnson (CGRH/RBTE), a professor of mechanical science and engineering, along with four co-PIs including Professor of Geology and of Microbiology Bruce Fouke (BCXT). Last year, Wagoner Johnson had the idea to apply her research on bone regeneration to coral research.

Above_Amy Wagoner Johnson, a professor of mechanical science and engineering.

"We thought it would be really interesting if we could take some of the things we've learned from tissue engineering—cells interacting with materials and what kinds of factors influence cells . . . and apply that to coral reproduction," she said. "Being able to more efficiently regenerate coral can contribute a little bit to resolving the issue of losing the coral reefs."

Damaged liver cells undergo reprogramming to regenerate

go.igb.illinois.edu/liver

In Greek mythology, Zeus punishes the trickster Prometheus by chaining him to a rock and sending an eagle to eat a portion of his liver every day, in perpetuity. This myth holds a kernel of truth: the liver has the ability to regenerate itself, though not overnight nor for eternity.

New research has determined how damaged liver cells repair and restore themselves through a signal to return to an early stage of postnatal organ development. The findings are reported in the journal *Nature Structural & Molecular Biology*.

Above_Biochemistry Professor Auinash Kalsotra, second from left, and his team, including, from left, graduate students Waqar Arif, Joseph Seimetz and Sushant Bangru, uncovered the molecular underpinnings of liver regeneration.

"The liver is a resilient organ," said lead author Assistant Professor of Biochemistry Auinash Kalsotra (GNDP/ONC-PM). "It can restore up to 70 percent of lost mass and function after just a few weeks . . . However, if the liver is damaged, the liver cells re-enter the cell cycle to divide and produce more of themselves."

Using a mouse model of a liver severely damaged by toxins, the researchers compared injured adult liver cells with healthy cells present during a stage of development just after birth. They found that injured cells undergo a partial reprogramming that returns them to a neonatal state of gene expression; fragments of messenger RNA, the molecular blueprints for proteins, are rearranged and processed in regenerating liver cells in a manner reminiscent of the neonatal period of development.

The NIH, March of Dimes and American Heart Association supported this research.

Unlocking the mysteries of the sugarcane genome

go.igb.illinois.edu/sugarcane

Above_ Modern hybrids of sugarcane are grown for food or biofuel production.

For centuries, sugarcane has supplied human societies with alcohol, biofuel, building and weaving materials, and the world's most relied-upon source of sugar. Now, researchers have extracted a sweet scientific prize from sugarcane: its massive and complex genome sequence, which may lead to the development of hardier and more productive cultivars.

Producing the comprehensive sequence required a concerted effort by over 100 scientists from 16 institutions; the work took five years and culminated in a publication in *Nature Genetics*. But the motivation to tackle the project arose long before.

"Personally, I waited for 20 years to get this genome sequenced," said Ray Ming (GEGC), the plant biology professor who instigated and led the sequencing effort.

"I dreamed about having a reference genome for sugarcane when I worked on sugarcane genome mapping in the late 1990s . . . This discovery will accelerate mining effective alleles of disease resistance genes that have incorporated into elite modern sugarcane hybrid cultivars, and subsequently the implement of molecular breeding [of sugarcane]."

Above_Ray Ming, plant biology professor.

Funding for this work was provided by the DOE, the EBI, Fujian Agriculture and Forestry University, the International Consortium for Sugarcane Biotechnology, the National Natural Science Foundation of China, the NSF, the Program for New Century Excellent Talents, and the 863 Program.

Classifying microbes differently leads to discovery

go.igb.illinois.edu/classification

According to a new study published in *mBio*, changing the way microbes are classified can reveal similarities among mammals' gut microbiomes and provide insight into human and environmental health.

Unlike many other organisms, microbial species are difficult to classify. Scientists often use a method pioneered by Carl Woese that uses 16S ribosomal RNA to sort microbes according to relatedness.

"If you're similar enough in genetic identity to another organism, you get clustered together," said James O'Dwyer (BCXT), an associate professor of plant biology and co-author of the NSF-funded study. **"The problem with that is we don't really know how closely that definition of a unit corresponds to the ecological differences between microbes."**

He and his co-authors proposed a different approach to classification that instead focuses on the microbes' evolutionary history. When the researchers grouped the microbes in this way, they learned more about the gut microbiomes of mammals. O'Dwyer hopes the field may one day come to an agreement on a better way to classify microbes, even if it's not the method this paper proposed.

World of Genomics at the St. Louis Science Center

go.igb.illinois.edu/
STLworldofgenomics

One of the IGB's most successful and comprehensive public engagement events, the World of Genomics, was showcased for three days at the St. Louis Science Center from October 18-20, 2018.

The World of Genomics featured six interactive learning stations spanning the breadth of our research in health, technology, and the environment. The

World of Genomics at the St. Louis Science Center
continued

Tree of Life station introduced visitors to genomic research, highlighting the overarching metaphor used by Darwin to describe the evolutionary relationships among all organisms, both living and extinct, and describing the discovery of the third domain of life by Illinois researcher and IGB namesake Carl Woese.

At other stations, guests examined concepts related to the human brain and behavior through the lens of bee research, learned how pets are being successfully treated with new cancer therapeutics, as well as how these treatments could be used to combat cancer in humans, and observed how a combination of traditional breeding, genetic engineering, and genome editing can create plants with higher yields that withstand drought and disease.

Two final stations examined types of interactions that were present between microbes and the environment during the emergence of life on Earth and featured hands-on visualizations of the unique microbial communities that live inside every person. Thousands of St. Louis community students, parents, teachers, community members, and University alumni enjoyed the event.

Stem cell proliferation controlled directly by nervous system

go.igb.illinois.edu/ANS

Somatic stem cells are microscopic workhorses, constantly regenerating cells throughout the body: skin and the lining of the intestine, for example. And to animal scientist Megan Dailey (RBTE) and graduate student Elizabeth Davis, they represent untapped potential.

Above_Megan Dailey, above, and Elizabeth Davis, below, both from the Department of Animal Sciences, demonstrate the autonomic nervous system has direct control over stem cell proliferation in the intestinal epithelium.

"If we could find a way to target and control stem cell proliferation in the body, there could be potential medical benefits, including turning off the proliferation of cancer stem cells or inducing proliferation of somatic stem cells where we want to grow tissue," said Davis, who with Dailey co-authored a study that demonstrates, for the first time, that stem cell proliferation is directly controlled by the autonomic nervous system—the same system that controls unconscious functions such as breathing and digestion.

