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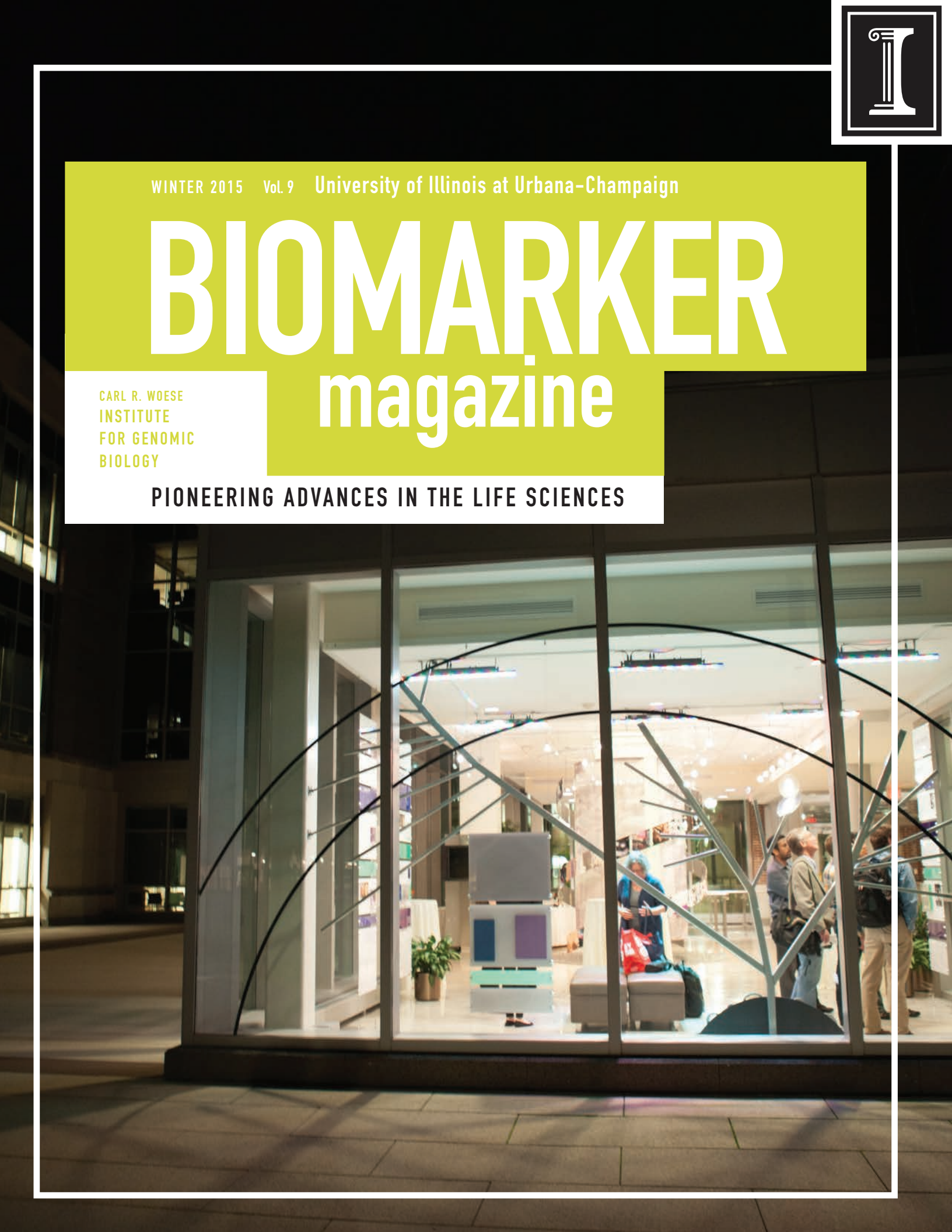
BIOMARKER magazine

CARL R. WOESE INSTITUTE FOR GENOMIC BIOLOGY

PIONEERING ADVANCES IN THE LIFE SCIENCES



Vision is the art of seeing things invisible.

–Jonathan Swift

IGB THEMES

BCXT	BIOCOMPLEXITY
BSD	BIOSYSTEMS DESIGN
CDMC	CELLULAR DECISION MAKING IN CANCER
CGRH	COMPUTING GENOMES FOR REPRODUCTIVE HEALTH
GNDP	GENE NETWORKS IN NEURAL & DEVELOPMENTAL PLASTICITY
GEGC	GENOMIC ECOLOGY OF GLOBAL CHANGE
MMG	MINING MICROBIAL GENOMES
RBTE	REGENERATIVE BIOLOGY & TISSUE ENGINEERING

IGB STRATEGIC INDUSTRY PARTNERSHIPS

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

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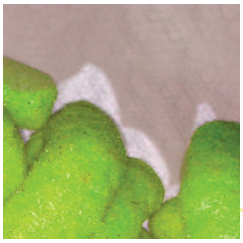



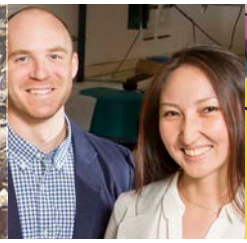



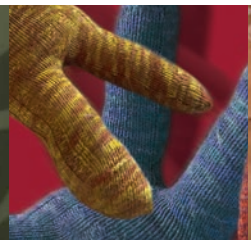



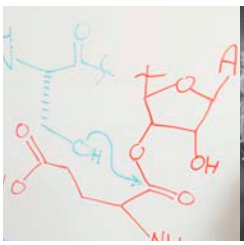
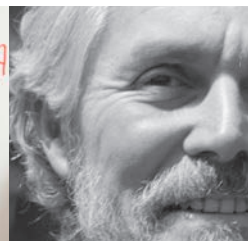

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DIRECTOR'S MESSAGE

THE ART OF SEEING THINGS INVISIBLE

When humans first developed scientific thought and began to construct quantitative models of the natural world, they encountered concepts of space and time far beyond everyday sensory experience. Attempts to calculate the size of the earth, the number of stars, and the movement of the planets forced early philosopher-scientists to grapple with orders of magnitude that the human mind can conceive of and analyze but cannot visualize. In the midst of the Information Age, these familiar challenges remain. They arise not only from the cosmic, but also the microscopic: the vastness of molecular data, much of it in the genomes that reside within all living cells.

Progress in genomic research has been accelerated by highly automated DNA sequencing technology. To make the most of the universe of genomic data now being illuminated, we need better computational tools designed for this scale of inquiry. This year, the Carl R. Woese Institute for Genomic Biology forcefully addressed this challenge, with members embarking on two separate large-scale collaborations funded by the National Institutes of Health Big Data to Knowledge Initiative. The funded projects are developing novel software to support the transformation of genomic big data into novel biomedical insights. One of these awards, which established a Center of Excellence for Big Data Computing in collaboration with the Mayo Clinic, falls under the auspices of the transdisciplinary CompGen Initiative, a partnership between the IGB and the Coordinated Science Laboratory.

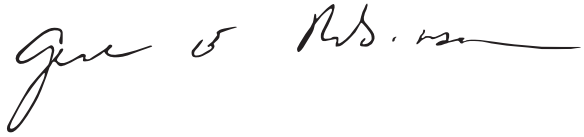
While these efforts in innovation are getting underway, genomic datasets of unprecedented scale are already dramatically increasing our power to make discoveries—and to upend our prior understanding of nature. Better data and better computational tools have allowed University of Illinois Founder Professor of Bioengineering and Computer Science Tandy Warnow, a member of the Biocomplexity and Computing Genomes for Reproductive Health research themes, to help rewrite the phylogenies of two major taxa, birds and plants. More comprehensive sequencing and analysis were also key to a new study, coauthored by Associate Professor of Anthropology Ripan Malhi, that has rewritten the history of human migration to the Americas. Malhi is a member of the Computing Genomes for Reproductive Health and the Regenerative Biology & Tissue Engineering research themes.

New ways of seeing and investigating the natural world lead to new research goals and lines of inquiry. At the IGB, these goals find representation in our research themes, interdisciplinary groups carefully assembled from around the campus expressly for the purpose of tackling some of the most fundamental problems in science. In this issue of *Biomarker*, we also reflect on the recent successes of our open, campus-wide proposal process in supporting the creation of robust, collaborative themes.

"New ways of seeing & investigating the natural world lead to new research goals and lines of inquiry."

