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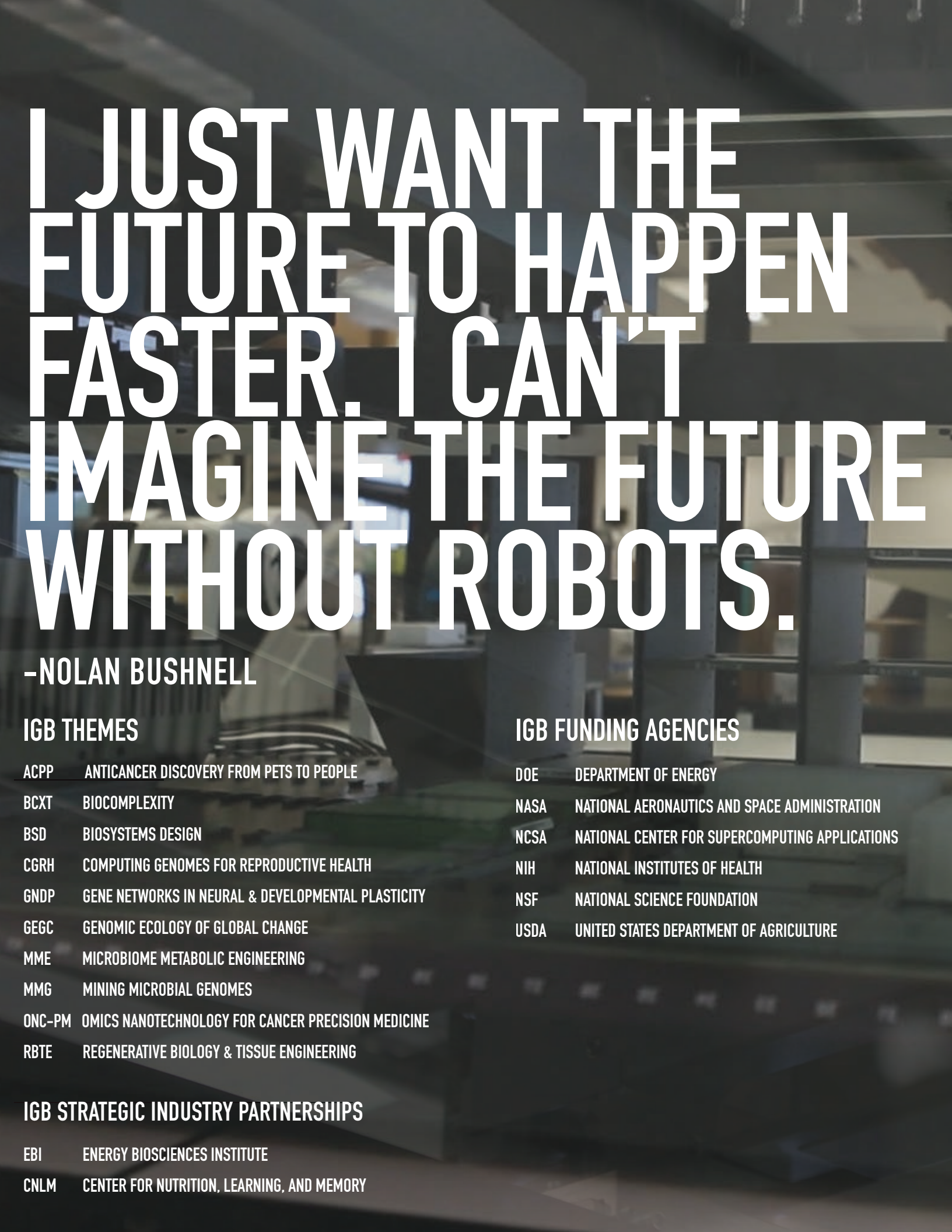
BIOMARKER magazine

CARL R. WOESE INSTITUTE FOR GENOMIC BIOLOGY

PIONEERING ADVANCES IN THE LIFE SCIENCES



I JUST WANT THE FUTURE TO HAPPEN FASTER. I CAN'T IMAGINE THE FUTURE WITHOUT ROBOTS.

–NOLAN BUSHNELL

IGB THEMES

ACPP	ANTICANCER DISCOVERY FROM PETS TO PEOPLE
BCXT	BIOCOMPLEXITY
BSD	BIOSYSTEMS DESIGN
CGRH	COMPUTING GENOMES FOR REPRODUCTIVE HEALTH
GNDP	GENE NETWORKS IN NEURAL & DEVELOPMENTAL PLASTICITY
GEGC	GENOMIC ECOLOGY OF GLOBAL CHANGE
MME	MICROBIOME METABOLIC ENGINEERING
MMG	MINING MICROBIAL GENOMES
ONC-PM	OMICS NANOTECHNOLOGY FOR CANCER PRECISION MEDICINE
RBTE	REGENERATIVE BIOLOGY & TISSUE ENGINEERING

IGB FUNDING AGENCIES

DOE	DEPARTMENT OF ENERGY
NASA	NATIONAL AERONAUTICS AND SPACE ADMINISTRATION
NCSA	NATIONAL CENTER FOR SUPERCOMPUTING APPLICATIONS
NIH	NATIONAL INSTITUTES OF HEALTH
NSF	NATIONAL SCIENCE FOUNDATION
USDA	UNITED STATES DEPARTMENT OF AGRICULTURE

IGB STRATEGIC INDUSTRY PARTNERSHIPS

EBI	ENERGY BIOSCIENCES INSTITUTE
CNLM	CENTER FOR NUTRITION, LEARNING, AND MEMORY

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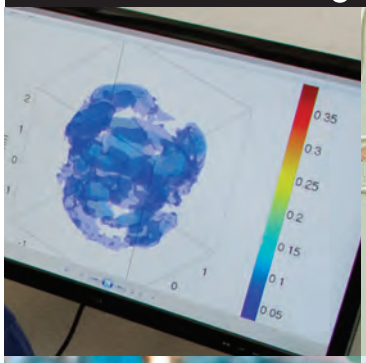

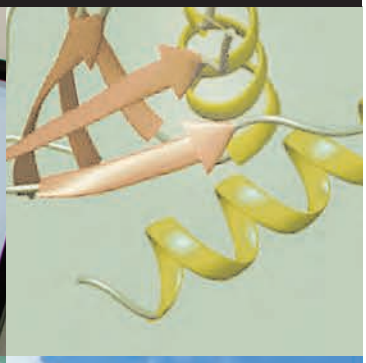

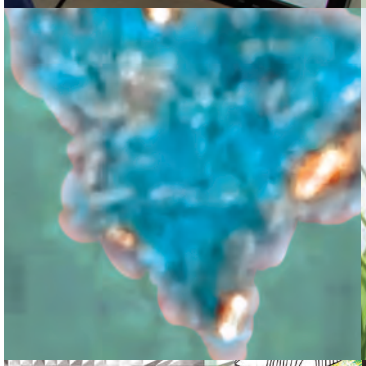

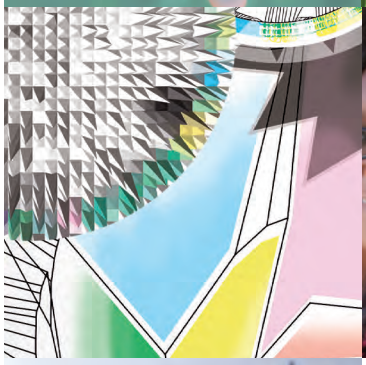

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DIRECTOR'S MESSAGE

SKILLFUL INVENTION & THE ESSENTIAL ELEMENT OF IMAGINATION

Why do we build robots? As our ability to build sophisticated machinery improves, we are automating tasks that were once entrusted only to skilled technicians. How do we identify endeavors that will benefit from automation? In science, this question takes on additional dimensions. Scientific research demands precision, consistency, tirelessness, and unbiased observation—all traits that are more closely aligned with the nature of robots than humans. It also demands creativity, adaptability, curiosity and passion—human traits that we may associate with the robots of science fiction, but not those we encounter in reality.

In the world of research-related technology, robots enable science of a scope and scale that would otherwise be impossible. One example of this comes from the Carl R. Woese Institute for Genomic Biology's Genomic Ecology of Global Change research theme, thanks to funding from the Department of Energy's Transportation Energy Resources from Renewable Agriculture (TERRA) program. With the creation of automated systems like the Mobile Energy-Crop Phenotyping Platform (MEPP), a self-driving crop-sensing robot developed by Gutgsell Endowed Professor of Crop Sciences and Plant Biology Stephen Long and colleagues, researchers will be able to engage in systems-level, large-scale crop development efforts that manual quantification of plant growth and yield could not support.

Another foray into robotics at the Institute, this one based in the Biosystems Design research theme, pushes the boundaries of biology and engineering at the molecular level. The Illinois Biological Foundry for Advanced Biomanufacturing (iBioFAB) was conceived and designed by Biosystems Design researchers, led by Steven L. Miller Chair of Chemical and Biomolecular Engineering Huimin Zhao, to automate key processes in synthetic biology. Beginning in 2013 with an award from the Roy J. Carver Charitable trust, they have built the iBioFAB into an adaptable platform that can precisely perform many of the key laboratory tasks involved in the production of designer organisms. Instead of slogging through the many tedious steps involved in genome editing only to discover that the tweak they've made is not optimal, researchers can ask iBioFAB to simultaneously build and test many iterations of an edited gene construct to discover which one makes the most antibiotic or the fastest-growing crop plant.

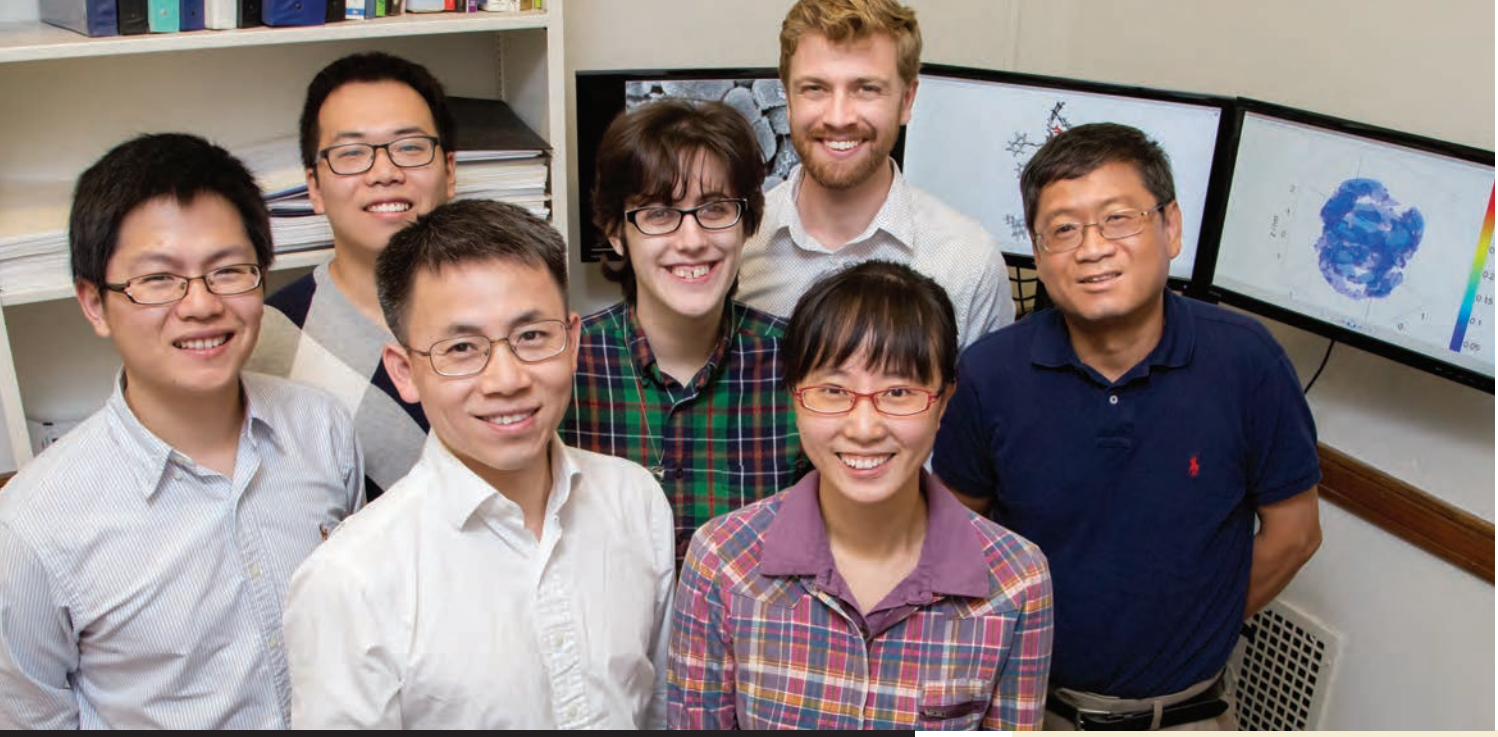
This issue of *Biomarker* explores the functionality of these and other cutting-edge technologies in detail, along with some of the innovative work they support. For example, an ongoing effort to accelerate the discovery and synthesis of novel antibiotics and other therapeutic drugs by leveraging the naturally occurring biochemical capabilities of microbial genomes can benefit greatly from the iBioFAB's ability to perform many genome editing experiments in parallel to uncover those capabilities.

"We create robots for the same reason that we create any other tool: to complement our own abilities, empowering us to reach new achievements and new discoveries."

Biomarker Volume 10 also offers a glimpse at some of the other highlights of our diverse portfolio of research this year: an innovative mathematical model that describes a key aspect of the emergence of life; an improved technique for producing *in vitro* environments for cell growth that enable translational cancer research; and a novel algorithm for the identification of genome sequence variants that predict disease. Each of these breakthroughs owes much to the technological developments that came before it, but would be impossible without the force of human ingenuity.

For now, creativity belongs to us, not to machines. We most often rely on robots for precision, organization, and repetition, leaving us free to think and to dream. It may not always be this way; we already use our smartest machines, such as IBM's Watson, to make some types of Big Data-driven connections that our minds cannot. No matter how this division of labor shifts, though, one thing will remain constant. We create robots for the same reason that we create any other tool: to complement our own abilities, empowering us to reach new achievements and new discoveries. The IGB continues to innovate and discover thanks to the creativity, the passion, and the other (for now) uniquely human strengths of its members.

GENE E. ROBINSON
Director
Carl R. Woese Institute for Genomic Biology



BACTERIAL HOLE PUNCHER COULD BE NEW BROAD-SPECTRUM ANTIBIOTIC

Front row, from left: Materials Science and Engineering Professor Jianjun Cheng and postdoctoral researcher Yan Bao. Back row, from left: postdoctoral researcher Menghua Xiong, graduate students Ziyuan Song and Rachael Mansbach, Materials Science and Engineering Professor Andrew Ferguson, and Biochemistry Professor Lin-Feng Chen.