In the study, which was published in *Physiological Reports* and supported by the USDA, the researchers focused on stem cells in the intestinal lining in mice. They found that neurotransmitters, signaling molecules of the nervous system, changed the behavior of the cells—just what they would expect to see for a direct relationship.

"We knew that nerves of the autonomic nervous system came into close contact with cells of the intestinal epithelium, including stem cells, but we didn't know if the neurotransmitters were able to bind to the stem cells. When we isolated the stem cells and found there were actually autonomic neurotransmitter receptors, we found that missing piece," Davis said.

A whole-system view of plant cold stress

go.igb.illinois.edu/coldstress

Above_Professor of Crop Sciences Gustavo Caetano-Anollés.

When temperatures drop, plants can't bundle up. Stuck outside, exposed, plants instead undergo a series of biochemical changes that protect cells from damage. Scientists have described these changes and identified some of the genes controlling them, but it's not clear how all the processes work together. Lacking this global view, plant breeders have struggled to engineer cold-tolerant crops.

A recent study in *Frontiers in Bioengineering and Biotechnology* lays the groundwork for a genome-wide approach to understanding and addressing cold stress in plants. The work was supported by the USDA and the NCSA.

"The chances are slim that breeders could successfully modify a single gene and achieve greater cold tolerance. We need to understand the entire system: not only the gene of interest but all the related genes that affect particular pathways and other biological activities involved in a plant's stress response," said Professor of Crop Sciences Gustavo Caetano-Anollés (GEGC), lead author of the study. "Our study identifies significant metabolites associated with important traits and is a step forward in metabolic profiling techniques."

The research team examined data points collected from *Arabidopsis thaliana*, a small plant commonly used to explore genetic and physiological processes, at four time points during a cold stress response. Using a database that annotates genes and gene products, the team was able to build a network of genes, metabolites, and pathways, identifying all the processes involved in the plant's cold stress response.

Pollen Power Camp

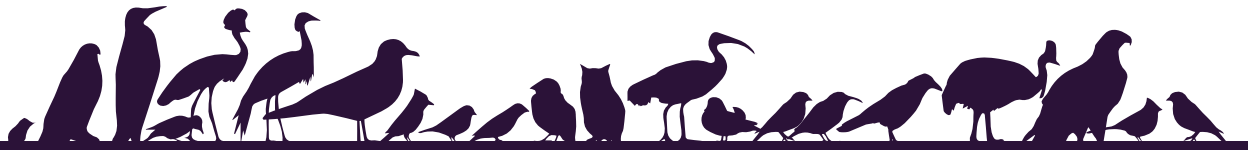
Right_During the Pollen Power summer day camp for middle school girls, participants took field trips to sites around campus, mapped evolutionary change, created television broadcasts reporting on climate change, and imaged pollen grains.

SCIENCE SPOTLIGHT

A LINEAGE TRACES THE HISTORY,
ANCESTOR TO DESCENDANT, OF A BIOLOGICAL ENTITY–
A GENE, A CELL, AN INDIVIDUAL, A POPULATION.
ELUCIDATED THROUGH THE ANALYSIS AND COMPARISON
OF GENOME SEQUENCES,

LINEAGES REFLECT POSSIBLE FUTURES

BY CREATING A COMPREHENSIBLE PROGRESSION
OF THE EVOLUTIONARY PAST.



THE ABCs OF LINEAGES

Every time a gene or a genome is copied as part of the act of reproduction, mutations, errors that change DNA sequence, spontaneously occur. Researchers can examine the genomes of related individuals and, through the distribution of different sequence changes, infer who is related to whom and how closely.

LINEAGES REFLECT POSSIBLE FUTURES

Researchers are using
knowledge of relationships between species
emerging from genome sequencing projects to

inform and improve efforts to conserve biodiversity around the world.

RIPE project receives additional $13 million

go.igb.illinois.edu/RIPE-reup

Above_RIPE Director Stephen Long (right) and Deputy Director Donald Ort (left) aim to enhance the photosynthetic productivity and yield of key food crops including rice, cassava, cowpea, and soybeans (pictured) to benefit farmers worldwide.

By improving how key crops transform sunlight into yield, Realizing Increased Photosynthetic Efficiency (RIPE) will one day help farmers put food on more tables worldwide, especially where it is needed most.

In 2017, a $45 million, five-year reinvestment from the Bill & Melinda Gates Foundation, the Foundation for Food and Agriculture Research, and the U.K. Government's Department for International Development ensured the international research project could continue to address the global food challenge. The Gates Foundation has now contributed an additional $13 million to add resources and personnel that will help accelerate the transfer of the RIPE project's successes into key food crops: soybeans, rice, cassava, and cowpea.

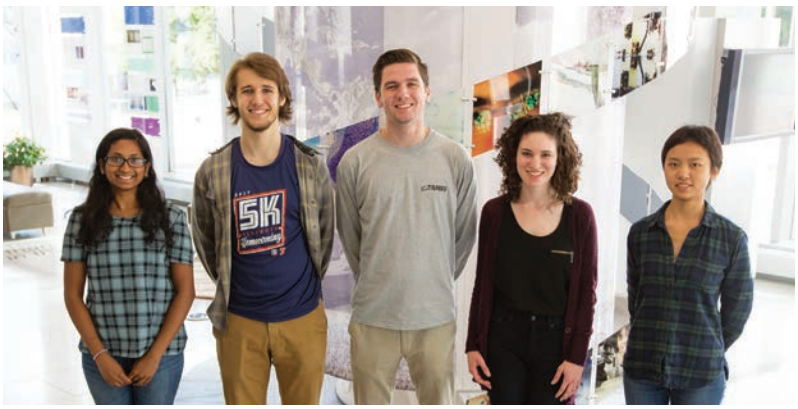
Above_Realizing Increased Photosynthetic Efficiency (RIPE).

"Time is of the essence—especially as we look to a future filled with more people and a dramatically different climate," said RIPE Director Stephen Long (BSD/CABBI/GEGC), Ikenberry Endowed University Chair of Crop Sciences and Plant Biology. "We must future-proof our food supply today to ensure that these technologies are available when we need them."

A key aim of the RIPE project is to provide farmers, particularly those in some of the world's poorest countries, with seed that will yield substantially more without requiring more inputs. RIPE is led by the University of Illinois in partnership with the Australian National University; Chinese Academy of Sciences; Commonwealth Scientific and Industrial Research Organisation; Lancaster University; Louisiana State University; University of California, Berkeley; University of Essex; and the U.S. Department of Agriculture, Agricultural Research Service.

Illinois team wins bronze at 2018 iGEM competition

go.igb.illinois.edu/iGEM-2018



Right_The 2018 iGEM Illinois team, from left to right: Pranathi Karumanchi, Alexander Ruzicka, Liam Healy, Amie Bott, and Ziyu Wang.