We have many other exciting developments to share with you in this issue of *Biomarker*. Our researchers have articulated their visions of crop plants that will someday adjust their own physiology according to their environment to maximize efficient use of light by entire fields of crops. They have explored the implications of mutations on the physical properties of DNA and how those might contribute to the disease process of cancer. They have reverse-engineered naturally occurring proteins to create better technologies for genome editing and antibiotic production.

This is a great time to be involved in genomic research. As our technological efforts advance, we will gain new ways to view and understand the biological world—approaches that are accessible and useful to researchers from many different backgrounds, with many different goals. We are excited to see what we will achieve next as a community, and we look forward to sharing our continued progress with you. ■



Gene E. Robinson
Director, Carl R. Woese Institute for Genomic Biology

A NOVEL ROADMAP THROUGH BACTERIAL GENOMES LEADS THE WAY TO DRUG DISCOVERY

For millennia, bacteria and other microbes have engaged in intense battles of chemical warfare. Doctors fight pathogens with an arsenal of weapons—antibiotics—co-opted from these microbial wars, but their efforts are frustrated by the development of drug resistance that outpaces drug discovery.

To address this, Illinois researchers teamed up with collaborators at Northwestern University to develop a better way to analyze microbial genome data and accelerate drug discovery.

Many medications used today were discovered by screening microbes for production of natural products, biologically useful compounds. In recent years, pharmaceutical companies have largely abandoned this strategy, focusing instead, often unsuccessfully, on synthetically created chemicals.

G. William Arends Professor in Molecular and Cellular Biology Bill Metcalf (MMG Theme Leader), a leading investigator in the new study, described the reason for pharmacological research's shift away from the exploration of natural products.

"There was a reason why they gave up . . . they kept discovering the same things over and over and over again," he said. "They were getting very diminishing returns."

In this way, natural products are like trading cards: it's easy to acquire a set of the common cards, but difficult to find the rare ones scattered among them. A collector might long to peek at all the cards hidden inside the wrappers and buy only the novel ones.

Genome sequence information, now available for an ever-increasing number of bacterial species, promises to allow antibiotic hunters to do just that. Clusters of genes within each genome code for enzymes, proteins that work together to synthesize a natural product for that bacterium. Part of the vision of the IGB's Mining Microbial Genomes research theme is to use bacterial genome sequence data as an index of its natural product repertoire.

If researchers could infer what type of product the bacterium is making by looking at its DNA sequence, they would not have to go through a lengthy screening process; they could just scan genomes for promising gene clusters. Unfortunately, this task is much harder than it sounds. Many clusters have similar sequences, making them indistinguishable by traditional comparative methods even though they enable the production of different compounds.

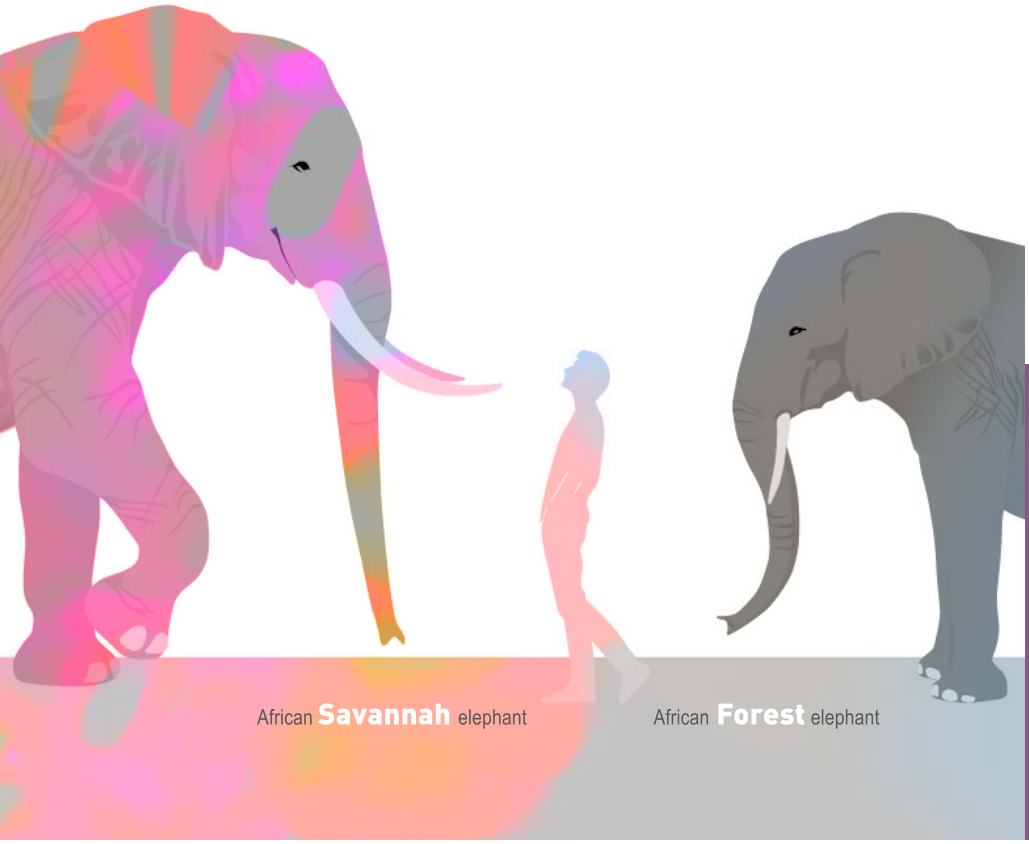
Metcalf, co-lead author, IGB Fellow James Doroghazi, and colleagues cleared this hurdle by combining multiple comparative metrics, each with a carefully calibrated weight, to produce an algorithm that sorted 11,422 gene clusters from 830 bacterial genomes into an orderly, searchable reference. Their work, which was funded by the IGB and the National Institutes of Health, was published in *Nature Chemical Biology*.

In the database created in the study, gene clusters predicted to make similar products were linked with each other in networks referred to as families. These predictions mesh almost perfectly with prior knowledge; gene clusters that produce similar known compounds were sorted by the new algorithm into the same family in every case but one.

The database is a huge step toward solving the "trading card" problem. By comparing the distribution of gene cluster families across bacterial species, researchers can now predict which species are most likely to contain novel antibiotics and target the richest strains for study.

"We've got the framework, we know the number of gene clusters, we know who has them and therefore we know where to look to find new drugs," said Metcalf. "It clearly leads to discovery." ■

FOR MILLENNIA, BACTERIA & OTHER MICROBES HAVE ENGAGED IN INTENSE BATTLES OF CHEMICAL WARFARE.



IN THE LAST DECADE, MORE THAN HALF OF ALL FOREST ELEPHANTS HAVE BEEN SLAUGHTERED FOR THEIR MARKET-PRECIOUS IVORY.

IN AT THE KILL

In the last decade, more than half of all forest elephants have been slaughtered for their market-precious ivory. Without action, this species will go extinct within our lifetime.

But it's hard to garner support for a species many do not know exists. Today the U.S. government and several conservation groups fail to recognize the forest elephant (*Loxodonta cyclotis*) as a species distinct from the African savannah elephant (*Loxodonta africana*) despite scientific evidence.

"By not recognizing two species, these organizations may be condemning the African forest elephant to extinction," said animal scientist Alfred Roca (CGRH/GNDP). "The time for governments and conservation agencies to recognize two species of elephants in Africa is long past due."

In a literature review published in the *Annual Review of Animal Biosciences*, Roca chronicled 15 years of genomic and morphological (physical) studies that confirm two species of African elephants that are as evolutionarily distinct as humans and chimpanzees.

This review prompted the Center for Biological Diversity, a public interest environmental organization, to petition the U.S. Fish and Wildlife Service (FWS) on June 10 to reclassify African elephants from one threatened species to two endangered species.

While elephants remain listed as threatened, the U.S. is able to import some ivory and elephant parts that may have been sourced illegally. The U.S. has one of the largest domestic ivory markets but lacks internal mechanisms to ensure elephant products are legal.

Reclassifying the two species as endangered would help stop illegal imports. It would also provide additional funding for elephant conservation and bring national and international attention to the current elephant crisis.