Bacteria have many methods of adapting to resist antibiotics, but a new class of spiral polypeptides developed at the IGB targets one thing no bacterium can live without: an outer membrane.

The polypeptides, which are short protein chains, act as bacterial hole-punchers, perforating the bacterial membrane until the cell falls apart. The antimicrobial agents are dressed for their mission in a positively charged shell that lets them travel in body fluids, protected from interacting with other proteins, and also attracts them to bacterial membranes.

Led by Professor of Materials Science and Engineering Jianjun Cheng (RBTE), the researchers published their findings in the *Proceedings of the National Academy of Sciences*. Cheng also is affiliated with the departments of chemistry and of bioengineering. NSF and NIH supported this work.

"When you have an infection, it can be very difficult for a doctor to know which bacteria is infecting you," said postdoctoral researcher Menghua Xiong, a co-first author of the paper. "Many antimicrobial agents can only cure one class of bacteria. A doctor may try one class, and if that doesn't work, try another class. We need more broad-spectrum antimicrobial agents."

SINCE THE SPIRAL STRUCTURES SIMPLY POKE HOLES IN THE PHYSICAL STRUCTURE OF THE MEMBRANE, IT WOULD BE MUCH HARDER FOR BACTERIA TO FORM RESISTANCE,

The new antimicrobial polypeptides are specially designed to fold into a rigid spiral, resulting in a rod-like structure ideal for punching holes in the bacterial membrane.

"We use a very set mechanism to puncture the bacterial membrane," Cheng said, "so the polypeptides don't really care whether the bacteria are gram-positive or gram-negative. They just kill the bacteria independent of their other surface properties."

Such structures have been investigated for various medical applications, but because they do not like water, they do not travel well in bodily fluids. In addition, other molecules in the cell could interact with the polypeptide to disrupt the spiral structure, making it ineffective in puncturing the membrane.

IGB researchers and their collaborators addressed these challenges by attaching positively charged ions to the backbone of the spiral, creating a protective shell around the polypeptide so that it is both water soluble and shielded from cross-reactions. The shielded spiral structures are resistant to changes in temperature or pH, so they have a stability and predictability that similar agents lack, Cheng said. Furthermore, the positive shell has the advantage of targeting bacterial membranes while decreasing interaction with human cells.

"At the molecular level, there are big differences between bacterial and human cells in the membranes," Xiong said. "The cell membrane lipids in bacteria have a lot of negative charges, and this polypeptide is positive, so it interacts with the negatively charged bacterial membrane. But with human cells, the interaction is weaker."

Many drugs are very targeted, interacting with a particular protein or interfering with a particular pathway in the bacterial cell. Bacteria can develop resistance to the antibiotic by circumventing the specific target. Since the spiral structures simply poke holes in the physical structure of the membrane, it would be much harder for bacteria to form resistance, Xiong said. In addition, the new antimicrobial agents could be coupled with other, targeted drugs to enhance their effectiveness.

"The polypeptides punch holes in the membrane, which makes it very easy for other drugs to go through and bypass some of the drug-resistant mechanisms," Cheng said. "Together, they work even better than a single agent."

Pictured from left to right: Nicolas De J. Corona, Adrell Núñez, Taras K. Oleksyk, and Yimell Corona.

CLOSE ANCESTORS ARE LONG GONE, AND TODAY'S SOLENODONS ARE THE ONLY REMNANT OF A VERY ANCIENT GROUP OF MAMMALS.

ENDANGERED VENOMOUS MAMMAL PREDATES DINOSAURS' EXTINCTION, STUDY CONFIRMS

The University of Illinois and University of Puerto Rico (UPR) have completely sequenced the mitochondrial genome for the *Hispaniolan solenodon*, filling in the last major branch of placental mammals on the tree of life.

The study, published in *Mitochondrial DNA*, confirmed that the venomous mammal diverged from all other living mammals 78 million years ago, long before an asteroid wiped out the dinosaurs. Animal scientist Al Roca (CRGH/GNDP) served as the lead researcher on the project.

"It's just impressive it's survived this long," said co-first author Adam Brandt, a postdoctoral researcher at Illinois. "It survived the asteroid; it survived human colonization and the rats and mice humans brought with them that wiped out the solenodon's closest relatives."

The study also supports recent findings that the Dominican Republic contains genetically distinct northern and southern populations that should be conserved as separate sub-species. Furthermore, the study found that the southern population has little diversity, whereas the northern population is much more diverse.

An offspring's nuclear DNA is a mixture of genes from each parent, while mitochondrial DNA is passed directly from mother to offspring without changes, creating a genetic record that researchers can use to trace back the lineage of organisms.

Brandt and co-first author Kirill Grigorev, a bioinformatician at the Caribbean Genome Center, analyzed the samples using two different methods to determine the sequence of nucleotides (building blocks that make up DNA) of the solenodon's mitochondrial genome. Independently, the two methods produced the exact same results.

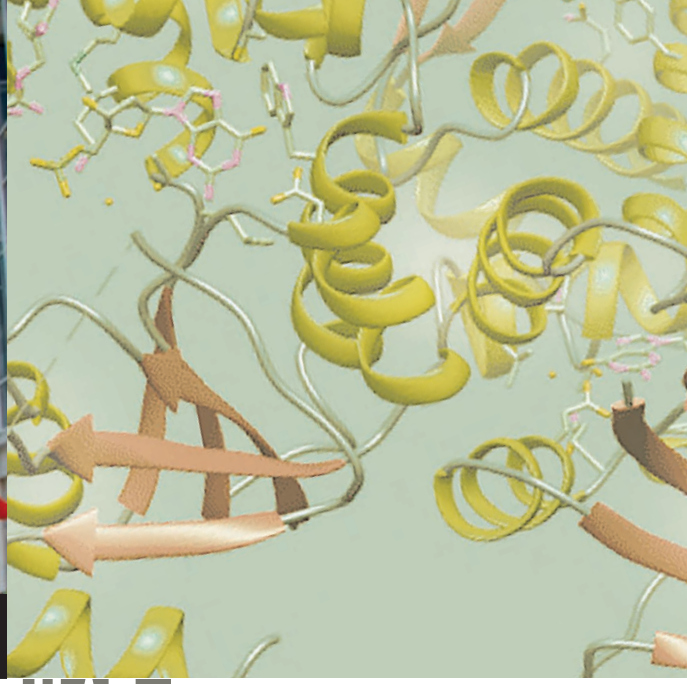
"IT SURVIVED THE ASTEROID; IT SURVIVED HUMAN COLONIZATION AND THE RATS AND MICE HUMANS BROUGHT WITH THEM THAT WIPED OUT THE SOLENODON'S CLOSEST RELATIVES."

A previous study used a different set of genes to estimate that solenodons diverged from mammals during the Cretaceous Period 76 million years ago. Working with an expert at Texas A&M, this study used a very different method but still established a similar estimate: 78 million years.

Interestingly, these two estimates align with a hypothesis regarding how the solenodon came to inhabit the island of Hispaniola. Some geologists speculate that the island was part of a volcanic arc connected to Mexico 75 million years ago and over time the arc has moved eastward.

"Whether they got on the island when the West Indies ran into Mexico 75 million years ago, or whether they floated over on driftwood or whatever else much later is not very clear," said Roca.

What they do know is that any close ancestors are long gone, and today's solenodons are the only remnant of a very ancient group of mammals. While the solenodon is venomous and resembles a "giant rat with Freddy Krueger claws" (according to Roca), it evolved in the absence of carnivores. Today, it is threatened by cats and dogs introduced by humans as well as habitat loss.



STUDY ADDS TO EVIDENCE THAT VIRUSES ARE ALIVE

A new analysis supports the hypothesis that viruses are living entities that share a long evolutionary history with cells, researchers report. The study offers the first reliable method for tracing viral evolution back to a time when neither viruses nor cells existed in the forms recognized today, the researchers say. The new findings appear in the journal *Science Advances*.

Until now, viruses have been difficult to classify, said crop scientist Gustavo Caetano-Anollés (GEGC), who led the new analysis with graduate student Arshan Nasir. In its latest report, the International Committee on the Taxonomy of Viruses recognized seven orders of viruses, based on their shapes and sizes, genetic structure and means of reproducing.

"Under this classification, viral families belonging to the same order have likely diverged from a common ancestral virus," the authors wrote. "However, only 26 (of 104) viral families have been assigned to an order, and the evolutionary relationships of most of them remain unclear."

Part of the confusion stems from the abundance and diversity of viruses. Fewer than 4,900 viruses have been identified and sequenced so far, even though scientists estimate there are more than a million viral species. Many viruses are tiny–significantly smaller than bacteria or other microbes–and contain only a handful of genes. Others, like the recently discovered miniviruses, are huge, with genomes bigger than those of some bacteria.

The new study focused on the vast repertoire of protein structures, called "folds," that are encoded in the genomes of all cells and viruses. Folds are the structural building blocks of proteins, giving them their complex, three-dimensional shapes. By comparing fold structures across different branches of the tree of life, researchers can reconstruct the evolutionary histories of the folds and of the organisms whose genomes code for them.

The researchers chose to analyze protein folds because the sequences that encode viral genomes are subject to rapid change; their high mutation rates can obscure deep evolutionary signals, Caetano-Anollés said. Protein folds are better markers of ancient events because their three-dimensional structures can be maintained even as the sequences that code for them begin to change.

By comparing fold structures across different branches of the tree of life, researchers can reconstruct the evolutionary histories of the folds and of the organisms whose genomes code for them.

The researchers analyzed all of the known folds in 5,080 organisms representing every branch of the tree of life, including 3,460 viruses. Using advanced bioinformatics methods, they identified 442 protein folds that are shared between cells and viruses, and 66 that are unique to viruses.

"This tells you that you can build a tree of life, because you've found a multitude of features in viruses that have all the properties that cells have," Caetano-Anollés, pictured above, said. "Viruses also have unique components besides the components that are shared with cells."

Using the protein-fold data available in online databases, Nasir and Caetano-Anollés used computational methods to build trees of life that included viruses.

The data suggest "that viruses originated from multiple ancient cells … and co-existed with the ancestors of modern cells," the researchers wrote. These ancient cells likely contained segmented RNA genomes, Caetano-Anollés said.

Some scientists have argued that viruses are nonliving entities, bits of DNA and RNA shed by cellular life. They point to the fact that viruses are not able to replicate outside of host cells, and rely on cells' protein-building machinery to function. But much evidence supports the idea that viruses are not that different from other living entities, Caetano-Anollés said.

"Many organisms require other organisms to live, including bacteria that live inside cells, and fungi that engage in obligate parasitic relationships – they rely on their hosts to complete their lifecycle," he said. "And this is what viruses do."

Some viruses also have genes for proteins that are essential to translation, the process by which cells read gene sequences to build proteins, Caetano-Anollés said. The lack of translational machinery in viruses was once cited as a justification for classifying them as nonliving, he said.

"This is no more," Caetano-Anollés said. "Viruses now merit a place in the tree of life. Obviously, there is much more to viruses than we once thought." ■

WATCHING 'JUMPING GENES' IN ACTION: REAL-TIME OBSERVATION OF TRANSPOSON ACTIVITY IN LIVING CELLS

"Jumping genes" are ubiquitous. Every domain of life hosts these sequences of DNA that can "jump" from one position to another along a chromosome; in fact, nearly half the human genome is made up of jumping genes. Depending on their specific excision and insertion points, jumping genes can interrupt or trigger gene expression, driving genetic mutation and contributing to cell diversification.

Since their discovery in the 1940s, researchers have been able to study the behavior of these jumping genes, generally known as transposons or transposable elements (TE), primarily through indirect methods that infer individual activity from bulk results. However, such techniques are not sensitive enough to determine precisely how or why the transposons jump, and what factors trigger their activity.

Reporting in the *Proceedings of the National Academy of Sciences*, scientists at the IGB have observed jumping gene activity in real time within living cells. The study is the collaborative effort of Illinois physics professors Thomas Kuhlman (BCXT) and Nigel Goldenfeld (BCXT Theme Leader/CGRH/GNDP). Their work was supported by NSF, NASA, and the Alfred P. Sloan Foundation.

"In this study, we were able to see that there is actually more of this jumping gene action going on than might have been expected from previous studies," said Kuhlman, whose team performed the *in vivo* experiments. "What's more, we learned that the rates at which these genes jump depend sensitively on how the cells are growing—if there is food available for the cells to grow, for example. In other words, jumping gene activation isn't entirely random, it's dependent on environmental feedback."

To observe these individual cellular-evolution events in living cells, Kuhlman's team devised a synthetic biological system using *E. coli*. The scientists coupled the expression of fluorescent reporters—genes that encode fluorescent proteins—to the jumping activity of the transposons.

The scientists could then visually record the transposon activity using fluorescent microscopy.

"These are genes that hop around and change location within the genome of a cell," said Kuhlman. "We hooked that activity up to a molecular system, such that when they start hopping around, the whole cell fluoresces. In our experiment, cells fluoresced most when they weren't very happy. One school of thought suggests that an increased mutation rate like this might be an advantage in such unhappy conditions, for cells to diversify."

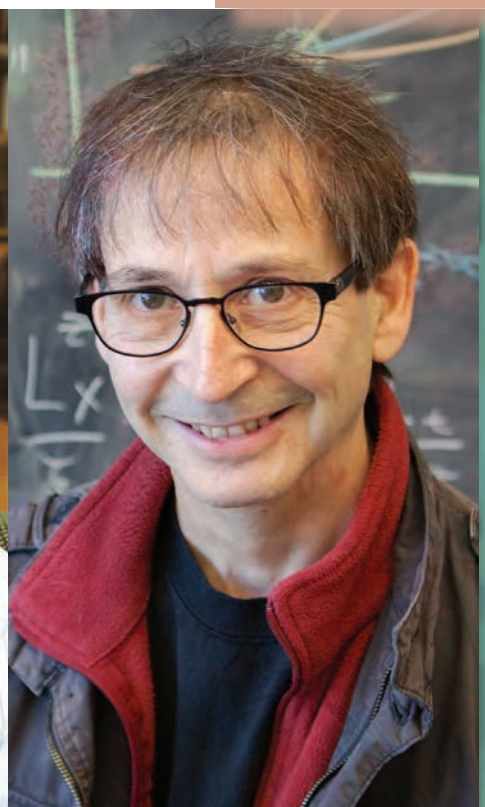
In order to help design the experiment and to calculate what would have happened if the jumping occurred in a purely random fashion, Goldenfeld's team developed computer simulations of the growth of bacterial colonies and predicted what the experimental signal would look like in the random case. These calculations showed that the experiments could not simply be interpreted as random transposon activity and even provided clues as to sources of non-randomness, including environmental feedback and heredity.