The Illinois iGEM team won a bronze medal at the 2018 International Genetically Engineered Machine (iGEM) competition for their work on the relationship between lactic acid bacteria and baker's yeast.

The iGEM competition brings together undergraduate students from across the world to present their research in synthetic biology. Pranathi Karumanchi, Ziyu Wang, Liam Healy, Amie Bott and Alexander Ruzicka represented Illinois this year, funded by CABBI.

Above_The Center for Advanced Bioenergy and Bioproducts Innovation (CABBI) is a DOE Bioenergy Research Center at the IGB.

The idea for the team's project came from the joint work of Associate Professor of Bioengineering Ting Lu (BCXT/BSD/MME) and Professor of Food Science and Human Nutrition Yong-Su Jin (BSD/MME), also a CABBI scientist. Lu is researching lactic acid bacteria, which is used in the production of cheese and yogurt, while Jin studies baker's yeast, which is used in baking bread. Their work contributes to the goal of one day engineering these organisms to create a range of valuable products.

The distance of microbial competitions shapes their community structures

go.igb.illinois.edu/microbialdistance

Above_IGB members shared the colorful biochemical lives of microbes at the World of Genomics at the St. Louis Science Center.

Inside the microbial communities that populate our world, microbes are fighting for their lives. Single-celled organisms constantly compete with each other for space, nutrients and other resources. Their competitions can occur across multiple spatial scales.

Ting Lu (BCXT/BSD/MME), an associate professor of bioengineering, wanted to know if the varying distances of interactions affect the organization of microbial communities. He and his lab members addressed this question in a recent publication in *Science Advances*. Their work was supported by the NSF, the Office of Naval Research, the American Heart Association, the Brain and Behavior Research Foundation, and the NCSA.

In the community where one type of microbe kills another, the researchers found that long-range competition was more effective, as it took less time for the microbe to kill its competitor at a long range than at a short range.

Next, they studied the community where two types of microbes kill each other. In such two-way competitions, the density of the microbial population matters. If the population is dense, microbes are forced to compete at a close range, and those who use contact-dependent devices win. If the microbes are more spaced out, they compete at a long range, and those using diffusible molecules win.

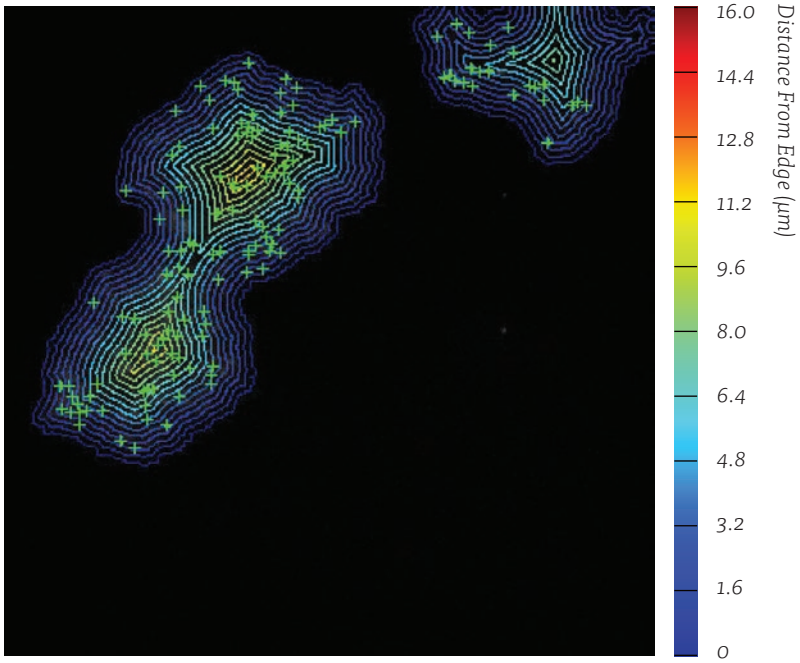
Above_Ting Lu, an associate professor of bioengineering.

The authors said that, to their knowledge, this is the first experiment to dissect the role of spatial interaction scale in the organization of microbial ecosystems. Lu said their results deepen their knowledge of how microbial communities assemble and function.

Jumping genes shed light on the evolution of complex genomes

go.igb.illinois.edu/jumpgene

A previously unappreciated interaction in the genome turns out to possibly drive evolution of the larger, more complex genomes of eukaryotic cells billions of years ago.



Right_This graph shows the location of jumping gene events (marked by green plus signs) in a growing colony of bacteria.

This discovery began with retrotransposons, known as "jumping genes," which are DNA sequences that copy and paste themselves within the genome, multiplying rapidly. Nearly half the human genome is made up of retrotransposons, but bacteria hardly have any. Nigel Goldenfeld (BCXT leader/CGRH/GNDP), Swanlund Endowed Chair of Physics, and Thomas Kuhlman, a former physics professor at Illinois now at University of California, Riverside, wondered why.

Above_Swanlund Endowed Chair of Physics Nigel Goldenfeld, top, and Professor in the Department of Physics & Astronomy at University of California, Riverside, Thomas Kuhlman.

"We thought a really simple thing to try was to just take one (retrotransposon) out of my genome and put it into the bacteria just to see what would happen," Kuhlman said.

Their results, published in the *Proceedings of the National Academy of Sciences*, revealed that retrotransposons are fatal to bacteria, which lack the protective mechanisms evolved by eukaryotic cells. Those mechanisms spurred the emergence of complex genomic features that grant more flexibility to how those cells use their genetic material.

This research was supported by the NSF Center for the Physics of Living Cells, the Alfred P. Sloan Foundation, and the NASA Astrobiology Institute.

New approach helps geneticists identify genes responsible for complex traits

go.igb.illinois.edu/SPAEML

In biomedical research, plant breeding, and countless other endeavors, geneticists are on the hunt for the specific genes responsible for disease susceptibility, yield, and other traits of interest. Essentially, they're looking for needles in the enormous haystack that is the genome of an organism.

A team of researchers have now developed a new approach, which they call SPAEML, that incorporates understanding of gene function into its analytical method. Their work was supported by the USDA and the University of Illinois and reported in the journal *Heredity*.

"The problem is the combinatorial explosion of possibilities that must be tested, because we're looking at pairs of markers," said co-author Liudmila Mainzer (IGOH), technical program manager for genomics at NCSA. "The algorithm needs to evaluate tens of thousands, hundreds of thousands, possibly millions of models in order to select the best one. It could take years in sheer computational time, which is why no one has ever done it."