"There's now no question that African elephants are two distinct species that should be managed according to their distinct needs," said Tara Easter, a scientist at the center, in a news release. "Both forest elephants and savannah elephants are vanishing quickly, so we must give them the stronger protections provided by endangered status or risk losing these intelligent and magnificent animals forever."

On July 29, 2015, the FWS proposed a revision to the Endangered Species Act that would create a "nearly complete ban" on commercial elephant ivory trade in the U.S.

At a news conference with Kenyan President Uhuru Kenyatta, President Barack Obama said, "Our countries are also close partners in the fight against poachers and traffickers that threaten Kenya's world-famous wildlife. The United States has a ban already on the commercial import of elephant ivory. I can announce that we're proposing a new rule that bans the sale of virtually all ivory across our state lines, which will eliminate the market for illegal ivory in the United States."

Still, poachers kill, on average, one elephant every 15 minutes. Fewer than 100,000 forest elephants and 400,000 savannah elephants remain. ■

FROM GENES TO CELLS TO SOCIETIES, STRENGTH IN NUMBERS

For most animals, the ability to navigate social situations is a vital trait, one that allows an individual to successfully court a mate, defend a territory, or cooperate to achieve a task. Every interaction is a labyrinth constructed from past experiences, the behaviors of fellow animals, and environmental context. What was the evolutionary pathway to the behavioral capability for these interactions and for the complex animal societies that they support in some species? What are the genomic roots of these behaviors, and how far back in evolutionary time do they extend?

The work of two IGB research themes, Biocomplexity and Gene Networks in Neural & Developmental Plasticity, has brought us closer to answering these and related questions. Three research efforts have spanned hundreds of millions of years of evolutionary time and examined cooperative behavior in organisms ranging from colonies of single-celled bacteria to a set of behaviourally rich and diverse bee species.

SPONTANEOUS COOPERATION IN A MICROSCOPIC WORLD

A clever combination of two different types of computer simulations enabled William and Janet Lycan Professor of Chemistry Zan Luthey-Schulten (BCXT), graduate student John Cole, and colleagues to uncover an unexpected group dynamic: the spontaneous emergence of resource sharing among individuals in a community. Who were the members of this friendly, digitally represented collective? *Escherichia coli*, rod-shaped bacteria found in the digestive systems of humans and many other animals.

The finding, initially predicted by mathematical models and then confirmed through empirical testing, was reported in *BMC Systems Biology*. Funding was provided by the U. S. Department of Energy, the National Institutes of Health, the Edelheit Foundation, and the National Science Foundation.

Three research efforts have spanned hundreds of millions of years of evolutionary time & examined cooperative behavior...

Bacteria such as *E. coli* adapt their metabolism—what they use as fuel and how they break it down—according to what resources they have available. Bacteria, like muscles, prefer to burn glucose in the presence of oxygen but can fall back on another metabolic pathway when they are without it. Similar to lactic acid production in a tired sprinter's legs, this pathway converts glucose into a chemical byproduct, acetate, that still contains some unharvested chemical energy.

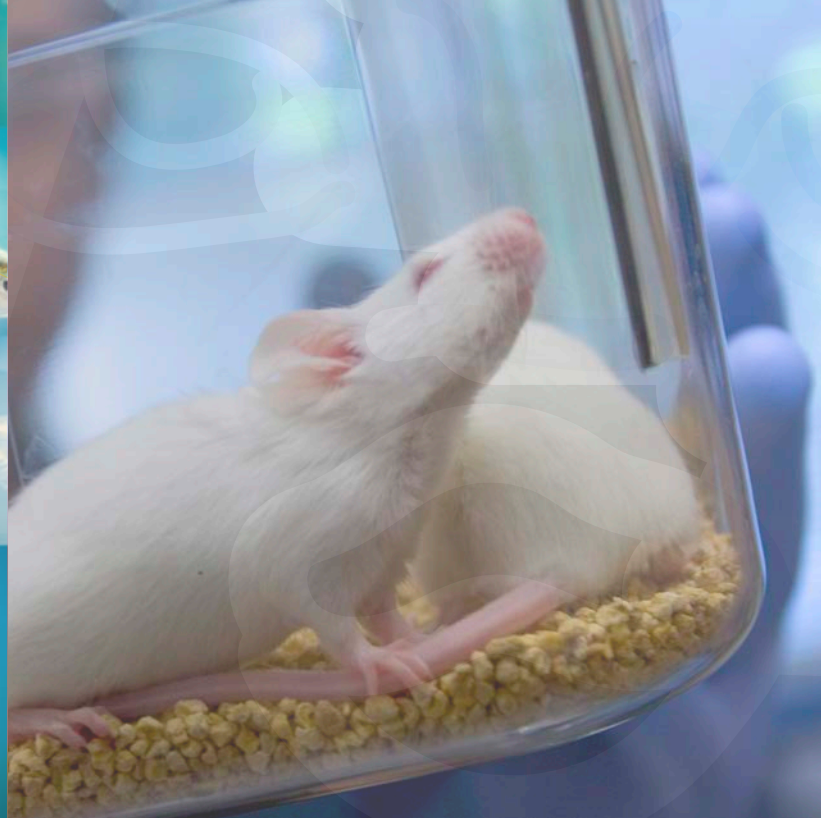
Cole and others wanted to know what happens inside a bacterial colony as it grows larger, making it harder for oxygen to penetrate to inside layers or for glucose from the growth substrate to reach the top. How do the cells respond?

The researchers built a molecular-level model of what was happening inside the colony that revealed something novel yet intuitive. Cells at the bottom, lacking oxygen, break down glucose into acetate. Cells at the top use their access to oxygen to metabolize acetate, extracting the remaining energy from the original glucose. Cells in the outermost ring, with access to both glucose and oxygen, expand the colony further. The bacteria in the model were cooperating.

To test their predictions, the researchers grew and monitored bacterial colonies in the lab in conditions that matched those they had simulated. The activity of the real-life colonies confirmed the predictions of their model. Exploring how cooperative task specialization quickly emerged among genetically identical or near-identical cells, said Cole, could help researchers understand and design new drugs to fight cancer-causing tumors.

A SHARED "GENETIC TOOLKIT" FOR BEHAVIOR

A team of IGB biologists and computer scientists are making strides in a more deliberate quest for deeply conserved origins of social behavior. The group is using three unlikely and seemingly unlike animals, the house mouse, stickleback fish, and honey bee, to ask whether there are



ON A MOLECULAR LEVEL, THE SOCIAL RESPONSES OF THESE THREE SPECIES LOOK MUCH MORE SIMILAR THAN THE EVOLUTIONARY DISTANCE BETWEEN THEM SUGGESTS.

common genetic "toolkits"—shared networks of genes in the brain—that direct social behaviors such as responding to intruders or caring for young.

The answer suggested by their findings so far? On a molecular level, the social responses of these three species look much more similar than the evolutionary distance between them suggests.

Cell and developmental biologist Lisa Stubbs (GNDP) led a study with animal biologist Alison Bell (GNDP), Swanlund Chair Professor of Entomology and IGB Director Gene Robinson, and computer scientist Saurabh Sinha (BSD/GNDP) to examine the brain gene network response in bees, mice, and fish after a territorial intrusion by a fellow species member. The work was funded by the Simons Foundation and published in *Proceedings of the National Academy of Sciences*.

"We knew that a variety of animals share genes for some common physical traits. Now it appears that different organisms share a 'genetic toolkit' for behavioral traits as well," Stubbs said.

After the aggressive encounter, activity of genes involved in brain growth, neural signaling, and energy use were altered in all three species. Among the genes identified were transcription factors, a type of gene whose protein product helps control the activity of many other genes, that may help orchestrate the molecular response to social challenges in diverse animal species.

FROM GENES TO NETWORKS, FROM BEES TO COLONIES

Patterns of gene regulation and activity may be able to provide a shared mechanistic explanation of social behaviors across diverse animal taxa. What can genes tell us about the diversity of animal lifestyles, from the nuclear families of mice to the crowded and coordinated societies of honey bees?

A genomic study of ten bee species representing this spectrum of social living, published in *Science*, offered new insights into the genetic changes that accompany the evolution of bee behavior. Primary funding sources of the project were BGI, the National Institutes of Health, and the European Union Framework Programme for Research and Innovation.

By sequencing and comparing the genomes of ten bee species that vary in social complexity, the multi-institutional team of researchers made three important discoveries.