"To extract signals and conclusions from the raw data, simulation and theoretical calculations were integral to the experimental design and interpretation," said Goldenfeld.

"The over-arching long-term research goal is a deeper understanding of how evolution works at the molecular level. Direct observation of how genomes in cells restructure themselves allows for a precise determination of adaptation rates and may shed light on a host of important evolutionary questions, ranging from the emergence of life to the spread of cancer, where cells undergo rapid mutations and transformations of their genomes," added Kuhlman.

JUMPING GENE ACTIVATION ISN'T ENTIRELY RANDOM, IT'S DEPENDENT ON ENVIRONMENTAL FEEDBACK.

Thomas Kuhlman (left) and Nigel Goldenfeld.



CHANGING GENETIC MEDICINE IN AFRICA

In collaboration with the National Center for Supercomputing Applications (NCSA), the IGB High-Performance Biological Computing group (HPCBio) is helping to change the way genomic medicine is researched and practiced in Africa.

Much of what is known about the genetics of diseases is based on people with European ancestry. Additionally, African populations face unique health challenges.

"The H3Africa project is looking at the relationship between genetics and susceptibility to disease in African populations," said former HPCBio Director Victor Jongeneel (CGRH/GNDP). "A large amount of time has been spent looking at these relationships in Caucasians and East Asians, but much of that research is irrelevant in the African context."

The Genome Analysis Working Group from the Consortium for Human Heredity and Health in Africa (H3Africa) has partnered with the Pan African Bioinformatics Network for H3Africa (H3ABioNet) and the Wellcome Trust Sanger Institute on research that will allow them to construct a genotyping chip to test for genomic variants found specifically in African populations.

Genomic variation plays a large role in disease predisposition and drug response. Thus, it is important to develop tools for genomic variant discovery in people of African descent, who have been underrepresented in many worldwide genetic diversity measurement projects.

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For the project, the researchers gathered 348 samples from both urban and rural parts of the continent that were then deeply sequenced by researchers at Baylor College of Medicine. The researchers also used publicly available sequence data from the 1000 Genomes project and over 2,000 low-depth whole-genome sequences from the African Genome Variation Project.

The research aims to make a list of genomic variants for a bead-array–based genotyping chip specific to people of African descent that will be built by Illumina. The chip will be a tool for rapid and inexpensive genotyping of individuals and will aid in studies of human evolution and of genomic bases of disease.

A group of bioinformaticians led by Professor Nicola initially planned to perform the data analysis at the University of Capetown. They quickly realized that they lacked the computing capacity, so they partnered with HPCBio and NCSA. Due to its international visibility and importance for global health, the project was granted a "strategic" allocation on NCSA's Blue Waters supercomputer.

The Mulder team, together with Manj Sandhu's team at the Wellcome Trust Sanger Institute, developed the computational workflow to extract genomic variants from the 348 samples sequenced at Baylor. HPCBio helped initiate this workflow on Blue Waters, and the NCSA teams monitored performance on the machine.

Besides limitations in physical hardware, the project researchers did not have a ready-to-use software for calling the variants. A variant calling pipeline that Illinois. developed in partnership with Mayo Clinic was modified to match the project requirements.

As part of the project, the NSCA and HPCBio teams also tested new methods of transferring data more efficiently from all over Africa to South Africa. The project also provided a testbed for some new tools that NCSA researchers have developed in the course of running Blue Waters that they hope to make more broadly available.

THE H3AFRICA PROJECT IS LOOKING AT THE RELATIONSHIP BETWEEN GENETICS AND SUSCEPTIBILITY TO DISEASE IN AFRICAN POPULATIONS

Victor Jongeneel

Even as larvae, honey bees are tuned in to the social culture of the hive, becoming more or less aggressive depending on who raises them, researchers reported in a recent study.

"We are interested in the general issue of how social information gets under the skin, and we decided to take a chance and ask about very young bees that are weeks away from adulthood," said IGB Director and Swanlund Professor of Entomology Gene Robinson, who led the research with Christina Grozinger, a professor of entomology at Pennsylvania State University, and Clare Rittschof, now an assistant professor of entomology at the University of Kentucky.

"In a previous study, we cross-fostered adult bees from gentle colonies into more aggressive colonies and vice versa, and then we measured their brain gene expression," Robinson said. "We found that the bees had a complex pattern of gene expression, partly influenced by their own personal genetic identity and partly influenced by the environment of the colony they were living in. This led us to wonder when they become so sensitive to their social environment."

In the new study, supported by the NSF and published in the journal *Scientific Reports*, Robinson and colleagues again cross-fostered bees, but this time, bees were transferred between colonies as larvae in order to manipulate their early life experiences. The larvae were from a variety of genetic backgrounds, with sister larvae divided between high- and low-aggression colonies.

THEY WERE SURPRISED TO SEE THAT THE BEES RETAINED THE SOCIAL INFORMATION THEY HAD ACQUIRED AS LARVAE...

The larvae were then removed from their foster hives and put into a neutral laboratory environment one day before they emerged as adults. The researchers tested their aggressiveness by exposing them to an intruder bee.

They were surprised to see that the bees retained the social information they had acquired as larvae. Those raised in aggressive colonies had an aggressive score that was 10 to 15 percent higher on average than those raised in the gentler colonies.

"Even sisters born of the same queen but reared in different colonies differed in aggression, demonstrating the potency of this environmental effect," Robinson said.

The aggressive honey bees also had more robust immune responses than their gentler counterparts, the team found.

"We challenged them with pesticides and found that the aggressive bees were more resistant to pesticide," Grozinger said. "That's surprising considering what we know from vertebrates, where stress in early life leads to a diminishment of resilience. With the bees, we saw an increase in resilience."

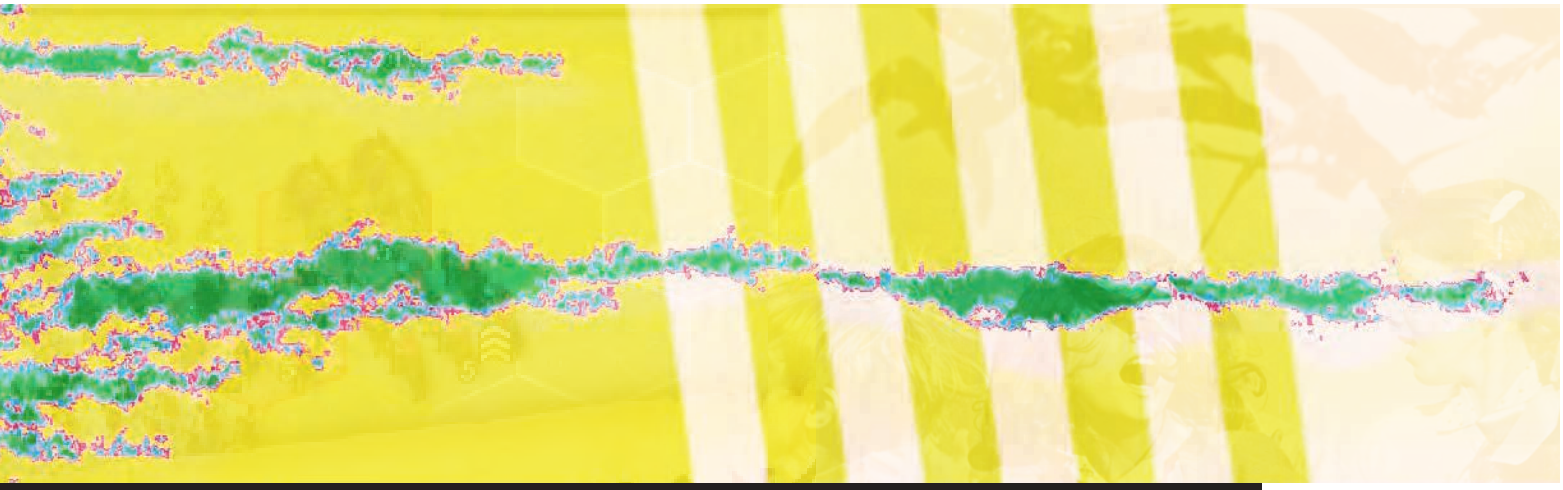
The researchers don't yet know how the social information is being transmitted to the larvae. They tested whether the bees differed in size, which would suggest that they had been fed differently, but found no size differences between aggressive and gentle bees.

"Adult honey bees are well known for their sociality, their communication skills and their ability to adjust their behavior in response to the needs of the hive," Rittschof said.

"In mammals, including humans, the effects of early life social interactions often persist throughout adulthood despite additional social experiences," she said. "A similar pattern in honey bees has broad implications for our understanding of social behavior within the hive and in comparison with other species."

From left: Clare Rittschof, & Christina Grozinger

WIMPS OR WARRIORS? HONEY BEE LARVAE ABSORB THE SOCIAL CULTURE OF THE HIVE



STRAIGHT UP, WITH A TWIST: NEW MODEL DERIVES HOMOCHIRALITY FROM THE BASIC REQUIREMENTS FOR LIFE

Life is quirky. Although the molecules that make up all living things obey physical and chemical laws, they do so with a puzzling twist. How did the distinctive molecular features of life emerge, and what can they tell us about life on Earth and elsewhere in the universe?

Swanlund Professor of Physics Nigel Goldenfeld (BCXT Theme Leader/CGRH/GNDP), graduate student Farshid Jafarpour, and postdoctoral researcher Tommaso Biancalani made a breakthrough in one of the most central chemical quirks of life as we know it: homochirality, the uniform "handedness" of biological molecules. Their new model addressing the emergence of this feature, published in *Physical Review Letters* and highlighted by *The American Physical Society*, suggests that homochirality can be used as a universal signature of life.

Many chemicals, organic or otherwise, are chiral; that is, if the structure of each was reflected in a mirror, its "looking-glass" copy could not be turned or flipped to match the original. Like a pair of gloves, the left-handed and right-handed versions of a chiral molecule are functionally equivalent, but their fundamental asymmetry makes them distinct.

Inorganic reactions produce and consume both versions of chiral molecules at equal rates. This is what makes the chirality of biological molecules, such as sugars produced by microbes and plants or the amino acids that make up proteins, so shocking. In every living thing on Earth, all amino acids are left-handed, and all sugars are right-handed.

Many scientists have proposed hypotheses for how this remarkable asymmetry became dominant. Perhaps the most prominent, put forward by noted physicist Sir Charles Frank in 1953, argued that homochirality could be produced by one of the fundamental properties of life—autocatalysis, the ability to self-replicate.

"FOR ME, THE MOST EXCITING THING IS THAT THIS MECHANISM SHOWS THAT HOMOCHIRALITY IS REALLY A BIOSIGNATURE OF LIFE," SAID GOLDENFELD.

He argued that in a system where one left-handed or right-handed molecule begets more like itself, and each type inhibits the self-replication of the other, an initial unevenness in the ratio, appearing by chance, would ultimately allow one handedness to completely outcompete the other.

Frank's work was ground-breaking, but it left unanswered questions that no subsequent work has adequately addressed. His idea appeared to rely on the inhibition of self-replication of each chirality by the other, a mechanism that might not have existed early on in life's history.

The Illinois team wanted to develop a simpler model, one based on only the most basic properties of life: self-replication and disequilibrium. They showed that with only these minimal requirements, homochirality appears when self-replication is efficient enough.

The work, which was funded by the NASA Astrobiology Institute for Universal Biology directed by Goldenfeld, leads to a key conclusion: since homochirality depends only on the basic principles of life, it is expected to appear wherever life emerges, regardless of the surrounding conditions.

"For me, the most exciting thing is that this mechanism shows that homochirality is really a biosignature of life," said Goldenfeld. "I think that looking for homochirality in the organic molecules that have been detected [on other planets] would be a fantastic way to look for life there."

Karen Sears

BEFORE NATURE SELECTS, GENE NETWORKS STEER A COURSE FOR EVOLUTION

WHAT HAPPENS WHEN A CHANCE EVENT, LIKE A MUTATION, CHANGES THE ACTIVITY OF ONE GENE. HOW MUCH WILL THE WHOLE NETWORK CHANGE, AND HOW WILL DEVELOPMENT BE AFFECTED?

Natural selection is a race to reproduce, a competition between individuals with varying traits that helps direct the evolution of a species. As scientists begin to explore the complex networks of genes that shape the form and function of each individual, they can ask a new question about evolution: How do the structures of these gene networks determine which individuals appear on the starting line, silently influencing evolution before competition has even begun?

Associate Professor of Animal Biology Karen Sears (GNDP/RBTE) and Associate Professor of Mathematics Zoi Rapti, along with collaborators at Illinois and four other institutions, have addressed this question by exploring the gene network that guides limb development in mammals. Their study was published in *PLOS Genetics*.

They found that during early development, when limbs are first forming, gene activity in this network varies little; later, when detailed limb structure is beginning to emerge, the network changes in structure, and gene activity varies more widely. This pattern may make it easier for evolution to tweak, rather than remodel, limb structure.

"When we look at the evolutionary record of animals, we find that there are some forms that have evolved repeatedly, and some that have never evolved," said Sears, who led the study. "I want to know the role that development has in generating these patterns."

Many genes encode proteins that influence or regulate each other's activity. These functional connections, and the genes that participate in them, can be imagined as the threads and intersections of a spider's web. Sears, Rapti, and colleagues wanted to know what happens when a chance event, like a mutation, changes the activity of one gene. How much will the whole network change, and how will development be affected?

This pattern may make it easier for evolution to tweak, rather than remodel, limb structure.

Using published data on developmental gene interactions, they created a model of how genes interact during early and late stages of limb development. The model allowed them to pluck at the spider web of genes, and watch how much the rest of the web is disrupted.

The researchers found that in early limb development, the network resists the spread of change; even when one gene's activity is altered, the network as a whole continues to function almost as usual. Later in limb development, however, the architecture of the network is different, and a change in one gene's activity has a more widespread impact.

In addition, an empirical investigation of gene activity during development in four different mammals—mice, bats, opossums, and pigs—showed that activity of developmental genes differs more in late development than in early development.

Together, these theoretical and empirical findings supported Sears' strongest initial hypothesis, that genomic mechanisms restrict the degree to which early limb development can vary in mammals. From an evolutionary perspective, this makes sense.

"If early development is disrupted, limb development will be severely disrupted," said Sears. "Later development, which doesn't have as many downstream impacts, might be expected to be more free to vary because the consequences of that variation would be less dire."

Sears, Rapti, and coauthors were brought together by the Illinois BioMathematics Program, an NSF-funded project that promotes research collaboration among biology and mathematics undergraduates and faculty members. The BioMath Program has led to a variety of innovative research efforts.

NEW SYNTHETIC TUMOR ENVIRONMENTS MAKE CANCER RESEARCH MORE REALISTIC

From left, Jeffrey Moore, Joshua Grolman, and Kristopher Kilian.