In the team's study, SPAEML could accurately detect the underpinnings of simulated traits with genetic sources similar to Alzheimer's disease in humans and flower structure in corn. Using custom-built software, which they have made freely available to other researchers and the computing power available at NCSA, the team confirmed that SPAEML could detect simulated markers of the traits in the dataset. Now, they are working with collaborators in the crop breeding industry and human health research to launch next steps.

Probing the secret lives of queen bees

go.igb.illinois.edu/secretbee

Above_Co-first author and postdoctoral researcher Hagai Shpigler holds a specially developed 3D-printed plastic honey comb that mimics the hive environment, used to monitor queen egg-laying behaviors.

More than a decade after the identification of colony collapse disorder, a phenomenon marked by widespread loss of honey bee colonies, scientists are still working to untangle the ecologically complex problem of how to mitigate ongoing losses of honey bees and other pollinating species. One much-needed aid in this effort is more efficient ways to track specific impacts on bee health. To address this need, a group of Illinois researchers has established a laboratory-based method for tracking the fertility of honey bee queens.

Co-first authors Julia Fine and Hagai Shpigler, both postdoctoral researchers at the University of Illinois, worked with others in the laboratory of IGB Director and Swanlund Professor of Entomology Gene Robinson (GNDP) to establish a laboratory setup that would mimic the key aspects of the hive environment and allow detection of egg-laying by honey bee queens living with small groups of worker bees. The resulting system, described in *PLOS One*, allowed them to demonstrate a relationship between worker access to protein sources and queen fertility.

Right_ A specially developed 3D-printed plastic honeycomb that mimics the hive environment enabled researchers to monitor queen egg-laying behaviors.

"The effect of the nutrition . . . was our first successful use of the system, giving us hope for more success in the future," Shpigler said. "The results show very nicely how the honey bee colony functions as one body, with shared digestive and reproductive systems. The workers are the ones that eat the food and the effect is on the queen egg laying—the superorganism in action!"

The work was supported by the Defense Advanced Research Project Agency; one coauthor also received support from LifeFoundry Inc.

DNA the theme of the day for DREAAM House visit

Right_DREAAM (Driven to Reach Excellence and Academic Achievement for Males) House is a school-to-college pipeline program for at-risk boys and teens. This year, IGB hosted 12 DREAAM students for a day of hands-on science.

SCIENCE SPOTLIGHT

A HIGH-THROUGHPUT TECHNIQUE IS ONE IN WHICH HUNDREDS OR THOUSANDS OF TESTS OR PROCEDURES ARE PERFORMED IN PARALLEL, GREATLY INCREASING THE EFFICIENCY OF THE WORK BEING PERFORMED.

HIGH-THROUGHPUT EXPANDS OUR VIEW

OF BIOLOGY; THESE TECHNOLOGIES EMPOWER SCIENTISTS TO OBSERVE AND EXPERIMENTALLY INFLUENCE ENTIRE LIVING SYSTEMS, CONSTRUCTING A MORE HOLISTIC UNDERSTANDING OF THEIR FUNCTION.

TAKING TIME WITH HIGH-THROUGHPUT

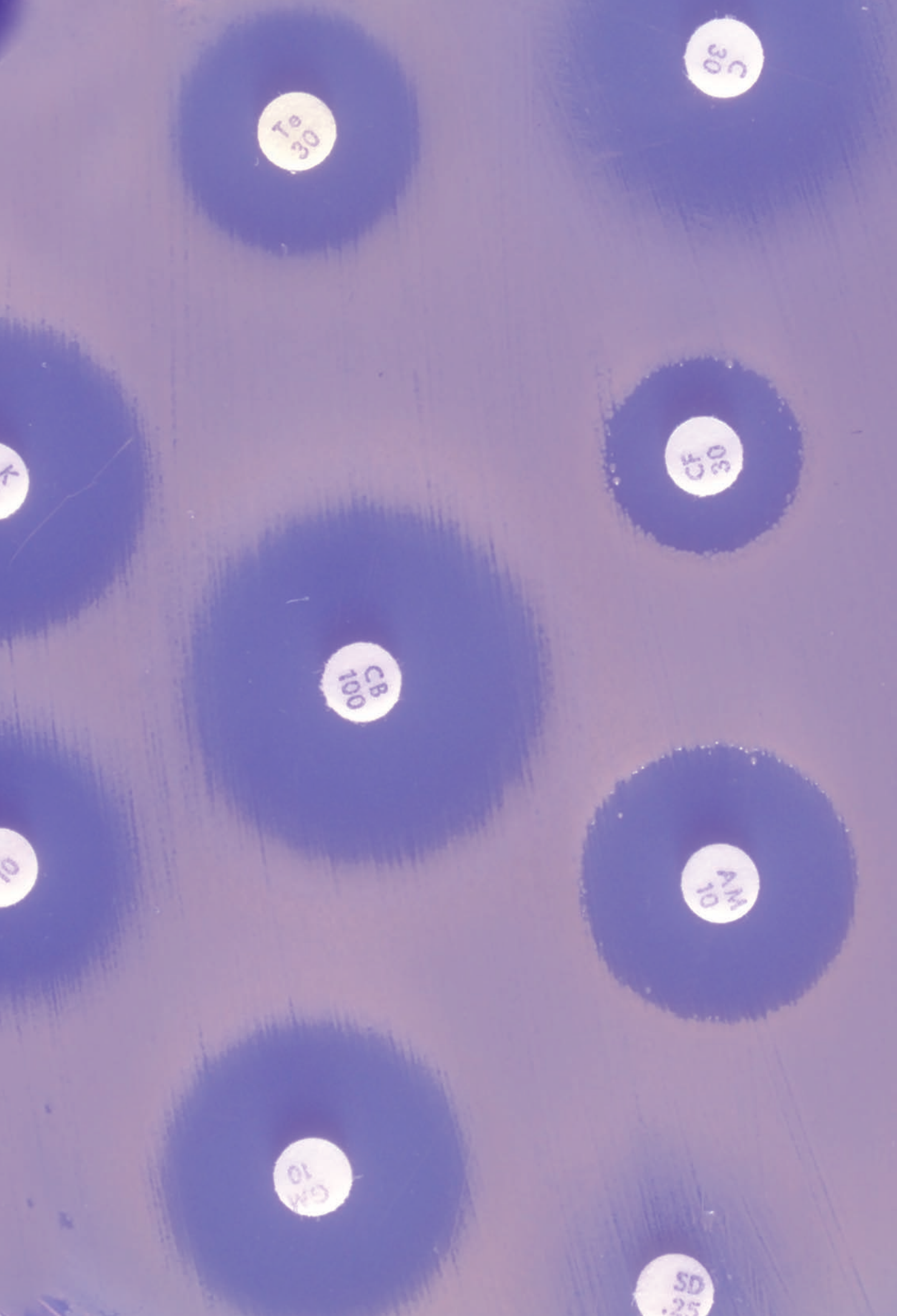
Some high-throughput methods rely on automation: laboratory robots dispense reagents, incubate cells, or monitor behavior of many experiments simultaneously. Others use quirks of molecular biology to quantify the activity of hundreds or thousands of genes at once.