"First, there is no single road map to eusociality–the complex, cooperative social system in which animals behave more like superorganisms than individuals fending for themselves," said Robinson; he and Sinha were lead authors on the bee study. "We found that independent evolutionary transitions in social life have independent genetic underpinnings." In other words, although the molecular origins of social behaviors may be deeply conserved, the detailed mechanics of societal structure may often be unique to each taxon.

The second insight involved changes in the evolution of gene regulation: as social complexity increased, so did the speed of changes to parts of the genome involved in regulating gene activity. By contrast, evolution seems to have put the brakes on changes in many parts of the genome that code for the actual proteins, Robinson said.

A third major finding was that increases in social complexity were accompanied by a slowing, or "relaxation," of changes in the genome associated with natural selection. This effect on some genes may be a result of the buffering effect of living in a complex, interdependent society.

This last finding speaks to the evolutionary argument for cooperation and complexity, among microbes and mice, bees and humans—in the struggle for life and fitness, there is sometimes strength in numbers. The genetic "tools" that structure social behaviors are good ones to have on hand. ■

THE LUCY ISLANDS IN BRITISH COLUMBIA, CANADA WERE THE DISCOVERY SITE FOR SKELETAL REMAINS OVER 6,000 YEARS OLD.

PAST & PRESENT GENOMES TELL THE STORY OF NATIVE AMERICAN BIOLOGICAL ORIGINS

An ancient shell midden found on the islands.

The first human inhabitants of the Americas lived thousands of years before the first written records, and the story of their transcontinental migration is the subject of ongoing debate and active research. A study published in *Science* by an international collaboration of researchers presented strong evidence, gleaned from ancient and modern DNA samples, that the ancestry of all Native Americans can be traced back to a single migration event.

The study was led by the Centre for GeoGenetics at the University of Copenhagen. More than 80 researchers contributed sequence data and analyses of key ancient individuals and from living individuals in the Americas and possible ancestral regions. Anthropologist Ripan Malhi (RBTE), one of the senior coauthors, focused on genome sequences obtained from 6,000-year-old skeletal remains found on Lucy Islands in British Columbia, Canada, and modern descendants of those individuals.

"There were multiple reasons why certain ancient individuals were selected," said Malhi. "We wanted a variety of locations as well as ages . . . individuals ranging from 6,000 years ago to more recent times show closer genetic affinity to the modern-day Native Americans in that same geographic region than anywhere else."

Researchers presented strong evidence, gleaned from ancient and modern DNA samples, that the ancestry of all Native Americans can be traced back to a single migration event.

This study confirmed two previously identified groups: Athabascans and northern Amerindians (comprising mainly northern populations) and other Amerindians (comprising mainly southern populations). The new results indicated that these groups diverged from their shared ancestors at about the same time, no earlier than 23,000 years ago, suggesting that a single group migrated to the Americas and subsequently split into two distinct populations.

Ancestral Native Americans traveled into the Americas via the Bering Land Bridge. The current study suggests that the migrating population remained isolated in this area for about 8,000 years before moving further into the Americas.

Analyses also suggested that traces of genetic similarity to East Asian and Australo-Melanesian populations found in some of the Native American groups were produced through sporadic contact between Native American and Eurasian populations, rather than two independent migration events.

Highlighting the difficulty of obtaining and analyzing these types of data, a study published simultaneously in *Nature* found support for two separate migration events. Malhi noted that the *Science* study had several strengths compared with other work: biparental genomic data, which are less vulnerable to bias, and an unusually large and diverse set of individuals.

A second study, which looked at the genetic characteristics of 84 individual dogs from more than a dozen sites in North and South America, suggested that dogs may have first successfully migrated to the Americas only 10,000 years ago, thousands of years after the arrival of humans. These results were published in the *Journal of Human Evolution*.

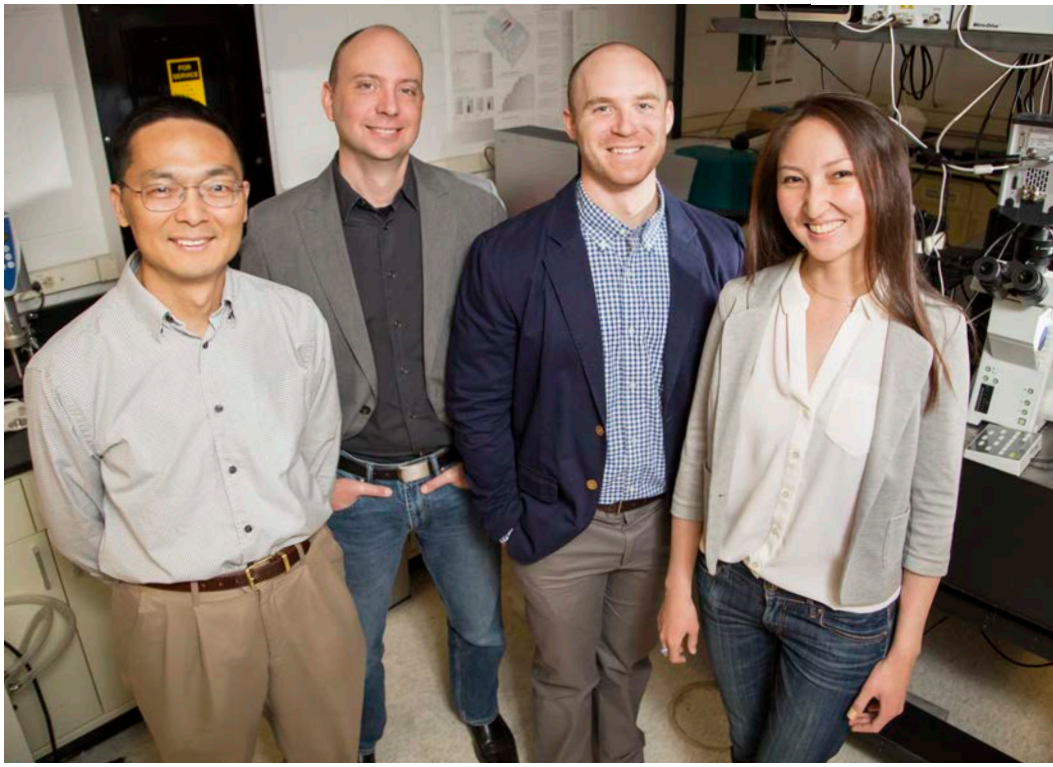
Human remains are not always available for study "because living populations who are very connected to their ancestors in some cases may be opposed to the destructive nature of genetic analysis," said graduate student Kelsey Witt, who coauthored the analysis of ancient dog remains. This type of study is often permitted when analysis of human remains is not, she said.

Malhi emphasized that the partnerships formed with modern Native American populations during his career have strengthened and informed his research program.

"A lot of my new thoughts and ideas, perspectives on genomic analysis of indigenous people in the Americas, come from interacting with Native Americans," said Malhi. ■

GENOME-EDITING PROTEINS SEEK & FIND WITH A SLIDE & A HOP

From left: Huimin Zhao, Charles Schroeder, Luke Cuculis, & Zhanar Abil.



Searching a whole genome for one particular sequence is like trying to fish a specific piece from the box of a billion-piece puzzle. Using advanced imaging techniques, IGB researchers in the Biosystems Design research theme have observed how one set of genome-editing proteins finds its targets, which could help them design better gene therapies to treat disease.

Chemical and biomolecular engineers Charles Schroeder (BSD) and Huimin Zhao (BSD Theme Leader/EBI/MMG), along with graduate students Luke Cuculis and Zhanar Abil, published their work in the journal *Nature Communications*.

TALE proteins, or transcription activator-like effectors, can be programmed to recognize and bind to specific DNA regions. Researchers use TALE proteins for synthetic biology techniques such as genome editing in plants or bacteria, or for gene therapy. For example, Zhao's group explores using TALE proteins to treat sickle cell anemia, which is caused by a mutation in one link of the DNA chain.

"People have been using this technique, but nobody fully understood the mechanism," Schroeder said. "The main question is, how do these proteins find their target sites? They are designed to bind to a particular site, but there's this big genome with billions of bases, so how does the protein find its site? If you understand the mechanism, you might be able to engineer better, more improved proteins."