Tumors are notoriously difficult to study in their natural habitat—body tissues—but a new synthetic tissue environment may give cancer researchers the next-best look at tumor growth and behavior. Researchers have developed a new technique to quickly create a cell habitat that mimics tissue environments in the laboratory.

"This is really the first time that it's been demonstrated that you can use a rapid methodology like this to spatially define cancer cells," said Assistant Professor of Materials Science and Engineering Kristopher Kilian (RBTE). "That's important, because once you have that architecture, then you can ask fundamental biological questions." Kilian said these questions range from the basic: how do macrophages signal to the breast cells? To the more long-term: can therapeutics be used to disrupt that communication?

Kilian, Professor of Chemistry Jeffrey Moore (BSD), graduate student Joshua Grolman, and colleagues developed a process for quickly synthesizing a customizable, three-dimensional hydrogel (a material similar to firm Jello that mimics many properties of living tissue) seeded with a range of multiple cell types typically found within an organ or tissue of interest. Their process combines the advantages of a more realistic experimental environment with the speed and convenience of a simple Petri dish.

To illustrate the potential of their more efficient and modifiable technique, Kilian and colleagues mixed breast cancer cells with cells called macrophages, which signal cancer cells to spread and grow into a tumor. They were able to observe the cells' activity and growth within the hydrogel.

The process the team came up with to produce the synthetic environments takes an estimated 15 minutes, discounting the time it takes to grow the cells and a few other steps, Grolman said. Using their method, the hydrogel can also be easily produced in any three-dimensional shape that suits the needs of a particular experiment. The researchers compared the freshly manufactured hydrogel to soft-serve ice cream leaving the machine; basic manipulation of the angle and rate of flow guides the resulting shape.

Not only is the process quick and simple to implement, but the device designed by the team to enable it is easy to manufacture. Grolman described it as a tool that could not only help expedite basic research, but also aid in drug screening.

"The microenvironment actually has a significant effect on how the cells respond to a drug," Grolman said. "These companies might have the next big drug, but they might not know it."

"The long-term vision would be: A patient goes in and finds out they've been diagnosed with some sort of solid tumor," Kilian said. "You take a biopsy of those cells, you put it into this device, grow them and see how they respond to different treatments."

Their research, supported by NSF and the American Cancer Society Illinois Division, was published in *Advanced Materials*.

HUMAN TRIALS OF CANCER DRUG PAC-1 CONTINUE WITH NEW INVESTMENT

Clinical trials of the anti-cancer agent PAC-1 are continuing to expand, thanks to a $7 million angel investment from an anonymous contributor who originally invested $4 million to help get the compound this far in the drug-approval pipeline.

The USDA also granted PAC-1 orphan drug status for the treatment of glioblastoma multiforme, a deadly brain cancer. This designation is meant to encourage development of drugs to treat rare diseases or conditions affecting a small subset of the population. Some steps in the approval process are aided or expedited for orphan drugs.

An estimated 12,120 new cases of glioblastoma are expected in the U.S. in 2016. The median survival with standard-of-care therapy is 14.6 months.

PAC-1 targets an enzyme, procaspase-3, that is elevated in cancer cells. When activated, this enzyme spurs cell death. The drug first showed promise in the treatment of pet dogs with spontaneously occurring cancers.

A Phase I clinical trial of PAC-1 in human cancer patients began in 2015 and has so far involved about a dozen patients with a variety of late-stage cancers. The human trial is being conducted at the University of Illinois Cancer Center in Chicago and at the Sidney Kimmel Cancer Center at Johns Hopkins University. A Champaign-based company, Vanquish Oncology, is the regulatory sponsor for the research.

Phase I trials are meant to determine the maximum tolerable dose of a cancer agent and are not tests of a drug's efficacy, said Illinois chemistry professor Paul Hergenrother (ACPP Theme Leader), who discovered PAC-1's anti-cancer properties more than a decade ago. He worked with veterinary clinical medicine professor Timothy Fan (ACPP) to first test the drug in pet dogs with cancer.

"There have been no unexpected toxicities and the dose escalation is progressing well," Hergenrother said of the human trials. "This new investment will enable us to provide more cancer patients with access to the drug as we move forward with the Phase I trials."

"We know that PAC-1 can be safely combined with curative intent radiation therapy and oral temozolomide in dogs with primarily glioma, or brain tumors," said Fan, who has worked closely with veterinary neurologist Dr. Michael Podell and veterinary radiation oncologist Dr. Jayme Looper of the Chicago-based MedVet Medical and Cancer Centers for Pets to conduct clinical trials of the drug in pet dogs.

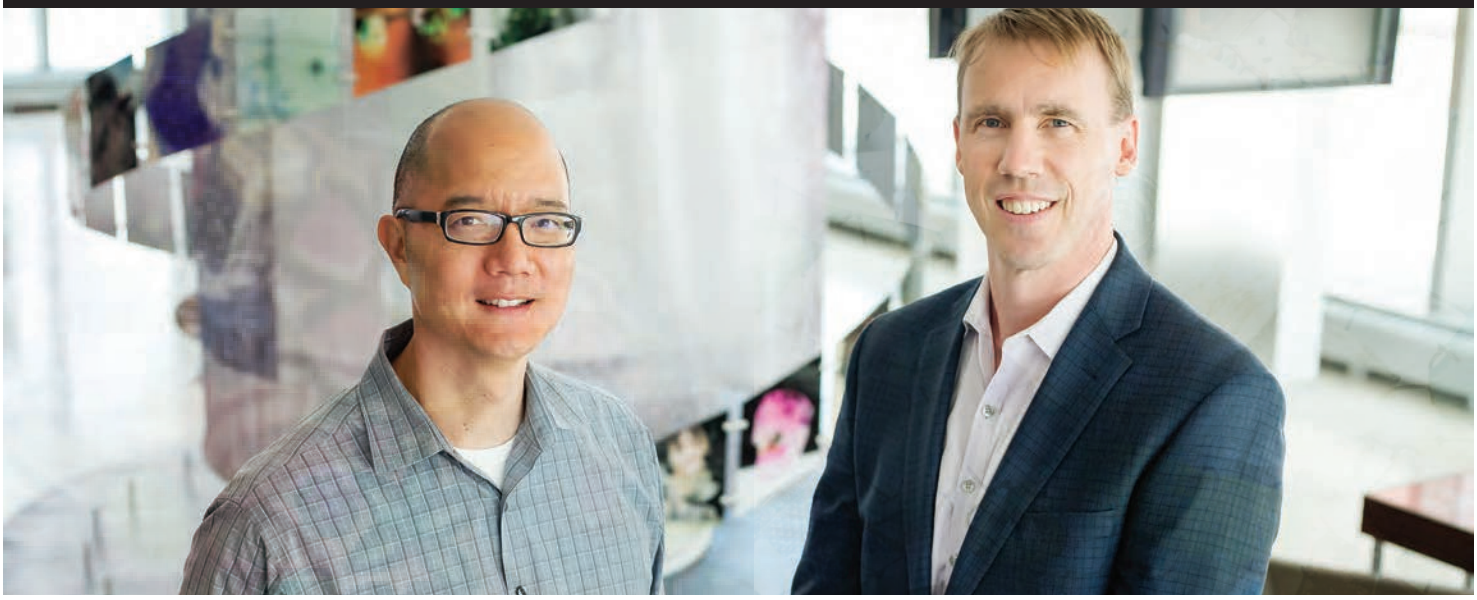
"Surgical resection, radiation and temozolomide is the standard treatment regimen for glioblastoma," Hergenrother said.

A second component of the Phase I trial will test PAC-1 in combination with temozolomide in human glioblastoma patients whose tumors have returned after standard treatment, he said.

"We've been at this now for more than 10 years, and we're excited to be able to continue down this road," Hergenrother said. "It takes a lot of time, a lot of effort and a lot of money to do human clinical trials. So to have the means to expand access to PAC-1 from a dozen patients to, we hope, hundreds, is very exciting. That is what will allow us to get some definitive data on the drug."

"PAC-1 is one of only a few drug agents developed and tested in animals and in humans at a single institution," said Dr. Arkadiusz Dudek, a physician and professor of hematology and oncology at the University of Illinois at Chicago who is directing the human clinical trials of the drug. "It is gratifying to see new funding to allow this work to continue."

The drug first showed promise in the treatment of pet dogs with spontaneously occurring cancers.



Timothy Fan and Paul Hergenrother

RUNNING ON SUNLIGHT: NEW RESEARCH ENDEAVORS BREAK TRAIL FOR BIOFUEL DEVELOPMENT

HIGH-POWERED ROBOTS THAT HELP BRING PLANT BREEDING TECHNIQUES INTO THE 21ST CENTURY;

America's oil consumption represents a lion's share of a global demand that our planet cannot sustain. Imagine, instead of acres of oil wells on barren land, endless fields of towering green sugarcane or sorghum, with each stalk producing renewable and sustainable biofuel. What innovations do we need to need to make this verdant dream a reality? Illinois's answer, growing to fruition at the IGB, involves seeing familiar crops in a new way; constructing high-powered robots that help bring plant breeding techniques into the 21st century; and taking advantage of a strong foundation in genomic information and technology.

In the last year, with support from the Department of Energy's (DOE) Advanced Research Projects Agency-Energy (ARPA-E) program, IGB faculty in the Genomic Ecology of Global Change research theme and the Energy Biosciences Institute have made significant progress toward the development of two alternative biofuel sources: sugarcane and sorghum.

OIL FROM AN UNLIKELY SOURCE

One of ARPA-E's forward-looking initiatives is Plants Engineered to Replace Oil (PETRO), which funds high-risk, high-reward projects that seek to develop plants that directly produce new drop-in fuels that could substitute for petroleum. Illinois researchers answered the call by imagining and successfully achieving a way to produce large quantities of oil from sugarcane. Their most recent study demonstrates the economic benefits of this technology relative to soybean oil.

"We thought that if we could go back to the drawing board, we'd need a very productive crop. And we would also need something that could grow on land that isn't being used intensively for food. We came up with sugarcane and sweet sorghum," recalled Gutgsell Endowed Professor of Crop Sciences and Plant Biology Stephen Long (BSD/EBI/GEGC).

Long leads PETROSS (the final two letters stand for sugarcane and sweet sorghum), a PETRO-funded project to develop these two plants as oil-producing crops. Other key researchers include Professor of Crop Sciences Steve Moose (BSD/GEGC), Robert Emerson Professor of Plant Biology Donald Ort (GEGC Theme Leader/BSD), Associate Professor of Crop Sciences Erik Sacks (EBI), Professor of Agricultural and Biological Engineering Vijay Singh (GEGC), and Steven L. Miller Chair Professor of Chemical and Biomolecular Engineering Huimin Zhao (BSD Theme Leader/EBI/MMG). Illinois' partner institutions on the project include the University of Florida, Brookhaven National University, and the University of Nebraska-Lincoln.

OILCANE COULD PROVIDE FUEL TO SATISFY MORE THAN TWO-THIRDS OF THE COUNTRY'S CURRENT DIESEL AND JET FUEL CONSUMPTION.

The team has already succeeded in altering sugarcane metabolism to convert sugars into lipids, fatty substances that include oils, which could be used to produce biodiesel. The natural makeup of sugarcane is typically a meager 0.05 percent oil. Within a year of starting the project, the team was able to boost oil production 20 times, to approximately 1 percent. This spring, the so-called "oilcane" plants were producing 12 percent oil. The ultimate goal is to achieve 20 percent. Long and colleagues have engineered oilcane to feature further advantages over sugarcane: increased cold tolerance and more efficient photosynthesis. The latter leads to greater biomass production and even more oil.

"If all of the energy that goes into producing sugar instead goes into oil, then you could get 17 to 20 barrels of oil per acre," Long explained. "A crop like this could be producing biodiesel at a very competitive price, and could represent a perpetual source of oil and a very significant offset to greenhouse gas emissions, as well." Another advantage of oilcane is that leftover sugars in the plant can be converted to ethanol, providing two fuel sources in one.

In an analysis published in the journal *Biofpr*, the team evaluated the land area, technology, and costs required for processing oilcane biomass into biodiesel under a variety of oil production scenarios, from 2 percent oil in the plant to 20 percent. These numbers were compared with normal sugarcane, which can be used to produce ethanol, and soybean.

The analysis showed that oilcane with 20 percent oil in the stem, grown on under-utilized acres in the southeastern United States, could provide fuel to satisfy more than two-thirds of the country's current diesel and jet fuel consumption. This represents a much greater proportion than could be supplied by soybean, even if the entire crop went to biodiesel production. Furthermore, oilcane could achieve this level of productivity on a fraction of the land area that would be needed for crops like soybean and canola, and it could do so on land considered unusable for food crop production.

Thanks in part to these results, PETROSS was granted a rarely-awarded third round of funding from the DOE this summer to continue developing oilcane and sorghum, as well as seeking additional investors and commercial partners. The project will continue work to increase yields and to improve cold tolerance to expand the growing region of oilcane, which is currently limited to small regions in Florida, Louisiana and Texas.

EXPANDING THE HORIZONS OF BIOFUEL CROP GROWTH

In April 2016, a group of researchers led by

Associate Professor of Plant Biology Andrew Leakey (EBI/GEGC) embarked on a closely related effort: with a 3-year, $5 million award from ARPA-E's OPEN funding initiative, Leakey and colleagues aimed to increase the water use efficiency (WUE) of sorghum, enhancing its utility as a bioenergy crop.

Sorghum is a versatile, drought-tolerant plant and a promising biofuel source. Like nearly all plants, sorghum transpires through stomata: small pores on the surface of the leaf that allow for gas exchange. By decreasing the stomata, researchers hope to increase WUE by reducing the amount of moisture lost. In addition, by shifting a larger percentage of photosynthetic activity to lower leaves, the higher local humidity will further reduce water loss.

By combining these approaches, the team predicts via its mathematical models that it may develop sorghum with a 40% improvement in WUE. "That means that we should be able to expand the growing area into regions that are currently too dry to produce a profitable crop," said Leakey. "And in the areas that are already suitable for growing, plants will suffer less in drought years, and make more biomass with the water that there is."

The project will identify naturally-occurring alleles that increase WUE and use biotechnology to manipulate sorghum genes for the same purpose. All in all, this research could unlock more than 9 million new acres currently unusable for energy crop production, and increase production on currently farmed land by nearly 30% on average. Much of the newly available land is located to the west of sorghum's current range, inspiring the project's name, WEST (Water Efficient Sorghum Technologies).

WEST's interdisciplinary research team includes Long, Ort, Assistant Professor of Plant Biology Carl Bernacchi (EBI/GEGC), Associate Professor of Crop Sciences Patrick Brown (EBI/GEGC), and collaborating scientists at the University of Wisconsin-Madison, the University of Nebraska-Lincoln, Cornell University, and USDA Agricultural Research Services in Lubbock, Texas.