CB
100

HIGH-THROUGHPUT EXPANDS OUR VIEW

High-throughput technologies are making it possible to discover and refine natural products with antibacterial and antifungal activity,

providing a boost that may allow us to keep pace with the rise of drug-resistant pathogens.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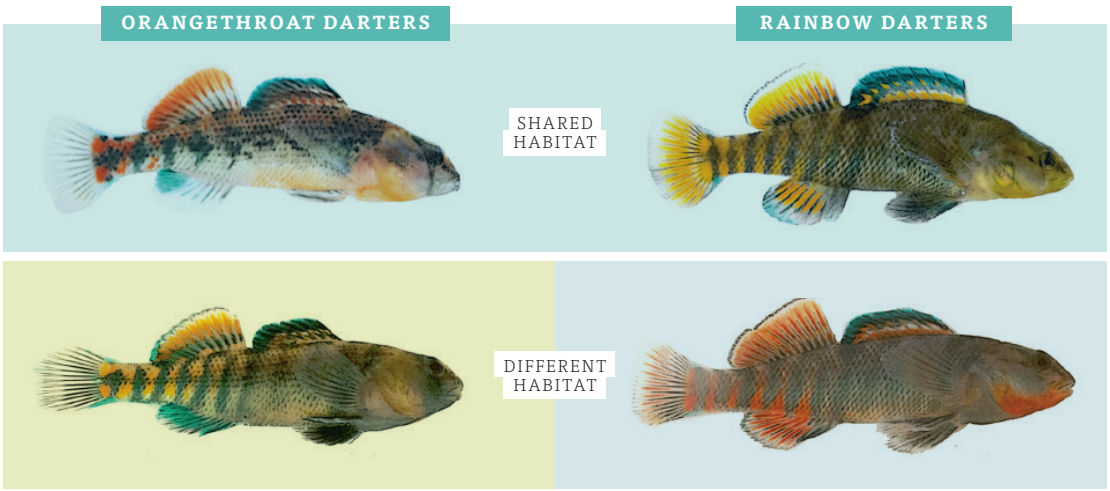


In darters, male competition drives evolution of flashy fins, bodies

go.igb.illinois.edu/darters

Above_When they share habitat with rainbow darters, male orangethroat darters learn to recognize their own and other species. They ignore other fish that look even slightly different from themselves, a behavior that appears to drive the evolution of their own color patterns.

Scientists once thought that female mate choice alone accounted for the eye-catching color patterns seen in some male fish. But for orangethroat darters, a new study has found that male-to-male competition is the real force behind the flash.

The research, conducted in the laboratory of Animal Biology Professor Becky Fuller (GNDP) and reported in the *Royal Society journal Proceedings B*, suggests that separate populations of orangethroat darters are evolving differing color patterns as a result of the males' ability to distinguish their own from other species.

Above_Animal Biology Professor Becky Fuller, left, and graduate student Rachel Moran study the factors that drive fish evolution in freshwater systems.

Darters are small, perch-like fish living in freshwater rivers and creeks in North America. The males are showy, with orange and blue-green stripes and patches, but the females are brown and tan.

Orangethroat darter males that coexist with a distantly related species, rainbow darters, have learned to distinguish between fellow orangethroat males and other darter males, but those who live away from other darters do not.

The researchers confirmed that when orangethroats gain this ability, their color patterns become more distinctive and diverge from those of separate orangethroat populations. These differences persisted across generations of lab-rearing in isolation, suggesting a genetic basis.

The NSF and the USDA supported this research.

Genomic study ties insect evolution to the ability to detect airborne odors

go.igb.illinois.edu/odors

A new study reveals that all insects use specialized odorant receptors that enable them to detect and pursue mates, identify enemies, find food and—unfortunately for humans—spread disease. This puts to rest a recent hypothesis that only some insects evolved the ability to detect airborne odors as an adaptation to flight, the researchers said.

The findings are reported in the journal *eLife*; the NSF and the USDA supported the research.

A human's nose or an insect's antenna is able to detect odors thanks to its odorant receptors, specialized proteins that grab onto the molecules of smelly substances and, in response, initiate nerve signals. Odorant receptors come in many different shapes, each able to bind to a particular type of odor-causing chemical.

Above_A new study from Professor of Entomology Hugh Robertson and colleagues at the University of California, Davis reveals that all insects have odorant receptors that enable them to detect airborne chemicals.

"We now know that odor detection was present at the very beginning of insect evolution and that it was probably a defining feature of insects as they became terrestrial," said Professor of Entomology Hugh Robertson (GNDP). "We found odorant-receptor genes in every insect species we looked at, including some that don't fly. We did not find these genes in any other arthropods, however, including other bugs with six legs." This finding contradicted a recent hypothesis that the evolution of insect odorant receptors was prompted by the emergence of flight.

Sequenced fox genome hints at genetic basis of behavior

go.igb.illinois.edu/foxgenome

For nearly 60 years, the red fox has been teaching scientists about animal behavior. In a long-term experiment, foxes at the Russian Institute of Cytology and Genetics have been selected for tameness or aggression, recreating the process of domestication from wolves to modern dogs in real time.

With the first-ever publication of the fox genome, scientists will begin to understand the genetic basis of tame and aggressive behaviors, which could shed light on human behavior, as well.

Right_Tame fox at Russian Institute of Cytology and Genetics in Novosibirsk.

"We've been waiting for this tool for a very, very long time," says Assistant Professor of Animal Sciences Anna Kukekova (GNDP), lead author of the paper, which was published in *Nature Ecology & Evolution*. She has been studying the famous Russian foxes since 2002.

Sequenced fox genome hints at genetic basis of behavior
continued

After sequencing and assembling the fox genome, the team turned to the Russian foxes to look for genetic regions differentiating the tame, aggressive, and conventional populations—farm-raised foxes ancestral to the tame and aggressive populations but not bred for any particular behavioral trait. They sequenced the genomes of 10 individuals from each population; the three groups differed in 103 genomic regions, some of which turn out to be responsible for the tame and aggressive behaviors.