The researchers used imaging techniques that let them watch through a microscope how individual TALE proteins interact with a string of DNA. They observed that the proteins seek and find DNA regions using a combination of sliding and hopping. The proteins bind to the DNA and slide along the helix, traveling down the DNA molecule like a highway. The researchers also observed that the proteins perform frequent, short hops along their paths, allowing them to move more efficiently but never straying far from the DNA.

TALE PROTEINS, OR TRANSCRIPTION ACTIVATOR-LIKE EFFECTORS, CAN BE PROGRAMMED TO RECOGNIZE & BIND TO SPECIFIC DNA REGIONS.

"The combination of sliding and hopping means they can cover more ground and potentially move past obstacles that might be in their way," said Cuculis, a co-first author of the paper.

"The combination of behaviors also would allow a TALE protein to switch strands of the DNA double helix and sample both strands, increasing the chance of finding its target site," said Abil, the other co-first author.

They also analyzed which parts of the protein did the work, finding a division of labor among the domains within the protein: one part searches, while another part binds to the specific target sequence. This finding gave the researchers insight into where to tweak the protein design so that it binds even more selectively.

The researchers are now planning further experiments that examine how the proteins work in live cells to see if the behavior changes when immersed in the bustling activity within the cell nucleus.

The IGB and the David and Lucile Packard Foundation supported this work. Schroeder and Zhao are also affiliated with the Department of Chemistry and the Center for Biophysics and Quantitative Biology. ■

HARNESSING THE POWER OF BIG DATA

Every silver lining has a cloud. Rapid advances in research technology have unleashed a river of valuable biomedical data—much more, in fact, than researchers have the tools to store, share, analyze, or interpret. This flood of Big Data includes high-resolution brain images, interactions within a social network, and millions of base pairs of DNA sequence.

Or is it that even this cloud has a silver lining? This glut of data has touched off a wave of technological creativity and innovation. In 2012, the National Institutes of Health created the Big Data to Knowledge (BD2K) Initiative to help harness the power of these new data types.

Perhaps no area of science needs this type of investment more urgently than genomics. Next-generation DNA sequencing technologies have turned the vision of precision medicine into a plausible reality but also threaten to overwhelm computing infrastructures with unprecedented volumes of data.

With its depth of expertise in computer engineering, data sciences, and genomics, the University of Illinois, and particularly the IGB, is well-equipped to begin tackling these growing challenges. In the past year, the IGB has received two BD2K Initiative awards. As part of the first wave of BD2K funding announced in fall 2014, Illinois and Mayo Clinic received a $9.34 million, 4-year award to create one of 11 new Centers of Excellence for Big Data Computing; in spring 2015, Illinois received a second, $1.3 million BD2K award for a separate software development project.

KNOWENG: A REVOLUTION IN GENOMIC DATA ANALYSIS

Google, Yahoo, and other internet search engines allow us to search and parse the collective knowledge of the world—they anticipate the user's questions, remember preferences, deliver information quickly and clearly. Why can't researchers trying to discover the most effective disease treatment employ the same analytical power to the knowledge discovery challenges of their work?

To the team of biologists, computer scientists, and bioinformaticians in Illinois' new Center of Excellence, this question sounds like an exciting opportunity. The group has begun work on a tool, the Knowledge Engine for Genomics (KnowEnG), that interprets new results by leveraging community knowledge of how genes interact.

Computer scientist Jiawei Han (GNDP) is the center's program director. Other principal investigators are computer scientist Saurabh Sinha (BSD/GNDP); physicist and bioengineer Jun Song (CDMC); and Richard Weinshilboum, M.D., interim director of the Mayo Clinic Center for Individualized Medicine and director of the center's Pharmacogenomics Translational Program. Victor Jongeneel (GNDP), Director of Bioinformatics at IGB and the National Center for Supercomputing Applications (NCSA), and Director of HPCBio, is executive director.

"By integrating multiple analytical methods derived from the most advanced data mining and machine learning research, KnowEnG will transform the way biomedical researchers analyze their genome-wide data," said Han. "The Center will leverage the latest computational techniques used to mine corporate or Internet data to enable the intuitive analysis and exploration of biomedical Big Data."

The Center combines the expertise of many units across the Illinois campus, including the IGB, Department of Computer Science, Coordinated Science Laboratory, College of Engineering, and NCSA. As a leader of biomedical research and structured data collection, Mayo Clinic is playing a vital role in design, testing, and refinement. The Breast Cancer Genome-Guided Therapy (BEAUTY) study at the Mayo Clinic will be the first to benefit from the KnowEnG technology.

Biomedical genomic studies often result in a list of genes—genes that differ in sequence or

activity in healthy and diseased individuals, for example. Researchers want to translate that list of genes into a better understanding of how disease works. How does a particular disease compare to other diseases at a cellular level? Are there specific functions inside the cell that are most affected? This knowledge could help predict disease risk or lead to new ideas for treatment.

When completed, KnowEnG will be unique in its integration of many disparate sources of gene-related data into one enormous network, a comprehensive guide against which a researcher's specific results can then be compared.

"There's a lot to do, and obvious challenges to overcome, and we're looking forward to those challenges," said Sinha, who leads the research arm of the project. "What I'm most excited about is the actual possibility that this could be a tool which everybody uses in the world."

DATA COMPRESSION: CUTTING BIG DATA DOWN TO A USABLE SIZE

Before data can be analyzed, they must be stored somewhere. Anyone who has struggled with the logistics of working with, saving, or sharing large computer files can empathize with the data storage challenges faced by today's biomedical researchers and medical practitioners. The genomic data files that these groups are beginning to produce on a routine basis are many orders of magnitude larger than the average movie or digital photo; a single human genome sequence takes up around 140 GB.

Olgica Milenkovic (BSD), an associate professor of electrical and computer engineering at Illinois, and Stanford University Professor of Electrical Engineering Tsachy Weissman are co-PIs on the second Illinois BD2K-funded project. Together, they are developing a suite of data compression software that will handle DNA sequence data, gene functional analyses, and other genomic data types. While compression of each data type requires a unique approach, their group hopes to identify aspects of compression strategies that are transferable across many types of genomic data.

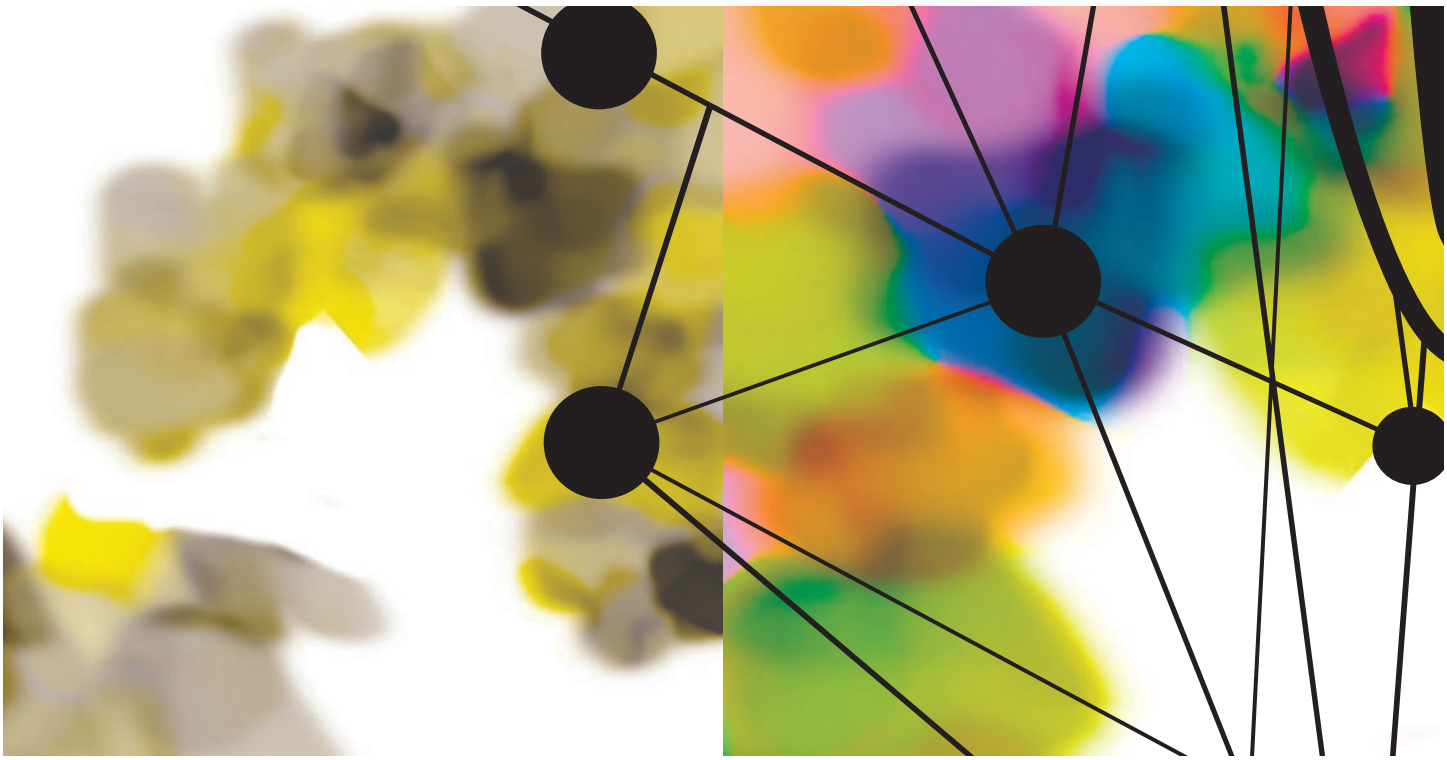
"Precision medicine requires that genomic, proteomic, and other types of health care-related data corresponding to many individuals be acquired, stored, and archived for many years," said Milenkovic. "[Our goal is] to develop a suite of software solutions for the next generation of biological data repositories and labs, which are currently facing enormous challenges with data storage, transfer, visualization, and wrangling."