"We can combine both natural alleles and those we've enhanced through genomic methods into novel lines," said Long, who is serving as co-director of WEST. "We anticipate that many of these genetic markers will be similar in other C4 crops, which means it would be possible to translate many of our findings to increase the efficiency of the closely related crops corn and sugarcane."

A ROBOTIC REVOLUTION IN PLANT BREEDING

Efforts to develop and improve any biofuel crop, including sugarcane and sorghum, relies on careful quantitation of how the plants actually do in the field. How well do they grow in different environments and weather conditions? How should they be managed to help them resist pests, diseases, and drought? A key step in answering these questions is phenotyping, obtaining accurate measurements of how well plants are actually growing and producing grain or biomass.

THIS RESEARCH COULD UNLOCK MORE THAN 9 MILLION NEW ACRES CURRENTLY UNUSABLE FOR ENERGY CROP PRODUCTION, AND INCREASE PRODUCTION ON CURRENTLY FARMED LAND BY NEARLY 30% ON AVERAGE.

ARPA-E's TERRA program aims to greatly accelerate agricultural research by supporting the creation of systems that will streamline the labor-intensive phenotyping step of farming and crop development, using bioenergy sorghum as a test crop. A third Illinois project, TERRA-Mobile Energy-Crop Phenotyping Platform (MEPP), is well on the way to addressing these challenges at the end of its first year of funding.

Automating tasks such as assessing the growth, health and biomass of individual plants and integrating these data with genetic and environmental information requires the concerted efforts of experts from multiple fields. The MEPP research team is led by Long, and includes Bernacchi, Brown, Ort, Singh, and researchers from Cornell University and Signetron Incorporated. Bernacchi is a co-director.

One of MEPP's main innovations is a semi-autonomous crop-monitoring robot, a rugged vehicle the size of a Golden Retriever equipped with miniature tank treads and a panel of miniature sensors, including hyperspectral, HD and thermal cameras, weather monitors, and LiDAR scanners, that will quantify key aspects of plants and the growing environment. The robot is based on autonomous rovers that search for accident victims in collapsed buildings and other confined, hazardous spaces.

The extensive data collected by the robot will be used to create a 3D reconstruction of each plant in a crop in order to estimate biomass yield. An analytical pipeline will associate these data with genome sequence information to identify high-yielding combinations of bioenergy plant lines, environmental conditions, and management practices.

"Some of the advantages of the platform that we have are its low cost and its high mobility," said Research Assistant Professor of Civil and Environmental Engineering Joshua Peschel, who led the first year of development of the robot. "The other thing to remember is that [the robot is] where the real action is happening, so if we can capture soil moisture and temperature in this general area and look up at how much light is coming through, then that's a game-changer."

At an inaugural field day event for the TERRA program, hosted this June by the University of Arizona, some of the most enthusiastic attendees were representatives of growers' associations for crops including sorghum, cotton, corn, and wheat. Growers spoke directly with researchers about how deliverables such as improved crop lines and cheap, automated monitoring systems like the TERRA-MEPP robot could positively and broadly impact agriculture.

ARPA-E Director Ellen Williams emphasized the importance of this type of technology transfer in her remarks at the event. "This technology has to work," she said, "but also be feasible." Efforts like MEPP, WEST and PETROSS continue to live up to ARPA-E's motto—"changing what's possible" for biofuel production, and for our society.

From left: Don Ort, Ellen Williams, and Steve Long

COMPGEN TEAM BUILDS ANCESTRAL TREES TO DETERMINE DISEASE-CAUSING GENETIC VARIANTS

VARIANTS CAN BE PASSED DOWN FROM GENERATION TO GENERATION, CREATING A MAP OF ANCESTRAL GENOMIC HISTORY.

Many of our most widespread diseases, such as diabetes, cancer, cardiovascular disease, and mental illness, are associated with variants in our genes. How do these variants in our genomes carry across generations, and how do they ultimately affect our health? IGB researchers are trying to unlock the mystery.

Parsing out ancestry-related genomic variations requires some data crunching. To put it in perspective, within each human genome, there are 46 chromosomes, and a single chromosome can have 6.5 million variants. Variants can be passed down from generation to generation, creating a map of ancestral genomic history. Each of those variants may play a unique role in our health.

Using novel algorithms, researchers from CompGen, a collaborative computational genomics initiative between the Coordinated Science Laboratory and the IGB, are employing the supercomputing power of NCSA's Blue Waters to scan 2,500 genomes to determine how variants transfer through ancestral ties.

Armed with this information, they can start to understand how our ancestry makes us either susceptible or resilient to diseases.

"How our genomic variants are partitioned across geographic and ethnic diversity is really important, both for understanding human evolutionary history and patterns of migration and globalization, but also very important for understanding health and disease, which is our major focus," said Derek Wildman (CGRH Theme Leader), a CompGen researcher and professor of molecular and integrative physiology at Illinois.

Wildman, who is working with Don Armstrong, a research scientist at the IGB, and Monica Uddin (CGRH), an associate professor of psychology, says past research examining ancestry and disease have relied upon self-reported ethnicity, a limiting factor.

Genomics is quickly becoming the discipline that generates the most data, surpassing other big data producers, like YouTube and Twitter, in scale.

"A lot of disease research has based ethnic categorizations along self-reported ethnicity, but genetic variation is more subtle and complex than socially constructed categories such as race," said Wildman. "We're all mixed to varying degrees with different histories, and that complexity, which we can determine using Blue Waters, likely plays a role in our health and disease."

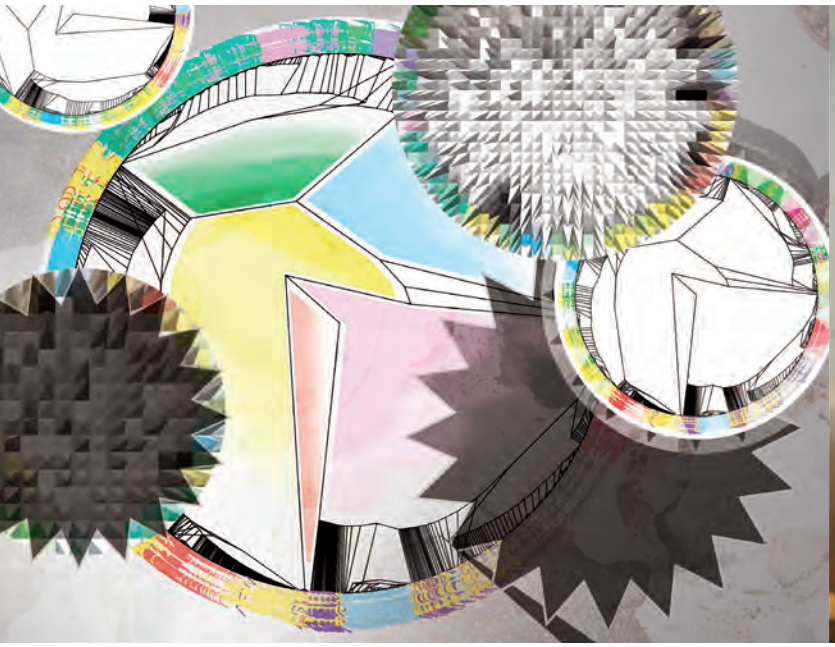
When looking at what causes disease, it is additionally important to disambiguate between genetic and external factors of particular ethnic groups. Wildman, for example, has found that in terms of pregnancy, African Americans are at a greater risk for pre-term birth than white Americans. The reason for this is something this team is still investigating.

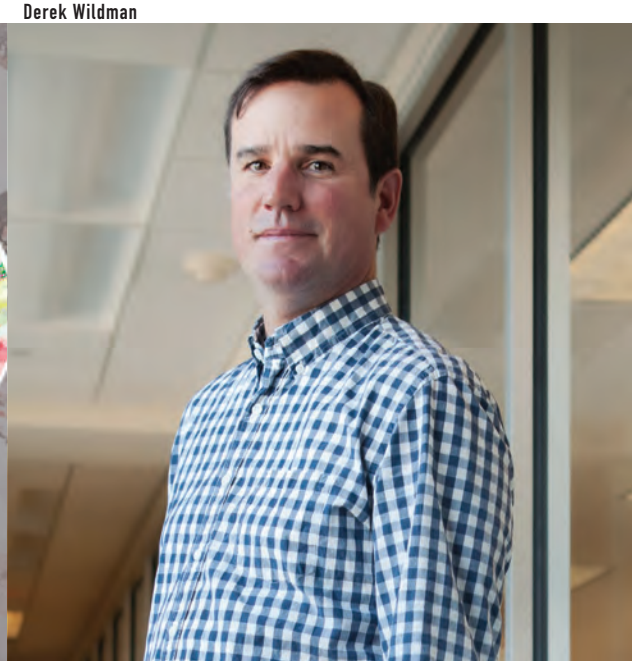
"We're not sure whether that's due to environment, psycho-social factors, a history of racism and segregation, or genetics," said Wildman. "We haven't been able to tease them apart, but it seems worthwhile to examine all those aspects. Having accurate ancestral trees in relation to genetic variants is a key component."

To determine disease-causing genetic variants, the team needs to solve another genetic problem that's emerging: genomics is quickly becoming the discipline that generates the most data, surpassing other big data producers, like YouTube and Twitter, in scale. That's where Blue Waters can help.

"There are more possible phylogenetic trees from the 2,500 genomes we're analyzing than there are electrons in the universe," said Wildman. "So looking at all of those would be prohibitive, but there are approaches on Blue Waters that allow you to simulate phylogenetic trees and get an idea of what the correct ones are."

"We're working to make better maps of ancestral and genomic history and to see the genetic landscape more accurately," said Wildman. "Ultimately, knowing what diseases you may be susceptible to, based on your genetics, means you can take action and make better informed decisions about your health."





Derek Wildman

From left: Shelby Clark, & Carleigh Frazier

THE PARTNERSHIP EXTENDS FISK'S COURSE OFFERINGS BY BROADCASTING BIOINFORMATICS SEMINARS TAUGHT AT ILLINOIS TO FISK STUDENTS AND FACULTY.

COLLABORATING TO STRENGTHEN THE RESEARCH WORKFORCE OF TOMORROW

The KnowEnG Big Data to Knowledge, Center of Excellence at the IGB is partnering with Fisk University in Nashville, Tenn., in an innovative program to promote diversity in the biomedical, behavioral, and clinical research workforce. IGB's collaboration aims to prepare underrepresented minority undergraduates for entry into competitive M.D. or graduate programs by teaching them to apply computational thinking and use statistical and informatics tools to address biomedical research challenges.

KnowEnG is one of 11 NIH-funded Big Data to Knowledge (BD2K) Centers of Excellence. NIH funds collaborations between institutions with BD2K Centers and institutions serving students from backgrounds that are underrepresented in research. These collaborations allow students to have learning and research experiences at the intersection of computer science and biology, biochemistry, molecular biology, and mathematics.

"Fisk has adopted a strategic STEM research and research training development plan that affirms the cross-disciplinary and enhanced quantitative and computational components of contemporary discovery," Lee Limbird, Dean of Fisk's School of Natural Sciences, Mathematics and Business explained. "We have intentionally fostered an interdisciplinary research culture that crosses all of our STEM areas of biology, chemistry, biochemistry and molecular biology, computer science, mathematics, and physics/ materials science."

The partnership extends Fisk's course offerings by broadcasting bioinformatics seminars taught at Illinois to Fisk students and faculty. Tools developed by the Center are being integrated in Fisk undergraduate courses and laboratories.

"Collaborating with Illinois … will give our students a chance to do research with top-notch scientists ... The program will also improve biology, chemistry, computer science and mathematics curricula at Fisk and enhance research collaboration between Fisk and Illinois faculty," said Fisk computer scientist Lei Qian.

The Fisk students work on research projects during the academic year under the mentorship of faculty whose research aligns with the BD2K Initiative. They also have the opportunity to do a summer internship with the Illinois High-Performance Biological Computing (HPCBio) group. Next year, Mayo Clinic, a KnowEnG partner, will also offer internships.

Carleigh Frazier and Shelby Clark were the first two Fisk interns to come to Illinois. Frazier hopes to be a dermatologist and do research in her own practice. Clark wants to be an obstetrician/ gynecologist helping women in developing countries. They both believe that what they learn through the program will help them in their future careers.

Frazier and Clark also participated in the Illinois Graduate College's Summer Research Opportunity Program (SROP), which helps students from populations underrepresented in graduate study to explore careers in research. SROP activities include writing workshops, GRE prep, and participation in research teams.

Fisk faculty attend summer short courses in data carpentry and computational genomics at Illinois, allowing them to establish collaborations that will provide them and their students with research opportunities, foster relationships, and work together on innovations in course design.

Ultimately, the collaboration's partners hope to increase diversity in Big Data biomedical research discovery through an evidence- and experience-driven program that will prepare professionally confident minority trainees.

Anticancer Discovery from Pets to People

NEW THEMES REFLECT THE RISING TIDE OF GENOMIC HEALTH INNOVATION AND PRECISION MEDICINE

To ensure that research initiatives at the IGB remain cutting edge and responsive to new avenues and technologies, members of Illinois' academic community are always welcome to propose new research themes. Three new themes were established within the last year, all focused on aspects of human health.

THREE NEW THEMES WERE ESTABLISHED WITHIN THE LAST YEAR, ALL FOCUSED ON ASPECTS OF HUMAN HEALTH.

Anticancer Discovery from Pets to People (ACPP) studies comparative tumor oncology and genomics in dogs and cats with naturally occurring cancer. Cancers that arise in pet animals more closely resemble human cancers than the diseases of laboratory animals, and findings from this work will eventually benefit both animal and human patients.

Professor of Chemistry Paul Hergenrother is leading this close-knit theme, which has pioneered a strategy to transform natural products into new compounds. Dramatic breakthroughs in cancer therapy come from new drugs that affect molecular processes in cancer cells; the theme employs genomic information and techniques to identify novel molecular processes to serve as targets for treatment, and uses new screening platforms to find chemicals that influence these processes and can be advanced as therapeutics.

Members have already validated a novel cancer target (activation of a protein called procaspase-3), and developed a promising drug (PAC-1) for otherwise untreatable cancers. They plan to move from target discovery and genomic validation to compound discovery, mechanistic studies in cell culture and rodents, and to treating pets with cancer. The most promising compounds will move to human clinical trials.

Microbiome Metabolic Engineering (MME) explores the relationship between the human microbiome (the complete collection of microbes within the body that determine many bodily functions like protection from disease and nutrition) and health, including how the microbiome can deal with negative environmental effects such as toxins, and how it reacts to positive changes such as increased fiber in diets. The theme is headed by Professor of Animal Sciences Isaac Cann, who is also a member of the Mining Microbial Genomes research theme and the Energy Biosciences Institute.