Funding was provided by the NIH, the USDA, the Russian Science Foundation, the Russian Academy of Sciences, the Chinese Academy of Sciences, and the University of Illinois.

Donor Spotlight: Sandra Perry Sigman

go.igb.illinois.edu/sigman

In 2009, Sandra Perry Sigman visited the University of Illinois campus with her husband David and son, Ryan. As an alumna of the School of Labor & Employment Relations graduate program, she was visiting then to be the commencement speaker for the program's commencement ceremony.

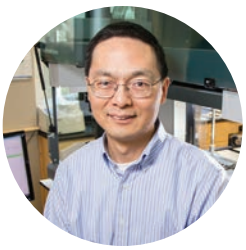
While visiting, her son's interest in genetics led them to take a tour of the IGB. They walked away impressed with the institute's interdisciplinary nature, which inspired them to become donors to the IGB.

Sigman and her late husband David, who was also an alumnus of Illinois, were employees of ExxonMobil for over 30 years. She worked in human resources, while David worked as a lawyer. As employees of a corporation with a science focus, they both had a strong interest in science.

"We believe in good science and I think the opportunity for good science in that arena was very high," Sigman said of the IGB. "I continue to be impressed with what they're doing."

Unique catalytic method opens doors to making useful compounds

go.igb.illinois.edu/catalysts



Above_Chemical and biomolecular engineer and leader of the IGB's Biosystems Design research theme, Huimin Zhao is also the leader of the Center for Advanced Bioenergy and Bioproducts Innovation (CABBI) Conversion Theme.

Researchers have developed a new method that aids in the process of making valuable compounds. A study published in *Nature* reported an innovative catalytic method that combines enzymatic catalysts with photocatalysts.

Huimin Zhao (BSD leader/CABBI/MMG), Steven L. Miller Chair in Chemical Engineering, led the research, which was supported by the NSF and the DOE.

Scientists often use combinations of enzymatic and chemical catalysts to cause reactions that result in higher yields than what can be achieved with enzymes alone. Higher yields are beneficial when scientists want to use these reactions to make useful products such as biofuels and pharmaceuticals. But enzymatic and chemical catalysts aren't naturally compatible; they work best under different conditions and temperatures.

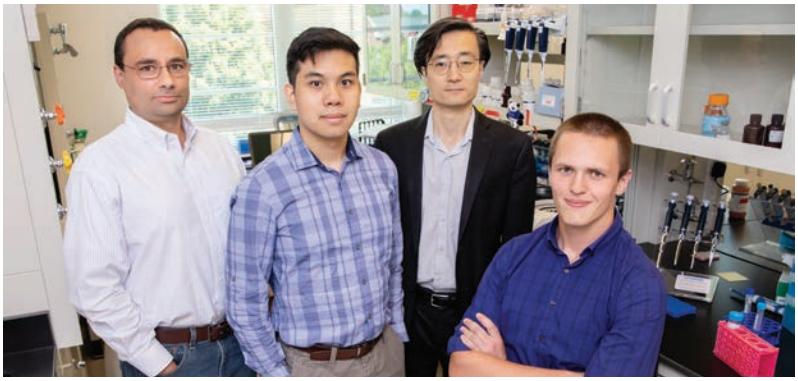
The team studied several enzymes and photocatalysts and found a pair that works together. They not only showed that enzymatic catalysts and photocatalysts can be combined, but that this combination can also be productive. Their method was able to create a few important active pharmaceutical intermediates for producing pharmaceutical drugs.

New CRISPR technique skips over portions of genes that can cause disease

go.igb.illinois.edu/crispr-skip

Researchers have adapted CRISPR gene-editing technology to cause the cell's internal machinery to skip over a small portion of a gene when transcribing it into a template for protein building. This gives researchers a way not only to eliminate a mutated gene sequence, but to influence how the gene is expressed and regulated.

The new CRISPR-SKIP technique, described in the journal *Genome Biology*, does not break the DNA strands but instead alters a single point in the targeted DNA sequence. The work was supported by the NIH, the NSF, and the American Heart Association.



Right_Researchers adapted CRISPR gene-editing technology to help a cell skip over mutated portions of genes. From left, Assistant Professor of Bioengineering Pablo Perez-Pinera, graduate student Alan Luu, Founder Professor of Physics Jun Song and graduate student Michael Gapinske.

"Given the problems with traditional gene editing by breaking the DNA, we have to find ways of optimizing tools to accomplish gene modification. This is a good one because we can regulate a gene without breaking genomic DNA," said bioengineer Pablo Perez-Pinera (ACPP), who led the study with physicist Jun Song (ACPP).

Such targeted editing could one day be useful for treating genetic diseases caused by mutations in the genome, such as Duchenne's muscular dystrophy, Huntington's disease or some cancers.

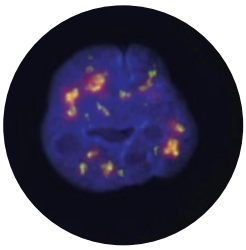
"Cytological ruler" builds 3D map of human genome

go.igb.illinois.edu/ruler

It has been almost 20 years since the human genome was first sequenced, but researchers still know little about how the genome is folded up and organized within cells. A publication in the *Journal of Cell Biology* has now described a new technique that can measure the position of every single gene in the nucleus to build a 3D picture of the genome's organization.

Researchers can examine the position of individual genes using a microscope, but determining the position of every gene at the same time is impossible this way. Professor of Cell and Developmental Biology Andrew Belmont (BSD) and

"Cytological ruler" builds 3D map of human genome continued



Above_Targeting horseradish peroxidase to nuclear speckles (green) produces a diffuse cloud of tyramide-containing molecules (red) that can label nearby DNA (blue). Sequencing the DNA can produce a map of the genome's organization.

colleagues have developed a technique called tyramide signal amplification sequencing (TSA-Seq) that allows the distance of any gene from specific nuclear landmarks to be measured simultaneously.

"The logic of this nuclear organization remains to be determined, but our model would suggest that chromosome movements of just a few hundred nanometers could have substantial functional significance," Belmont says.

A small shift in a gene's position could be sufficient to dramatically enhance the gene's activity, for example.

The researchers say that the technique still needs to be improved, but they hope to use TSA-Seq to map the positions of genes in other cell types and examine how these positions change as cells develop or become diseased. The work was supported by the NIH and the Netherlands Organization for Scientific Research.

Unusual biosynthetic pathway offers a key to future natural product discovery

go.igb.illinois.edu/pathway

Above_Richard E. Heckert Endowed Chair in Chemistry and HHMI Investigator Wilfred van der Donk.