Genomic data sets pose a unique set of challenges and opportunities for data compression. They have a large amount of repetition and a very small alphabet; just four nucleotide bases, or "letters," in raw DNA sequence. Repetitions within data provide opportunities for shortcuts in representation.

In addition, some genomic data sets are linked to a reference—a genome sequence from a similar species, the same species, or even the same individual, to which DNA or RNA sequences can be compared. A reference-based algorithm can then encode only the differences between these sequences and the reference, rather than every nucleotide of the sequence, to greatly reduce the size of the data set.

Milenkovic, Weissman, and colleagues will explore strategies that combine existing compression algorithms, focusing on those that handle these data characteristics well, with algorithms that will be newly developed as part of the project. ■

KnowEnG will be unique in its integration of many disparate sources of gene-related data into one enormous network.



REVISING THE TREE OF LIFE

In 1977, Carl Woese rewrote the tree of life. Nearly 40 years later, scientists are still revising it, one phylogenetic reconstruction at time.

"You never put all your heart and soul into any reconstruction because better data and better tools can change it," said Founder Professor of Bioengineering and Computer Science Tandy Warnow (BCXT/CGRH). "The analyses are evolving, the data are increasing, and the methods are improving."

By developing new computational methods, Warnow helped two teams reconstruct branches on the tree of life to understand the evolution of birds and plants, respectively. "We couldn't address these questions using off-the-shelf methods," she said.

MODERN BIRDS FIND THEIR PLACE

With the help of nine supercomputers and 400 years of CPU time, more than 100 researchers created the most accurate avian tree of life to date based on 14,000 genes from 48 species of birds. Their results were published in *Science*.

"It is not just about what happened with the birds but what is underlying all of that evolution," Warnow said. "With good methods, you can understand things about how genes and phenotypes evolve; you get more information about fundamental science."

Genomes of different species evolve over time, and these differences are a sign of evolutionary changes that create new species. However, when species diversify in a short period of time, their genomes remain relatively similar, making it hard to infer the phylogeny. In addition, these rapid speciations can make gene trees different from each other due to a process called "incomplete lineage sorting."

To make sense of the genome-scale avian data, Warnow helped develop a method called statistical binning. Using this method, similar genes are grouped into "bins," each bin produces a tree, then these trees are combined into a phylogenetic tree. In this study, they divided 14,000 genes into 2,000 bins of seven genes.

"NEVER PUT ALL YOUR HEART & SOUL INTO ANY RECONSTRUCTION BECAUSE BETTER DATA & BETTER TOOLS CAN CHANGE IT."

The resulting tree shows how birds diversified after the mass extinction that killed off the dinosaurs. Among the results, they found that flamingos are more closely related to pigeons than pelicans, and falcons are more closely related to parrots and a group of songbirds than to eagles and vultures.

THE EVOLUTION OF PLANT LIFE

Warnow also developed a method to help an international team construct a phylogenetic tree for 100 plant species as part of the 1000 Plants (1KP) initiative, an effort to generate sequencing data for more than 1,000 species of plants. Their work was published in *Proceedings of the National Academy of Sciences*.

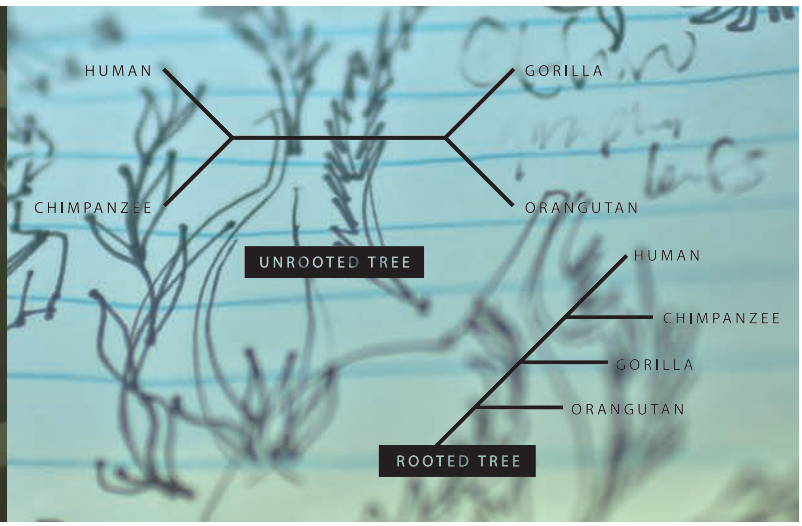
The main obstacle in constructing the land plant species tree was the large amount of missing data, which made the most popular species tree estimation methods inapplicable (because they require rooted gene trees). Therefore, Warnow and her students developed a new method for computing species trees from gene trees, called ASTRAL, that combines unrooted phylogenetic trees from many genes into a single family tree. Many research groups have adopted ASTRAL, which is faster and more accurate than previous methods. The group has already launched ASTRAL-2, which they are working to improve even more.

AN EVER-EVOLVING DRAFT

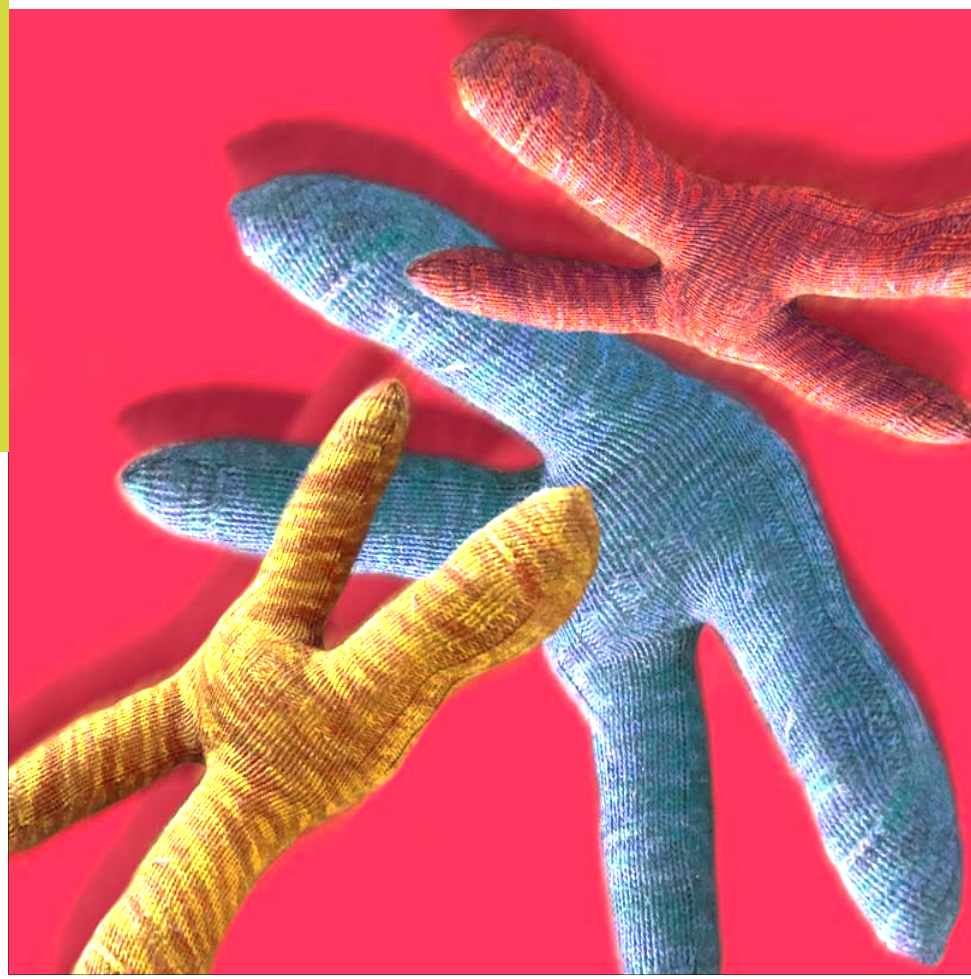
Just as the tree of life is continually evolving, so is our understanding. As data and methods improve, scientists will discover new evolutionary relationships. Each new method will yield a better draft.