MME members will examine not only adult microbiomes, but also the establishment and development of microbiomes in infants and children. In collaboration with two ongoing research initiatives at Illinois–STRONG (Synergistic Theory and Research on Obesity and Nutrition Group) Kids and IKIDS (Illinois Kids Development Study)–the researchers will identify unique pathways in the human/microbiome milieu that impact human health and nutritional status.

Knowledge generated by MME may eventually lead to strategies to establish and maintain healthy, beneficial microbiomes, thereby promoting overall wellbeing and helping to cure or prevent serious disorders, such as infection.

Omics Nanotechnology for Cancer Precision Medicine (ONC-PM), led by Professor of Electrical and Computer Engineering Brian Cunningham with the Macro and Nanotechnology Laboratory (MNTL) develops new technology to use personalized medicine (individually custom tailored healthcare based on genes, environment, and lifestyle) to identify and manage cancerous tumors. They are pioneering novel low-cost genomic "liquid biopsies" involving finger sticks to collect blood samples in the home.

Selecting optimal therapeutic regimens remains challenging. Often, there are many therapies that can slow disease progression, but they work only for some patients. Moreover, tumors can develop mutations that allow them to evade the treatment. There are no reliable predictive factors, and performing a biopsy on a tumor is invasive and expensive.

ONC-PM theme members focus on using genomics and nanotechnology to develop methods to characterize tumors and monitor how they grow, and to design tools that track material shed in the blood by tumors (biomarkers). The theme is collaborating with clinicians at the Mayo Clinic and leading experts in biomarker identification and validation from the University of Wisconsin to translate their findings into cancer treatments for patients.

BUILDING A FULLY-AUTOMATED TOMORROW WITH IBIOFAB

ILLINOIS BIOLOGICAL FOUNDRY FOR ADVANCED BIOMANUFACTURING PROVIDES A NEW MANUFACTURING PARADIGM FOR CHEMICALS, MATERIALS, AND BIOLOGICS.

"We think the future should be something automated, or even autonomous. We believe in full automation, and we want to build versatility and flexibility into that system."

It might sound like dialogue from a science fiction novel, but that's actually IGB graduate student Ran Chao, talking about the Illinois Biological Foundry for Advanced Biomanufacturing, or iBioFAB. Designed and built by PI and Steven L. Miller Chair of Chemical and Biomolecular Engineering Huimin Zhao (BSD theme leader/MMG/EBI) and Co-PI Christopher Rao (BSD/EBI/MME/RBTE), Professor of Chemical and Biomolecular Engineering, iBioFAB is a one-of-a-kind robotic platform for rapid prototyping and manufacturing of biological systems and parts.

As part of the Global Biofoundry Consortium (see sidebar), iBioFAB represents a new breed of technology in synthetic biology: one that prioritizes standardization, modularity, and above all, automation. "[iBioFAB] has the potential to really accelerate our biological engineering work—I think this is the future of our field," said Zhao.

iBioFAB wasn't the first robot at the IGB. That honor goes to a liquid handling system—a machine that handles pipetting tasks involving samples and reagents much faster than a human could—in the EBI. Zhao and Rao had both used that machine as part of their work within the EBI, but were frustrated by its limitations: "It was not very customizable and there were lots of bugs in the program," said Zhao. "The functions were very restricted."

This was fresh on the researcher's minds when the opportunity emerged to apply for funding from the Roy J. Carver Charitable Trust in 2013, a private philanthropic organization that supports biomedical and scientific research as well as youth educational needs.

"I worked on the proposal with a few colleagues," recounts Zhao, "but we weren't sure what we actually wanted to build. That kind of funding isn't always available: it's a custom-designed system, not something like a Liquid Chromatography Mass Spectrometer [a commonly used piece of equipment]. It was hard to justify an application, because you don't know what kind of applications it could have."

The team received $2 million to realize their dream, and set out to build a robot with far more potential than any stock machine. Components came from several vendors, with substantial help from Thermo Fisher in solidifying the design.

"Our first idea was that we wanted to automate DNA cloning," says Zhao. "But we wanted to build something that could do more than just DNA cloning. That's why we built this as an integrated robotic system—it's not just for cloning, not for one application. It can do many things, and it can evolve to do new things."

> **"It's not just for cloning, not for one application. It can do many things, and it can evolve to do new things."**

As it is today, iBioFAB consists of a platform with over 20 modular instruments. Plate readers detect and measure changes, while "peelers and sealers" wrap and unwrap samples to prevent contamination. Incubators, a centrifuge, a liquid-handling system and thermocyclers round out the rest of the most-used equipment.

But the most important, and most distinctive, part of iBioFAB is its central robotic arm, which is approximately seven feet long and able to move up and down a 16-foot-long track to interact seamlessly with various instruments. More impressively, the arm features six degrees of freedom, giving it a range of motion equivalent to a human arm.

"The robotic arm is basically the link between different equipment, and each piece of equipment is handling some elementary steps—in chemical engineering we call them unit operations," explains Chao. These units of operation combine to form "process modules," each of which represent a standard technique such as DNA assembly, that's common to many avenues of research.

Though they look seamless, these process modules are driven by extensive programming that tells the robot what to do and where to go, down to the last millimeter. Much of the work is incredibly precise, and that precision must be replicated in the code. For now, Chao does most of the programming himself; because it requires thorough knowledge of both the programming language and the experimental procedure, it takes a special person to be able to code for iBioFAB, a "biologist-programmer."

"In the beginning, we had to program—no matter how complex or how many steps it takes the program to finish—we had to program it in one complete go and try to debug that," explains

Chao. “And that takes a long time—weeks—to have a stably running program for some of these longer workflows.”

“But with our standardized process modules,” he adds, “we’re able to program, debug, and test them separately.” That means when the robot needs to perform a complicated experiment, researchers can assemble the program by combining the appropriate process modules in a matter of days, rather than programming it from scratch. As more parts are added and more diverse experiments are performed, the library of modular programs will increase in size, cutting down on future coding time.

Though still growing, iBioFAB has proved itself a valuable resource in a number of diverse research projects. One of its earliest jobs, and one that it was in many ways built for, is the synthesis of transcription activator-like effector nucleases, or TALENs. TALENs are restriction enzymes used to cut DNA at specific sites for use in genome editing within the cell—a highly useful tool for work in synthetic biology.

Though TALENs can be (and often are) produced by humans in the lab, the process is long and tedious, and the number of steps often results in high error rates. “When our lab was synthesizing TALEN by hand, someone could probably produce ten TALENs in a week,” recounts Chao, “and that’s already kind of a stretch. Even just those ten involve hundreds of pipetting steps, and the success rate is not too good.

“But with the robot, consistency is one of its strengths, and unlike a human, it can run 24/7. With our workflow, the robot can produce two batches of about 200 TALENs in a day, with pretty much no mistakes. That’s a two order of magnitude increase in throughput.” Though the pipetting steps had previously been automated by other groups, this represents the first time the whole process could be completed by a machine, and its efficacy speaks for itself.

The robot has been instrumental in another project out of Zhao’s lab: engineering a better yeast genome, one with improved hardiness to some inhibitors—though that project is still in pre-publication review. iBioFAB is also in use on campus as part of Professor of Cell and Developmental Biology Andrew Belmont’s NIH-funded 4D Nucleosome project, studying the structure, function and dynamics of chromatins within the cell nucleus.

And it’s getting bigger to tackle new projects: to accommodate future growth and its expanding footprint, iBioFAB moved from its 2nd floor space to the concourse research lab in October. The move was no easy feat-windows were removed on both the second floor and concourse, and the robot was lowered down using a crane. Its new workspace allows for an increase in size of 30-50%, with the planned addition of new incubators, another liquid-handling system, and a second robotic arm among other improvements.

The second arm is a critical feature for one of iBioFAB’s upcoming projects: raising bee larvae, feeding and caring for them with its robotic hand in a collaboration with Swanlund Chair of Entomology and IGB Director Gene Robinson (GNDP). “It will be an automated, artificial environment,” describes Zhao. “Honey bees in the environment are exposed to a lot of factors, especially toxins, herbicides, and pesticides that accumulate in the honeycomb, in the wax. This is part of the reason we see declining bee populations: each generation is weakened by this exposure.”

By replacing caretaker worker bees with the robot, young bees can be raised in a sterile environment without outside contaminants, eventually producing hardier hives that can be used in agricultural settings. “It’s an interesting idea, to use the robot to replace the uncontrollable-ness of nature,” adds Chao. “This is a really novel idea [...] no one is doing things like this yet, but I really think it will start to happen.”

There’s no direct equivalent to iBioFAB in the U.S., at least not within academia. iBioFAB’s fully-automated process is a rare quality: most similar systems require human intervention at a much higher level. “We recently competed for a grant for similar biofoundries, we made it to the final selection process,” said Zhao. “Ours was the only proposal that described a fully integrated—fully automated-robotic system, and showed it actually worked.”

“In industry too, as far as I’m aware, companies are only working with partially integrated systems. Our vision is more ambitious.”

Though iBioFAB might not have a competitor in the United States, it does, however, have a

peer overseas: the Edinburgh Genome Foundry features a very similar robotic platform modelled after it. “They heard my talk at a conference in Spain and got in contact with us,” says Zhao. “They kind of replicated our system. But they’re the only other group working in full automation.”

Ultimately, the team believes that iBioFAB—and robots like it—will be the future of technology. They’re faster, they’re more reliable, and they’re becoming smarter: one of the next steps in evolving iBioFAB will be machine learning, allowing it to begin to perform some of the design and computational steps itself. “I really believe that other labs will begin to see the use of machines like [iBioFAB],” said Zhao.

“When I was a student, we did so much by hand, we were always in the lab. Already, we’ve seen the shift toward partial automation, but there’s still a lot to do in the lab. The potential of full automation will free up researcher’s time to focus on the ideas and challenges of synthetic biology.”

GLOBAL BIOFOUNDRY CONSORTIUM EMBRACES GRAND CHALLENGE OF SYNTHETIC BIOLOGY

Synthetic biology has emerged from the intersection of engineering and biology, with its emphasis on standardization, modularization and automation. The newly established Global Biofoundry Consortium, led by Steven L. Miller Chair Professor of Chemical and Biomolecular Engineering Huimin Zhao (BSD Theme Leader/ EBI/MMG), is investing in the systematized approach of engineering to touch off the next wave of biological discovery and innovation.

The consortium, whose founding members include the University of Illinois, Boston University, the University of Manchester, Tianjin University, the Tianjin Institute of Industrial Biotechnology of Chinese Academy of Sciences, and corporate partner Thermo Fisher Scientific, held its inaugural meeting on April 15, 2016. Participants gathered at the IGB to develop a strategic plan to achieve the consortium’s central aim: to develop biofoundries for accelerated biological engineering and fundamental research.

“I expect that this consortium will grow rapidly in the near future,” Zhao said, “because many universities and companies have established, are establishing or will establish biofoundries for various biotechnological applications.”

Biological foundries like the one Zhao and his colleagues have established within the IGB combine cutting-edge robotics, standardized parts and protocols, and computational methods; the resulting experimental platform makes it possible to perform automated engineering at the DNA, protein, pathway and genome levels on a massive scale.

“We were honored to host the inaugural meeting of this important consortium,” said IGB Director and Swanlund Professor of Entomology Gene Robinson. “Synthetic biology holds great promise to help address some of the most important problems in health, agriculture, energy, and the environment, and we are very excited about its prospects for advancement, at the IGB and with the consortium partners throughout the world.”

NEWS & OUTREACH

IGB WELCOMES TWO WOESE UNDERGRADUATE RESEARCH SCHOLARS

Not every student dreams of spending their summer on the beach. Some would rather pursue their passions on campus, spending the long summer days in an air-conditioned lab crunching numbers or plating cells. For two lucky undergraduates researching at the IGB that dream was realized, made possible by the Carl R. Woese Undergraduate Research Scholarship.

The Woese Undergraduate Research Scholarship offers exceptional students a stipend to fund their room and board for a ten week summer program. Recipients continue work begun with an IGB member or affiliate during the academic year, with the intention of completing a largely independent project and final report by the end of the summer.

Rebecca Wipfler (Molecular and Cellular Biology) and Elijah Karvelis (Chemical and Biomolecular Engineering) were chosen via a competitive application process: over 30 students already working in IGB labs applied. Wipfler and Karvelis are the first two scholars in what will become an annual tradition.

ILLINOIS GROUP TO STUDY BRAIN HEALTH AS PART OF NIH BRAIN INITIATIVE

Martha Gillette (GNDP), a professor of cell and development biology at Illinois, has studied the brain for most of her career. Her current work focuses on improving the lives of those affected by brain disorders.

Gillette, an IGB affiliate and Beckman Institute member, and colleagues including chemist Jonathan Sweedler (MMG/BSD) and bioengineer Rohit Bhargava were awarded more than $2 million from the NIH Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative to develop an analytical platform that can lead to new developments in neuroscience, and create diagnostic and therapeutic opportunities in treating neurological diseases.

“BRAIN awards are collaborative grants involving people from different disciplines and a lot of innovative technology,” said Gillette. “This innovation award was possible because of the vigorous collaborative nature of research at the Beckman Institute and the investigators' drive to interact beyond their usual disciplines. One of the exciting aspects is that students are attracted to working at the interface of neuroscience, chemistry, and engineering."

ILLINOIS AND SYNGENTA SIGN AGREEMENT FOR ACCESS TO RIPE INTELLECTUAL PROPERTY

The University of Illinois and Syngenta Crop Protection, LLC, have signed an agreement to implement a commercialization strategy for intellectual property developed under the "RIPE: Realizing Increased Photosynthetic Efficiency for Sustainable Increases in Crop Yield" project, which is funded by the Bill & Melinda Gates Foundation. Illinois will be collaborating with seven other institutions to improve photosynthetic efficiency in food crops in an effort to help resource-poor farmers increase their sustainable yields.

The Illinois and Syngenta collaborative partnership brings leading academic groups working in the area of photosynthesis together with a major agriculture industry partner to evaluate and advance the technologies developed by the RIPE project. Syngenta will serve as a commercialization partner by providing research materials and facilities to support RIPE project goals, as well as bring the industry perspective for bridging key, fundamental photosynthetic research to commercial product development.

“This is a win-win-win deal, the synergies giving the academic partners, Syngenta and the Gates Foundation, benefits that none of the partners alone could gain,” said RIPE Project Director Steve Long (BSD/EBI/GEGC), Gutgsell Endowed Professor of Crop Sciences and Plant Biology. “It is a unique alliance that will accelerate the cause of increasing global crop yield potential, and provide a new model for industry-academia collaboration for the mutual benefit of society and industry.”