Bacteria are master engineers of small, biologically useful molecules. A new study in *Nature Communications* has revealed one of the tricks of this microbial trade: synthesizing and then later inserting a nitrogen-nitrogen bond, like a prefabricated part, into a larger molecule.

The discovery was made by a collaborative group of chemists at the University of Illinois and Harvard University. Together, they confirmed that two otherwise unrelated, bacterially-produced compounds shared an unusual set of steps in their biosynthetic pathways. The coordinated research efforts that produced this work were supported by the NIH, the HHMI, the Research Corporation for Scientific Advancement, and the Camille and Henry Dreyfus Foundation.

"It's a molecular handle or genetic handle if you wish to now go after other new molecules that people haven't found before," said Wilfred van der Donk (MMG), Richard E. Heckert Endowed Chair in Chemistry and Investigator of the HHMI. "So we're pretty excited both about what's in the paper and also what it allows us to do going forward."

Finding this improbable commonality in the way two dissimilar molecules are produced increased the researchers' confidence in the functional roles of the genes involved. They now have a new genomic signature to add to their lexicon, something they can scan for in other bacterial genomes as they continue the search for useful natural products.

Harnessing microbial communities' division of labor for biofuel, chemical production

go.igb.illinois.edu/division

Above_Associate Professor of Bioengineering Ting Lu, top, with Professor of Food Science and Human Nutrition Yong-Su Jin.

Much like human society, microbial communities have a division of labor. In these complex groups of microorganisms, different microbes are responsible for different tasks, such as the organization or delivery of cell functions.

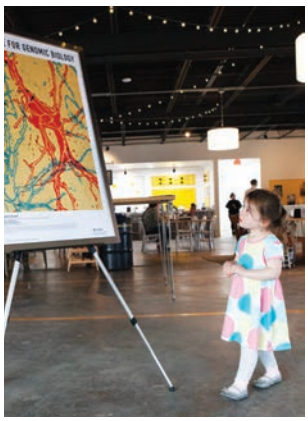
Researchers at the IGB aim to understand more about the division of labor in microbial communities in a new project led by Ting Lu (BCXT/BSD/MME), an associate professor of bioengineering, and Yong-Su Jin (BSD/MME), a professor of food science and human nutrition. Their work is funded by a $1.5 million grant from the DOE.

Microbial communities, which contain a diverse range of species, can do things that individual species can't do on their own, like increasing the strength of the ecosystem. This parallels what happens in nature.

"When we look at the microbes in nature, we know that they do not exist in a single cell or a single population," Lu said. "Instead, they always present in the form of complex communities." The researchers' goal is to uncover the design principles behind the division of labor in these communities. They also plan to use these principles to engineer microbial communities to produce chemicals through a process known as metabolic engineering.

Bold colors and open spaces at Art of Science 8.0 opening

go.igb.illinois.edu/AoS2018



Right_Science buffs and art enthusiasts united to appreciate the annual Art of Science exhibit, which featured images of research subjects ranging from single molecules to communal-living creatures.

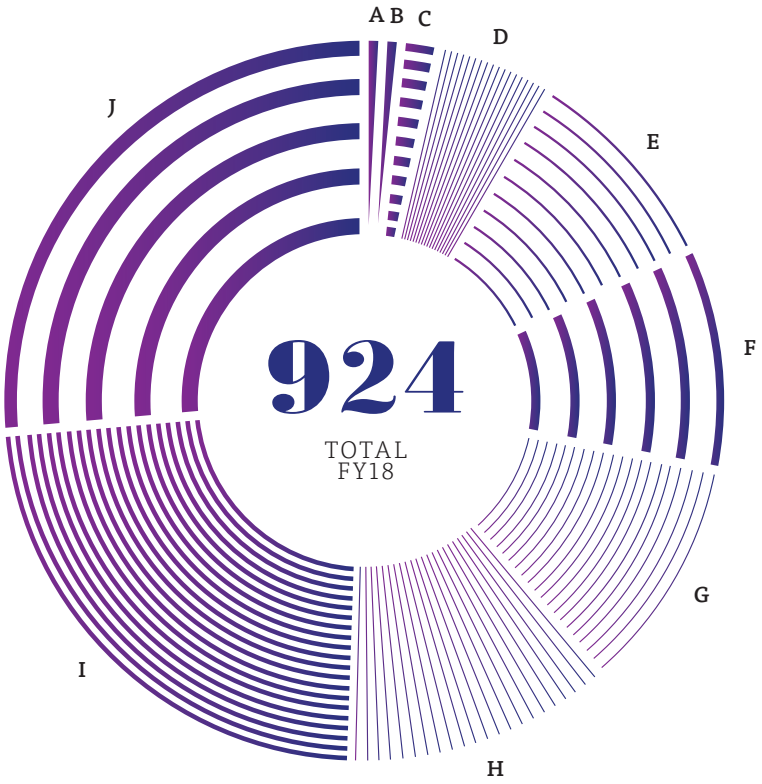
NUMBERS FROM 2018

LOOK OUT FOR

People

Total **924**

- **A** Student Staff_8
- **B** IGB Fellows_9
- **C** Visiting Researchers_15
- **D** Administration_48
- **E** Postdoctoral Researchers_87
- **F** Faculty_93
- **G** Affiliates_99
- **H** Research Staff_109
- **I** Graduate Students_213
- **J** Undergraduates_243



FY18 Economic Development

15 Disclosures

11 Patent Applications

1 License Optioned

4 Patents Issued

Thermostable *C. Bescii* Enzymes
Isaac K. O. Cann, Roderick I. Mackie

Altered Microbiome of Chronic Pelvic Pain
Bryan A. White

Biosynthesis of Oligosaccharides
Yong-Su Jin

Phosphonic Acid Compounds and Screening Method
Wilfred A. van der Donk, William W. Metcalf

Publications

982
Papers published

7 *Science*
5 *Nature*

IGB Faculty in bold

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Arrival routes of first Americans uncertain
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Nature, Vol. 561, No. 7723, 20.09.2018, p. 387-390.

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Nature, Vol. 560, No. 7718, 16.08.2018, p. 355-359.

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continued

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Terminal Pleistocene Alaskan genome reveals first founding population of Native Americans *Nature*, Vol. 553, No. 7687, 11.01.2018, p. 203-207.	Moreno-Mayar, J. Víctor; Potter, Ben A.; Vinner, Lasse; Steinrücken, Matthias; Rasmussen, Simon; Terhorst, Jonathan; Kamm, John A.; Albrechtsen, Anders; Malaspinas, Anna Sapfo; Sikora, Martin; Reuther, Joshua D.; Irish, Joel D.; **Malhi, Ripan S**; Orlando, Ludovic; Song, Yun S.; Nielsen, Rasmus; Meltzer, David J.; Willerslev, Eske.