"Developing new methods is a combination of inspiration and luck," Warnow said. "We were lucky that we had some inspiration and could come up with approaches that worked." ■

Tandy Warnow



COLLABORATIVE RESEARCH TEAM SOLVES CANCER-CELL MUTATION MYSTERY



APPROXIMATELY 85% OF CANCER CELLS OBTAIN THEIR LIMITLESS REPLICATIVE POTENTIAL THROUGH THE REACTIVATION OF A SPECIFIC PROTEIN CALLED TELOMERASE (TERT).

Cancer-related causes kill more than 500,000 people in the United States each year. Emerging research has identified the mechanism behind one of the most common mutations that help cancer cells replicate limitlessly.

Approximately 85 percent of cancer cells obtain their limitless replicative potential through the reactivation of a specific protein called telomerase (TERT). Recent research has shown that highly recurrent mutations in the promoter of the TERT gene are the most common genetic mutations in many cancers, including adult glioblastoma and hepatocellular carcinoma.

TERT stabilizes chromosomes by elongating the protective element at the end of each chromosome in a cell. Cells harboring these mutations aberrantly increase TERT expression, effectively making them immortal.

Now, a collaborative team of researchers in the IGB Cellular Decision Making in Cancer research theme and at the University of California, San Francisco (UCSF), have been looking at why this happens. The team's findings, published in *Science*, have exciting implications for new, more precise, and personalized cancer treatments with reduced side effects.

The team's findings, published in *Science*, have exciting implications for new, more precise and personalized cancer treatments with reduced side effects.

By integrating computational and experimental analyses, the researchers found that the mechanism of increased TERT expression in tumor tissue relies on a specific transcription factor—a protein that binds specific DNA sequences and regulates how its target genes are expressed—that selectively binds the mutated sequences. The TERT mutations act as a new binding site for the transcription factor that controls TERT expression. The newly identified transcription factor does not recognize the normal TERT promoter sequence and thus, does not regulate TERT in healthy tissue.

The researchers at Illinois include H. Tomas Rube, Alex Kreig, Assistant Professor of Bioengineering Sua Myong (CDMC), and Founder Professor of Bioengineering and of Physics Jun Song (CDMC). The first author, Robert Bell, is a UCSF graduate student co-advised by Song.

The team's work further showed that the same transcription factor recognizes and binds the mutant TERT promoter in tumor cells from four different cancer types, underscoring that this is a common mechanism of TERT reactivation.

The identified transcription factor and its regulators have great potential for the development of new precision therapeutic interventions in cancers that harbor the TERT mutations. A treatment that would inhibit TERT in a targeted cancer, cell-specific manner would bypass the toxicities associated with current treatments that inadvertently also target TERT in normal healthy cells.

Based on these new findings, the team is now conducting a variety of experiments designed to test whether inhibiting the transcription factor activity would not only turn down TERT expression but might also result in selective cancer cell death. ■

AN EXPERIMENT IN COOPERATIVE RESEARCH

DIFFERENT VIEWPOINTS CAN LEAD TO NEW WAYS TO APPROACH COMPLICATED PROBLEMS

Social behavior evolved as a means for a cooperative group to profit from resources that would be inaccessible to individuals. Honey bees amass large food stores. Termites construct terrific nests. Interdisciplinary scientists address grand challenges.

The latter is the idea on which the Carl R. Woese Institute for Genomic Biology (IGB) was founded. It makes sense: Scientists working together can share resources and expertise. Different viewpoints can lead to new ways to approach complicated problems.

"Groups of scientists identify questions that are bigger than what individual scientists are able to address themselves–ideas that require expertise and perspectives from different disciplines. At the IGB, these collaborations are formalized in the form of a functioning unit, called a thematic research group, or theme," said IGB Director Gene Robinson, Swanlund Chair Professor of Entomology.

A theme is composed of researchers from diverse disciplines across the Illinois campus. Theme leaders help coalesce members into a team, and each team is housed in a large, shared laboratory to promote collaborations and the exchange of ideas.

IGB themes have the potential to solve the global energy crisis, explain how climate change will affect food crops, develop regenerative therapies, and more. But how they go about addressing these problems varies. Each theme, with its unique inception, composition, and goals, is an experiment in cooperative research—an ongoing effort to prove that for team science, the whole can be greater than the sum of its parts.

IGB themes come together in many different ways. Three of the most recently formed exemplify the many paths to success:

- **BIOSYSTEMS DESIGN (BSD):** Start with a question.
- **GENE NETWORKS IN NEURAL & DEVELOPMENTAL PLASTICITY (GNDP):** Start with a team.
- **COMPUTING GENOMES FOR REPRODUCTIVE HEALTH (CGRH):** Start with a leader.

START WITH A QUESTION

How can we employ engineering principles to design biological systems (such as DNA molecules and custom cells) more quickly and efficiently?

As researchers at Illinois began to think about this question, Centennial Endowed Chair of Chemical and Biomolecular Engineering Huimin Zhao (BSD Theme Leader/EBI/MMG) and Robert W. Schaefer Scholar Professor Chris Rao (BSD/EBI/RBTE) helped establish a new theme, called BSD, for the emerging field of synthetic biology.

The theme's vision: combine the university's expertise in engineering, biology, and agriculture to establish a theme in synthetic biology. "The vision is very important," Zhao said. "You need to know what you are really good at, how you can compete [for grants] nationwide, or even worldwide. You have to have the vision, but you also have to build a team that can work together."

With support from the Roy J. Carver Charitable Trust, the theme created the Illinois Biological Foundry for Advanced Biomanufacturing (iBioFAB) where custom molecules and cells are designed and created automatically, using a high-tech robotic system.

To differentiate themselves from other synthetic biology centers, which at the time focused mostly on prokaryotic cells, they set their sights on eukaryotic cells, including mammalian cells for biomedical research and plant cells for agricultural research.

Today they work to enhance the functionality and capabilities of the iBioFAB. They design the cell, build it, and then test it to see if the cell matches their design. They are also developing fully automated methods to design and construct large DNA molecules, such as natural product gene clusters, plasmids, and bacterial artificial chromosomes.

"But of course, we are a relatively young theme," Zhao said. "We are very diverse; we have faculty from quite a few engineering departments, including electrical engineering, industrial engineering, and computer science. But we still want to broaden our collaborations and involve more people."