STEPHEN LONG SPEAKS AT PARIS CLIMATE CONVENTION

Agricultural innovation is needed now—not later—to avoid food shortages in a world with an ever-changing climate and a growing population.

That’s the message Illinois Gutgsell Endowed Professor of Crop Science and Plant Biology Stephen Long (BSD/EBI/GEGC) shared with an audience of lawmakers, thought leaders, political staff members, and concerned citizens at a Wednesday, Dec. 2, 2015, public session of the Paris Climate Change Conference.

“With the projected increase in global food demand—which the United Nations says will be 70 percent more by 2050,” said Long, “we have to increase productivity per unit area of land we’re using now.”

One of his key points was that society has managed to keep up with agricultural demand over the last two centuries through a series of innovations. “Right now society is pushing back on agricultural innovations,” he said. “We actually need to overcome that; otherwise, we’re going to create more problems for ourselves.”

ART OF SCIENCE EXTENDS ITS REACH

The “Art of Science: Images from the Carl R. Woese Institute for Genomic Biology” is a celebration of common ground between science and art. Now in its 6th year, researchers and members of the public attended an all-ages opening reception in April, where they had the chance to view genomics through an unconventional lens.

The exhibition comprised images from research addressing significant challenges in the areas of environment, medicine, and energy use and production. Images were selected to highlight the beauty and fascination encountered daily in scientific endeavors.

The Art of Science 7.0 exhibition will take place on April 13th, 2017 at Gallery 217. Current images can be viewed at the I-Hotel and Conference Center in Champaign.

ST. ELMO-BRADY STEM ACADEMY

Last fall, the IGB partnered with the Department of Chemical and Biomolecular Engineering to present two week-long programs for the St. Elmo-Brady STEM Academy. Named for the first African American to earn a Ph.D. in Chemistry from the University of Illinois, the academy exposes underrepresented fourth and fifth grade boys to science, technology engineering and mathematics in an after-school and Saturday program at Champaign’s Booker T. Washington STEM Academy and Garden Hills Elementary School.

The IGB Outreach team met the boys at their schools to lead them in hands-on activities about DNA, inheritance, cell structure and evolution. On Saturdays, the students’ fathers were invited to join in the fun, to help establish intergenerational learning and strong role models. The IGB will be organizing another program through the St. Elmo-Brady STEM Academy this fall.

NEWS & OUTREACH

DECIPHERING GENOMICS: A VITAL JOB SKILL FOR THE 21ST CENTURY PROFESSIONAL

Three years ago, in recognition of the growing impact of genomic science and technologies on modern society, the IGB created the "Genomics for" program, a public education effort that offers engaging, accessible introductory genomics workshops and learning opportunities. Each event is tailored to fit the professional development needs and interests of a particular professional group; this year, the IGB offered two new opportunities, Genomics for MBA Students and Genomics for Clinicians, in partnership with the Illinois College of Business and Carle Foundation Hospital, respectively.

In spring 2016, Professor of Business Administration and Diane & Steven N. Miller Centennial Chair Madhu Viswanathan served as lead instructor for "Business Applications of Genomics," an eight-week course for which IGB Director and Swanlund Professor of Entomology Gene Robinson and four other IGB faculty members acted as co-instructors.

"The deeper you go into an arena such as genomics," said Viswanathan, "the broader you can take that learning across different technologies." Students in the course explored the research and development opportunities, constraints, and ethics of genomic technologies such as transgenic food and fuel crops, innovations in tissue engineering and drug discovery, and consumer genomics.

Genomics for Clinicians, a day-long intensive workshop, was held on the Carle Hospital campus in July 2016. Health care professionals participated in sessions focused on omics technologies, their applications in the areas of nutrition, reproductive health, and cancer, and related legal and ethical considerations. Each session was led by a faculty member of the IGB or the University of Illinois College of Medicine.

"We are further along in understanding the genome than I thought," said one participant, reflecting on lessons learned during the workshop. Some attendees noted that in addition to the knowledge gained during the event, their participation had inspired them to be more aware of further research and innovations in genomics and how those might inform their practice.

DECODING THE UNIVERSAL LANGUAGE OF LIFE, COMING SOON TO COURSERA

What is a genome? What did the first genetic material on earth look like, compared with the diversity of genomes found in life on earth today? How can we use genomics to discover new drugs, heal injuries, grow better crops, and construct more robust communities, whether microbial or human?

All of these questions and more will be explored by a new Massively Open Online Course (MOOC), scheduled to be released on Coursera in January 2017. The course, titled "Genomics: Decoding the Universal Language of Life" has been developed by IGB in collaboration with the Illinois Center for Innovation in Teaching & Learning. IGB Director and Swanlund Professor of Entomology Gene Robinson is lead instructor for the course.

Access to the course will be free to the general public, and content has been designed to be inviting and accessible, with no requirement for background knowledge in biology. The educational goal is that students who complete the course will be empowered to understand and evaluate news about ongoing discovery and innovation related to genomics.

The course will present a series of videos that explore both basic science concepts in genomics and their research applications, featuring IGB faculty members as guest lecturers. Colorful, quirky animations help reinforce complex scientific concepts. Students will be invited to engage in forum discussions exploring current science and science policy news.

BIG SUCCESS AT GENOME DAY 2015

Genome Day, an annual IGB event held at the Orpheum Children's Museum in Champaign, had over 400 individuals in attendance to learn about genomics with their families in an all-ages setting.

Chaired by crop scientist Patrick Brown (EBI/GEGC), Genome Day was staffed by over 130 volunteers from all of the IGB research themes, IGB staff, HPCBio, NCSA, the Center for the Physics of Living Cells, and the Biomedical Engineering Society. Volunteers from the Society for the Advancement of Chicanos/Hispanics and Native Americans in Science were on hand to provide bilingual support for all activities to make the event accessible to more of the community.

This coming year, the IGB will have the special opportunity to bring hands-on learning for all ages to Chicago, as part of the World of Genomics at the Field Museum, presented by the IGB. Please join us May 19-20, 2017 to take part in this one-of-a-kind event.

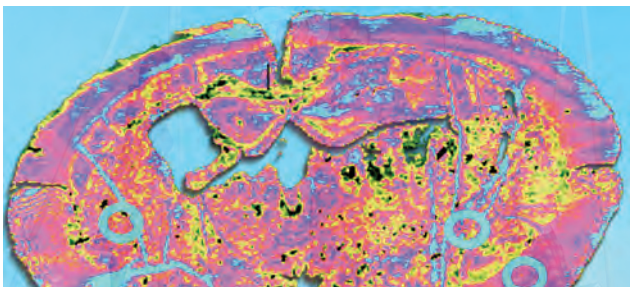
IGEM TEAM WINS SILVER MEDAL

Digital memory versus analog: it's a question that's plagued music lovers for years. In biology, however, the focus is overwhelmingly digital: 0 or 1, on or off, genes expressed or not expressed. But what would analog memory look like in a cell, and how might it be useful?

Last summer, the UIUC_Illinois International Genetically Engineered Machine (iGEM) team set out to create a novel genetic part that would allow bacteria to record their environment in analog. Their completed project, SCRIBE (Synthetic Cellular Recorders Integrating Biological Events), was presented at the iGEM Giant Jamboree in Boston, where it received a silver medal.

The International Genetically Engineered Machine (iGEM) Foundation is a non-profit organization that promotes synthetic biology technologies and collaborative, open-sourced study in the context of high school and undergraduate education. The University of Illinois iGEM team, hosted by the IGB, is now in its eighth year, and has won several medals at both the regional and international level.

"If you want a truly fundamental and yet frontier-pressing extracurricular as an undergraduate, and are interested in molecular biology or genetic engineering," said team member Sameer Andani, "there's nothing else you can do that's more beneficial for your education than participating in iGEM."



IGB RESEARCH BRIEFS

LIGHT ILLUMINATES THE WAY FOR BIO-BOTS

A new class of miniature biological robots, or bio-bots, has seen the light – and is following where the light shines.

The bio-bots are powered by muscle cells that have been genetically engineered to respond to light, giving researchers control over the bots' motion: a key step toward their use in applications for health, sensing and the environment. Led by Rashid Bashir (ONC-PM/RBTE), Abel Bliss Professor of Engineering and Head of Bioengineering, the researchers published their results in the *Proceedings of the National Academy of Sciences*.

"Light is a noninvasive way to control these machines," Bashir said. "It gives us flexibility in the design and the motion. The bottom line of what we are trying to accomplish is the forward design of biological systems, and we think the light control is an important step toward that."

This work was part of the Emergent Behaviors of Integrated Cellular Systems (EBICS) project, funded by the NSF. EBICS received a five-year, $25 million renewal in fall 2015, allowing Bashir and colleagues to continue to develop bio-bot technology for a variety of applications in diagnostics, medicine and sensing.

THE PROOF OF THE PLANT BREEDING IS IN THE (DIGITAL DROPLET) PCR

The first human farmers needed hundreds of years and a lot of good luck to shape the first domesticated crops; modern agricultural researchers need months or weeks. A study supported by the Bill & Melinda Gates Foundation has explored the potential ability of a new molecular method, digital droplet PCR (ddPCR), to further speed the development of food crops.

The work, led by Illinois postdoctoral fellows Kasia Glowacka and Johannes Kromdijk and published in *Plant, Cell and Environment*, addressed a central challenge of transgenic plant development: how to reliably evaluate whether genetic material has been successfully introduced. Glowacka, Kromdijk, and collaborators at Illinois, the Polish Academy of Sciences, the University of Nebraska-Lincoln and the University of California, Berkeley compared the traditional method to several new ones that have emerged from advances in genomic technology they identified one that is much faster than the standard approach, yet equally reliable.

"For plants with long life cycles, such as our food crops, this will greatly speed the time between genetic transformation or DNA editing, and development of pure breeding lines," said Gutgsell Endowed Professor of Crop Sciences and Plant Biology Steve Long (BSD/EBI/GEGC), the principal investigator of the study. Long hopes that his group's demonstration that ddPCR is a "reliable, fast and high throughput" technique will help it to become the new standard for those developing transgenic crops.

FRIEND OR FOE? NOVEL GENOMIC PLATFORM HELPS TO IDENTIFY DANGEROUS E. COLI STRAINS

In August 2015, three children in three separate northern Indiana counties were sickened by *Escherichia coli O157:H7*, and one of them died. Health threats like these send public health officials into overdrive as they search for information about the source of the contamination that could help them end the outbreak.

The difference between the potentially deadly O157:H7 strain and its more benign cousins stems from just a few genome sequence changes, explained Sergei Maslov (BCXT), a professor of bioengineering and Bliss Faculty Scholar. The team's research was published in the *Proceedings of the National Academy of Sciences* and funded by the Office of Biological and Environmental Research of the DOE and by Brookhaven National Laboratory, where Maslov holds a joint appointment.

Maslov, also an NCSA affiliate, and his colleagues recently analyzed O157:H7 and 31 other *E. coli* strains to gain insights into the evolution of bacteria and the development of benign and pathogenic strains. They identified stretches of the *E. coli* genome that were present across all strains, and whose small variations in sequence could be used to characterize differences among existing or novel strains.

"This is key because, in the event of an outbreak of a new strain of pathogenic *E. coli*, medical researchers will be able to run a single comparison of the new strain against this basic platform to quickly find what is new, what is lost or replaced by another strain," Maslov said.

SHAPE OF TUMOR MAY AFFECT WHETHER CELLS CAN METASTASIZE

Only a few cells in a cancerous tumor are able to break away and spread to other parts of the body, but the curve along the edge of the tumor may play a large role in activating these tumor-seeding cells, according to a new study led by Kristopher Kilian (RBTE), a professor of materials science and engineering, and Timothy Fan (ACPP/ONC-PM), a professor of veterinary medicine.

Using engineered tissue environments in various shapes and patterns, the study found that the more curved the cell cultures were, the more cancer cells at the edges displayed markers of stem cell characteristics—the key to spreading to other tissues. This has potential for furthering our understanding of cancer as well as developing personalized treatment plans.

“The most dangerous part of cancer is metastasis,” Kilian said. “Some cells that we call cancer stem cells adopt deadly characteristics where they can travel through the bloodstream to other tissue and form new tumors. There’s a need for ways to find these cells and to study them, and importantly, to develop drugs that target them, because these cancer stem cells are resistant to chemotherapy drugs that target the main tumor. This causes recurrence: the cancer comes back.”

The American Cancer Society and the NSF supported this work, which was published in the journal *Nature Materials*.

RESEARCHERS FIND CULTURAL VARIATIONS PRODUCE DIFFERENCES IN GUT MICROBIOME

Our growing understanding of human microbiomes, the communities of microscopic living things that thrive inside our bodies and contribute to our physiological functions, has reinforced the idea that you are what you eat.

A recent publication in *Cell Reports* compared the gut microbiomes of two neighboring societies from the Central African Republic: a hunter-gatherer society, and a farming society with access to Westernized foods. These two types of microbiomes were also compared with that of a typical Western society. The findings suggested that characteristics of diet may influence microbial community composition more strongly than geographic or other cultural factors; traits of the species that make up microbiomes, including the ability to digest fibrous material, correlated with diet.

From top, Illinois postdoctoral fellow Kasia Glowacka; a Lego model of the human liver; and two staple foods from the Central African region – Gozo, a bitter manioc root, and Koko leaves in peanut sauce.

Andres Gomez, first author and microbial ecologist and staff scientist at the J. Craig Venter Institute in California, published the findings with colleagues including Illinois’ Professor of Animal Sciences Rex Gaskins (RBTE), Professor of Microbiology Brenda Wilson (MMG), Professor of Anthropology Rebecca Stumpf (BCXT/CGRH), Professor of Animal Sciences Bryan White (BCXT/CGRH), and Adjunct Professor of Anthropology Steven Leigh. Their findings could further support the understanding of the impact of diet and lifestyle in relation to metabolic and colonic disorders.

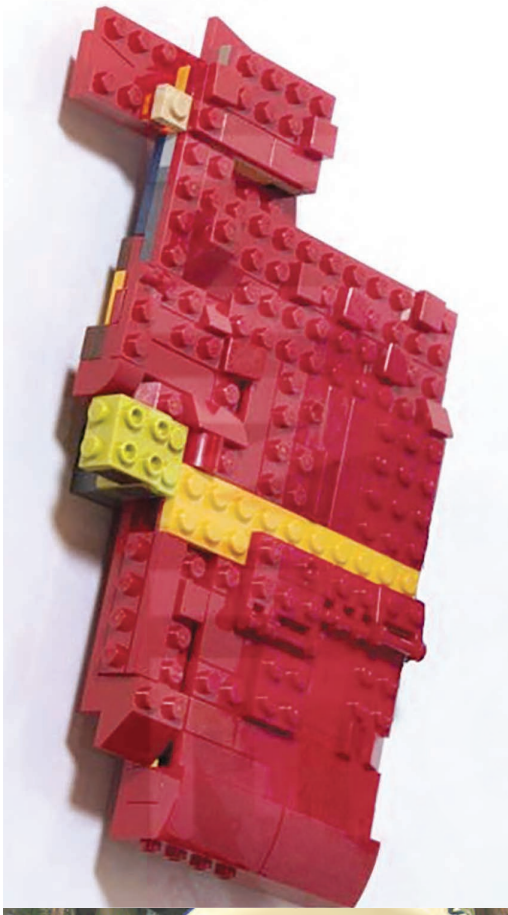
SCIENTISTS UNCOVER MECHANISM THAT PROPELS LIVER DEVELOPMENT AFTER BIRTH

Any expectant mother will tell you that she wants her baby's organs to develop properly in the womb. What she may not realize is that a child's internal organs continue to develop for months and years after birth.