Core Facilities Use

111
Research groups

298
Users

Outreach

9,000+ people
reached

226
science volunteers

3-92
ages reached

16 connections
with groups at the University of Illinois

13 connections
with community organizations

1,793 hours
science volunteer time

360 hours
of outreach activities

115 days
of outreach events

68
outreach events

22
different locations

Events in 9 cities
Champaign, Urbana, Savoy, Rantoul, St. Louis, Boston, Chicago, Seattle, Mahomet

Events in 4 states
Illinois, Washington, Massachusetts, Missouri

FY18 IGB Grant Awards

Total **$52,081,858**

A DOE_$19,427,601
B NIH_$9,448,581
C NSF_$1,061,981
D EBI/BP & Shell Oil_$2,036,719
E Gates_$15,861,035
F Others (plus USDA)_$4,245,941

Awards

Rashid Bashir, Dean of the University of Illinois College of Engineering and Grainger Distinguished Chair in Engineering (ONC-PM/RBTE) elected National Academy of Inventors Fellow, and Royal Society of Chemistry Fellow.

Alison Bell, Associate Professor of Animal Biology (GNDP) named University Scholar.

Martin Burke, Professor of Chemistry (MMG) named University Scholar.

Brian Cunningham, Donald Biggar Willett Professor of Engineering and Professor of Electrical and Computer Engineering (ONC-PM leader/ MMG) named to Institute of Electrical and Electronics Engineers Photonics Society Distinguished Lecturer Program.

Brendan Harley, Professor, Chemical & Biomolecular Engineering (RBTE leader) received Campus Distinguished Promotion Award, College of Engineering Dean's Award for Excellence in Research, and College of Liberal Arts & Sciences Dean's Award for Excellence in Undergraduate Teaching.

Hannah Holscher, Assistant Professor of Nutrition (MME) received Young Investigator Award from the journal *Nutrients*, and appointed to the Scientific Advisory Board of uBiome.

Princess Imoukhuede, Assistant Professor of Bioengineering (RBTE) received Distinguished Leadership Award from Illinois Mathematics and Science Academy (IMSA).

Paul Kenis, William H. and Janet G. Lycan Professor and Head of Chemical & Biomolecular Engineering (RBTE) named Elio Eliakim Tarika Endowed Chair in Chemical Engineering.

Andrew Leakey, Professor of Plant Biology (GEGC/ CABBI) elected Fellow of the American Association for the Advancement of Science and named University Scholar.

Ting Lu, Associate Professor of Bioengineering (BSD/BCXT/MME) received American Chemical Society Infectious Diseases Young Investigator Award.

Zan Luthey-Schulten, William H. and Janet G. Lycan Professor of Chemistry (BCXT) elected Fellow of the Biophysical Society.

Olgica Milenkovic, Professor of Electrical and Computer Engineering (GNDP/BSD/ ONC-PM) elected Fellow of the Institute of Electrical and Electronics Engineers.

Ray Ming, Professor of Plant Biology (GEGC) elected Fellow of the American Association for the Advancement of Science.

Douglas Mitchell, Professor of Chemistry (MMG) named Alumni Research Scholar Professor of Chemistry, and received Campus Distinguished Promotion Award.

Jeffrey Moore, Murchison-Mallory Professor of Chemistry and Professor of Materials Science and Engineering (BSD) received U.S. Secretary of Energy Achievement Award for the Center for Energy Storage Research project, and received Stephanie L. Kwolek Award from the Royal Society of Chemistry.

Stephen Moose, Professor of Crop Sciences (BSD/CABBI/ GEGC) awarded Karl E. Gardner Outstanding Undergraduate Adviser Award from the College of Agricultural, Consumer and Environmental Sciences.

Gene Robinson (Director/GNDP) elected to the National Academy of Medicine, and awarded Wolf Prize in Agriculture.

Saurabh Sinha, Professor of Computer Science (GNDP/ BSD) elected American Institute for Medical and Biological Engineering Fellow, and named University Scholar.

Amy. J. Wagoner Johnson, Associate Professor, Mechanical Science and Engineering (CGRH/ RBTE) received College of Engineering Dean's Award for Excellence in Research.

Giving and Donor Roll

July 1, 2017 – June 30, 2018
Including corporate gifts related to
World of Genomics

*** Deceased**

Abbott Laboratories

AbbVie Inc.

Bayer CropScience LP

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Tracy BioConsulting LLC

Mark Tracy and Wendy Putnam

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Abbreviations and Acronyms

About the Icons

The success of the IGB depends on collaborations that transcend traditional disciplines and close partnerships between researchers and support staff. Throughout this annual report, we use the icons below to indicate connections to five major research impact areas.

Health

Research that seeks to understand the origins and mechanisms of disease and discovers new ways to promote wellness.

Technology

Research that imagines, develops, and refines new tools that enable discovery and create solutions.

Environment

Research that explores and protects ecosystems, especially those we rely on for food and fuel.

Fundamental Research

"Blue Sky" research that creates the knowledge base needed for future progress.

Community Engagement

Programs that promote open dialogue between genomic research and society.

Research Themes and Centers

ACPP	Anticancer Discovery from Pets to People
BCXT	Biocomplexity
BSD	Biosystems Design
CABBI	Center for Advanced Bioenergy and Bioproducts Innovation
CGRH	Computing Genomes for Reproductive Health
EBI	Energy Biosciences Institute
GEGC	Genomic Ecology of Global Change
GNDP	Gene Networks in Neural and Developmental Plasticity
IGOH	Infection Genomics for One Health
MME	Microbiome Metabolic Engineering
MMG	Mining Microbial Genomes
ONC-PM	Omics Nanotechnology for Cancer Precision Medicine
RBTE	Regenerative Biology and Tissue Engineering

Other Abbreviations and Acronyms

DOE	Department of Energy
IGB	Carl R. Woese Institute for Genomic Biology
HHMI	Howard Hughes Medical Institute
IUB	NASA Astrobiology Institute for Universal Biology
NIH	National Institutes of Health
NSF	National Science Foundation
USDA	United States Department of Agriculture

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Nicholas Vasi

Design
Mirhee Lee

Writing
Claudia Lutz and Emily Scott

Printing
Curtis 1000

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WHERE
SCIENCE
MEETS
SOCIETY

UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN
CARL R. WOESE INSTITUTE FOR GENOMIC BIOLOGY
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