This critical period is full of cellular changes that transform tissue organization and function, but the exact mechanisms underlying postnatal organ maturation are still a mystery. Recently, researchers reported that postnatal development of liver cells relies in part on a mechanism called "alternative splicing," which alters how genes are translated into the proteins.

"This mechanism is different from simply turning gene expression on or off," said Professor of Biochemistry Auinash Kalsotra (GNDP/ONC-PM), who led the study. “You are making the same amounts of RNA, but of different kinds."

Alternative splicing is a lot like building with LEGOs, where bits and pieces of DNA (called exons) can be pieced together or have parts removed to produce different assortments of proteins; in this case, the proteins that direct the maturation of the liver tissue, preparing it for its adult functions. These findings, which were made possible by funding from the NIH, March of Dimes, and Roy J. Carver Charitable Trust and appeared in the journal *Nature Communications*, were the first to provide a direct link between splicing regulation and liver maturation.



IGB GRANTS

BRENDAN HARLEY
MATTHEW WHEELER
US ARMY MEDICAL RESEARCH AND MATERIAL COMMAND
"Polycaptrolactone-collagen Composite Biomaterials for Mandible Regeneration"

DEREK WILDMAN
ROMANA NOWAK
SUSAN SCHANTZ
NATIONAL INSTITUTES OF HEALTH
"Placental RNA Expression as a Function of Gestational Age and Environmental Exposures"

RIPAN MALHI
MONICA UDDIN
DEREK WILDMAN
NATIONAL SCIENCE FOUNDATION
"IBSS-L: Epigenomic Effects of European Colonization on Alaskan Native"

GENE ROBINSON
HUIMIN ZHAO
DARPA
"Protecting the National Food Supply: Advanced Bio-Manufacturing to Produce Deployable Pollinating Units: Seedling Proposal"

ANDREW LEAKEY
CARL BERNACCHI
PATRICK BROWN
STEPHEN LONG
DONALD ORT
DOE ARPA-E
"Novel Technologies to Solve the Water Use Problem of High Yielding C4 Bioenergy and Bioproduct Feedstocks"

HYUN JOON KONG
KOREA INSTITUTE OF INDUSTRIAL TECHNOLOGY
"The Development of Smart Hydrogel Patch for the Patient-managed Treatment of Incurable Wound"

JIAWEI HAN
JUN SONG
NATIONAL INSTITUTES OF HEALTH
"UIUC KnowEnG BD2K Center–Mayo Clinic Partnership with Fisk University"

JUN SONG
NATIONAL BRAIN TUMOR SOCIETY
"Functional Characterization of Germline Risk Variants in Oligodendroglioma"

ANDREW LEAKEY
NIGEL GOLDENFELD
DANFORTH PLANT SCIENCE CENTER/ NATIONAL SCIENCE FOUNDATION
"An Integrated Phenomics Approach to Identifying the Genetic Basis for Maize Root Structure and Control of Plant Nutrient Relations"

JOHN GERLT
JOHN CRONAN
NATIONAL INSTITUTES OF HEALTH
"Novel Strategies for the Discovery of Microbial Metabolic Pathways"

DONALD ORT
AMERICAN SOCIETY OF PLANT BIOLOGISTS
"Silencing of XRCC4 Using VIGS for T-DNA Insertion of Homologous Recombination Facilitated by CRISPR/CAS9 Genomic Editing System"

BARBARA HUG
REBECCA FULLER
NATIONAL INSTITUTES OF HEALTH
"PAGES (Progressing through the Ages: Global Climate Change, Evolution, and Societal Well-being)"

ALISON BELL
NATIONAL SCIENCE FOUNDATION
"Workshop: Integrating Molecular Mechanisms and Quantitative Genetics in Order to Understand Consistent Individual Differences in Behavior"

IGB AWARDS

RASHID BASHIR, Bioengineering Professor and Department Head (ONC-PM, RBTE) was named a Fellow of the Biomedical Engineering Society (BMES).

MARNI BOPPART, Associate Professor of Kinesiology and Community Health (RBTE) received a Campus Excellence in Undergraduate Teaching Award from the University of Illinois.

STEPHEN A. BOPPART, Abel Bliss Professor of Engineering (RBTE) received the 2016 Technical Achievement Award from the Institute of Electrical and Electronics Engineers (IEEE) Engineering in Medicine and Biology Society.

ROY DAR, Assistant Professor in Bioengineering (GNDP) received a Career Transition Award from the National Institutes of Health (NIH) National Institute of Allergy and Infectious Diseases.

LEE DEVILLE, Associate Professor of Mathematics (BCXT) received a Campus Excellence in Undergraduate Teaching Award from the University of Illinois.

REBECCA FULLER, Associate Professor of Animal Biology (GNDP) received a Campus Award for Excellence in Guiding Undergraduate Research from the University of Illinois.

REX GASKINS, Professor of Immunobiology, Departments of Animal Sciences and Pathobiology (RBTE) received a Distinguished Scientist Award from the Society for Experimental Biology and Medicine (SEBM).

PAUL HERGENROTHER, Kenneth L. Rinehart Jr. Endowed Chair in Natural Products Chemistry (ACPP Theme Leader) received the Innovation Transfer Award from the 2016 Innovation Celebration, a joint venture between the Champaign County Economic Development Corporation, University of Illinois, and Parkland College.

PRINCESS IMOUKHUEDE, Assistant Professor of Bioengineering (RBTE) received a Scientist Development Grant from the American Heart Association.

AUINASH KALSOTRA, Assistant Professor of Biochemistry (GNDP/ONC-PM) was named a 2016-17 Center for Advanced Study Fellow.

MADHU KHANNA, Professor of Agricultural and Consumer Economics (EBI) was selected as an Agricultural & Applied Economics Association (AAEA) 2016 Fellow.

HYUNJOON KONG, Associate Professor and Centennial Scholar in Chemical and Biomolecular Engineering (RBTE) received the 2016 Campus Distinguished Promotion Award, as well as the College of Engineering Dean's Award for Excellence in Research.

STEPHEN LONG, Gutgsell Endowed Professor in the departments of crop sciences and plant biology (BSD/EBI/GEGC) was named by Thomson Reuters as a Highly Cited Researcher for 2015.

TING LU, Assistant Professor in Bioengineering (BCXT/BSD/MME) received a 2016 Young Investigator Award from the Office of Naval Research, as well as a National Science Foundation Faculty Early Career Development (CAREER) award.

RUBY MENDENHALL, Associate Professor, African American Studies of Sociology (CGRH/GNDP) was named a 2016-17 Center for Advanced Study Associate.

WILLIAM METCALF, G. William Arends Professor in Molecular and Cellular Biology was named a Fellow of the American Association for the Advancement of Science.

DOUGLAS MITCHELL, Assistant Professor of Chemistry (MMG Theme Leader/EBI) received the National Fresenius Award, administered by the American Chemical Society.

DONALD ORT, Robert Emerson Professor of Plant Biology (GEGC Theme Leader, BSD) was named to the Agricultural Research Service Science Hall of Fame, as well as being named by Thomson Reuters as a Highly Cited Researcher for 2015.

GENE ROBINSON (Director) was awarded the 2016 IBANGS Distinguished Investigator Award.

KAREN SEARS, Associate Professor of Animal Biology (RBTE, GNDP) received a Campus Excellence in Undergraduate Teaching Award from the University of Illinois, as well as the Lynn Martin Award for Distinguished Women Teachers from the College of Liberal Arts and Sciences.

VIJAY SINGH, Professor of Agricultural and Biological Engineering (GEGC) was named a University Scholar.

REBECCA STUMPF, Associate Professor of Anthropology (BCXT, CGRH) was named a University Scholar.

TANDY WARNOW, Founder Professor of Bioengineering and Computer Science (BCXT, CGRH) was named a 2015 Fellow of the Association for Computing Machinery (ACM).

MATTHEW WHEELER, Professor of Animal Sciences (RBTE) received a Campus Award for Excellence in Faculty Leadership from the University of Illinois.

CHENGXIANG ZHAI, Professor of Computer Science (BSD) received a Campus Award for Excellence in Graduate Student Mentoring from the University of Illinois.

HUIMIN ZHAO, Centennial Endowed Chair Professor of Chemical and Biomolecular Engineering (BSD Theme Leader, MMG) was selected by the University of Illinois as the Steven L. Miller Chair in Chemical Engineering, as well as receiving the 2016 Charles Thom Award.

IN MEMORIAM: DR. SHARON GRAY

Sharon Gray, a postdoctoral scholar in plant biology at the University of California, Davis and a former member of the Genomic Ecology of Global Change research theme working with Professor Andrew Leakey at the IGB, was killed on October 4, 2016 after a civil unrest altercation in Ethiopia. Sharon was traveling to begin a new research project in the area with charitable organizations including the Netherlands Institute of Ecology when protesters attacked her car.

"Sharon was one of those people who went the extra mile in everything," Leakey said. "She mentored an incredible number of undergraduate students in the group. She taught them how to do science. She was one of those people who people turned to for advice on any topic. Professionally, she was incredibly successful, but maybe most significantly, personally she was an extraordinarily warm and kind person. She was just someone who enriched the lives of all around her."

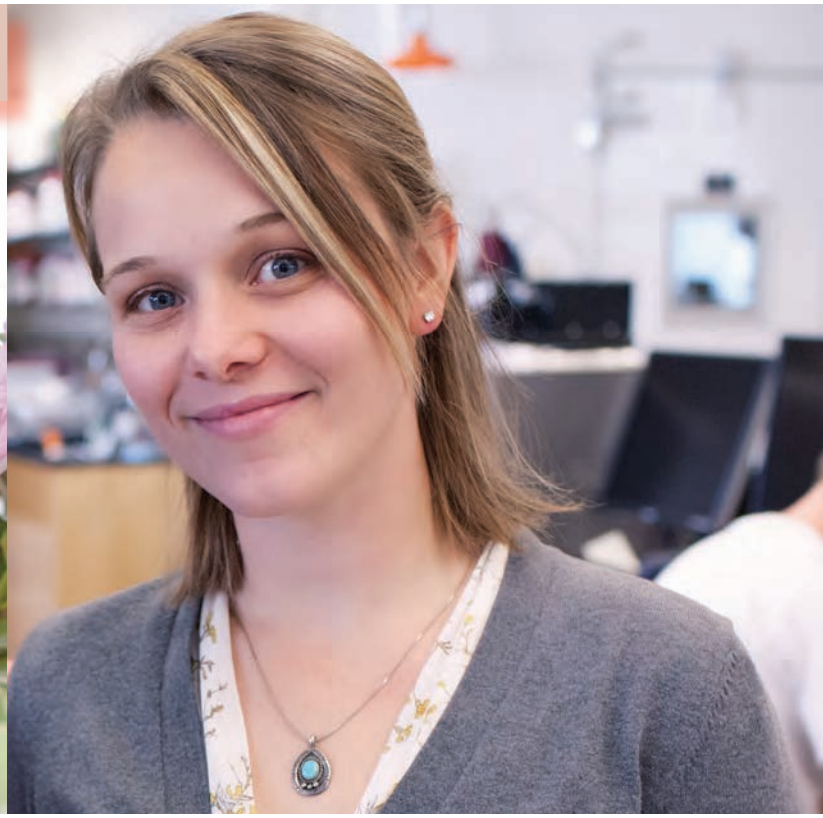
"Sharon was one of those people who went the extra mile in everything,"

Sharon was a promising young scientist, highly respected among her peers, and one of the IGB's first participants in the OLLI Citizen Scientist program. Sharon led by example in both her research and her interaction with others.

Our deepest condolences to the Gray family, to Sharon's husband Cody Markelz who was also a member of the Leakey group, and to her friends, colleagues, and fellow researchers here at Illinois and at UC Davis. She will be missed.

UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN
B.SC. INTEGRATIVE BIOLOGY, 2006
PH.D. PLANT BIOLOGY, 2013

1985-2016





From left: DNA Day Participants, and Woese Scholars:Elijah Karvelis & Rebecca Wipfler

Thank you for YOUR support

GIVE TO IGB

The vision of scientific research is limited by the pace of innovation. New technologies let us see the physical world more clearly, in greater detail, in finer scales of space and time. Genomic research, around which the IGB is focused, is particularly tied to advancing technologies.

To continue our record of high-quality research, we need to maintain our position at the forefront of the field. We move past traditional divisions between disciplines of study by constructing a network of collaborations. With your help, we will continue to forge a path toward our vision of a better world.

FOR MORE INFORMATION, VISIT:

WWW.IGB.ILLINOIS.EDU/GIVING

OR CONTACT:

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SHAPING THE FUTURE OF SCIENCE & SOCIETY

Carl R. Woese Research Fund

Donations may be made to the Carl R. Woese Research Fund to support research on evolution, systems biology, and ecosystem dynamics at the IGB. Prof. Woese approved this fund in his name to help the next generation of scientists and to recognize his discoveries and work that spanned nearly half a century at the University of Illinois at Urbana Champaign.

IGB Annual Fund

Gifts to the IGB help us to foster the collaborative environment that we believe is vital for progress in genomic research. Philanthropy helps us create opportunities for building strong working relationships with intelligent, talented researchers from our own campus, and from across the world. It allows us to provide grants for promising, but risky, research projects that more traditional funding agencies might be hesitant to support. Research needs evolve quickly and unrestricted gifts to the IGB Annual Fund permit us to optimize funds by allocating them for the projects that need them most.

iGEM Undergraduate Team

The IGB hosts a team of undergraduates from multiple departments to participate in the International Genetically Engineered Machine (iGEM) competition. This opportunity provides students the development of open community and collaboration for the advancement of synthetic biology. Funds for the iGEM team will give undergraduates the chance to present their research to an international audience in Boston.

STAY CONNECTED WITH THE IGB

Stay connected to news, events, and program information at the Carl R. Woese Institute for Genomic Biology. By joining our mailing list, you'll receive our e-newsletter and Biomarker with details about seminars, workshops, and symposia at the IGB.

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