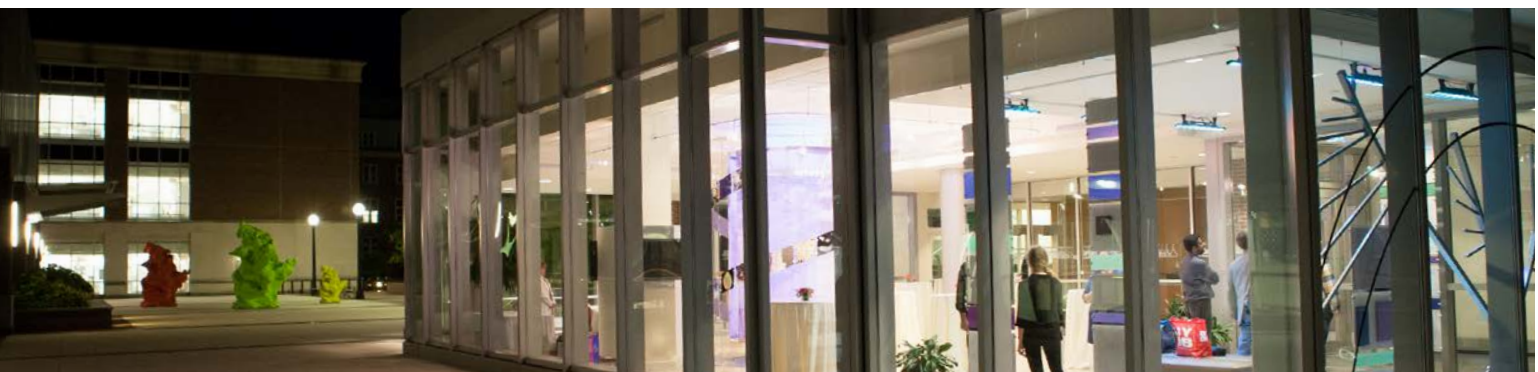
START WITH A TEAM

In 2011, when several members of the Genomics of Neural and Behavioral Plasticity (GBB) theme moved on and theme leader Robinson assumed the role of IGB interim director, the team was left with a choice: reenvision their collaborations or close shop.

"We all automatically said we want a new theme, but that it should grow out of the old one," said cell and developmental biologist Lisa Stubbs (GNDP Theme Leader), who stepped up to lead the new theme. "We decided to retain the momentum we had developed in neurogenomics and behavior, but that we would focus more on the subject of gene regulatory networks and their evolutionary dynamics rather than on behavior *per se*."

According to Stubbs, new themes should sprout from these "kernels" of collaboration.

The reimagined theme looks very different than the original, starting with its new name, GNDP. It studies the evolution of regulatory networks that are active in the brain and asks how those networks have evolved to influence similar



behaviors across species.

The group studies behaviors such as reactions to intruders and caring for offspring. They are hunting for the molecular tools that trigger an "emotional learning experience" that tells an animal how to respond to a social stimulus (such as intruders or young) during a future encounter.

According to Stubbs, new themes should sprout from these "kernels" of collaboration. "We have data sets that we generated together, and so we all have a vested interest in each other's activities," Stubbs said. "That is basically what makes the theme work. I care what's going on with my theme members' data sets. It's not just something that is going on down the hall. I am involved in those projects, and the outcome of those projects is really informative to mine and vice versa."

The trick is finding the right people. "They can't just be people that you think are smart or well known or accomplished because those people may not have time," she said. "You need people who will actually spend time here and actually have the motivation to devote 10 or 20 percent of their time to the theme. I am taking a risk by putting 20 percent of my precious time into something that is a little bit outside my 'comfort zone'; I am really hoping that I am going to get a lot back. And I have."

START WITH A LEADER

After an international search, Derek Wildman (CGRH), a professor of molecular and integrative physiology, was tasked with identifying the right topic for a new theme and the right people to be a part of it.

"The IGB recognized a need to have a theme in the broad area of computational genomic medicine," he said. "It could be many things, but I had to figure out what kind of theme I was going to lead."

For several months, he talked with potential members from across the university: engineers, computer scientists, biologists, animal scientists, and others. "In talking to people, I felt that what we all had in common is that we are interested in how complex interactions shape biology," Wildman said. "Those could be maternal-fetal interactions during pregnancy; those could be gene interactions at the cellular level."

Finally it was decided. CGRH, capitalizing on Wildman's background in the evolution of pregnancy and reproduction, would leverage the university's expertise in computational, biological, and social science to study reproductive health and disorders across biological levels.

Their long-term goal is to answer some of the big remaining questions surrounding pregnancy, such as how to predict when a woman will go into labor. They are also interested in the underpinnings of disease as well as resiliency: Why do some women have "good" pregnancies and others don't?

For Wildman, many of these questions can be posed as a zero-sum game; what one gains the other loses, resulting in punishments and rewards. The reward for the mother may be passing her genes to the next generation; the reward for the fetus may be healthy growth; and punishments may include the development of obstetrical syndromes that can harm both mother and offspring.

Wildman plans to recruit more theme members to help model these reproductive games and their outcomes to better understand pregnancy and ultimately to ensure that both mother and child can win.

THE POINT IS TO START

According to Robinson, there is no single best way to start a theme. "We have had questions bubble up from faculty. We have had collaborations form and flower into larger ones. We have had new individuals come on campus and take an idea and run with it. And we have ideas that originated with the director."

"The marketplace of ideas is complex and lively, and I think there is no one way that works best," he said. "The key is to imagine a problem that is big enough to envelop a group of individuals and motivate and animate them in a way that really brings forth their best efforts."

With its proposal development team, business office, and communications group, Robinson said the IGB has the resources to empower researchers to form collaborations that perform "high-impact, grand-challenge-type team science."

"Everything at the IGB is designed to facilitate getting big grants and performing team science," Robinson said. "To the extent that we are successful in doing that, the IGB is fulfilling our part of a social contact. Faculty that are part of the IGB are stretched even more than usual, because they are expected to maintain active research and teaching programs in their home departments in addition to their work in the institute. But in return for being stretched, the faculty are able to realize bigger dreams, and everyone benefits: students, postdocs, faculty, departments, the IGB, and the whole campus."

GOT A BIG DREAM? DISCUSS IT WITH ROBINSON & PERHAPS YOU, TOO, CAN BUILD A TEAM & SUBMIT A 10-PAGE WHITE PAPER.

Got a big dream? Discuss it with Robinson and perhaps you, too, can build a team and submit a 10-page white paper. The white paper identifies a potential theme's major scientific objective, theme leader, and faculty members, as well as requests for fellowships and faculty hires to gain expertise not represented on campus. Anyone (including you) can propose a new theme, and existing themes are always looking for new members with complementary interests and expertise.

Regardless of whether a potential theme is based on an idea, a team, or a will to start something bigger, the point is to start, Robinson said. Odds are, someone else at Illinois is dreaming the same dream right now. ■

IT'S TIME TO STOP THINKING IN TERMS OF FOOD VS. FUEL

THE "FOOD VERSUS FUEL" DEBATE AFFECTS US ALL

Whether you have taken a side or a backseat in the discussion, the "food versus fuel" debate affects us all. Some say growing more biofuel crops today will decrease greenhouse gas emissions but will make it harder to produce food tomorrow, which has prevented the U.S. from maximizing the potential of environmentally beneficial biofuels.

In a recent article published by the National Academy of Engineering, University of Illinois' Gutgsell Endowed Chair of Plant Biology and Crop Sciences Steve Long (EBI/GEGC/BSD) and University of California's Philomathia Professor of Alternative Energy Chris Somerville predict that farmers can sustainably, and affordably, meet humanity's growing demand for food and fuel.

"It is not possible to control which fields are affected by climate change, but we can decide which fields could produce biofuels without impacting food production and which crops will benefit the environment most," said Long, who also directs the Realizing Increased Photosynthetic Efficiency (RIPE) project.

Biofuel crops capture and store carbon dioxide from the air, lowering greenhouse gases (GHG). This is especially true of the perennial biofuel crops, such as Miscanthus and prairie cordgrass. As a clean-burning alternative to gasoline, biofuels also reduce GHG emissions from your car.

NOT ALL BIOFUEL IS CREATED EQUAL

Today, ten percent of your car's fuel (or more if you use E85) comes from ethanol, a fuel often made from fermenting corn and sugarcane. An alternative–called cellulosic ethanol–is produced from plants (called feedstocks) that are not grown for food.

Corn ethanol produces 34-44 percent less GHG emissions than gasoline. Sugarcane ethanol reduces GHG emissions by more than 50 percent; some estimate it reduces GHG by as much as 82 percent. Cellulosic ethanol, when combined with carbon capture and storage, may be a carbon-neutral source of fuel with no net GHG emissions.

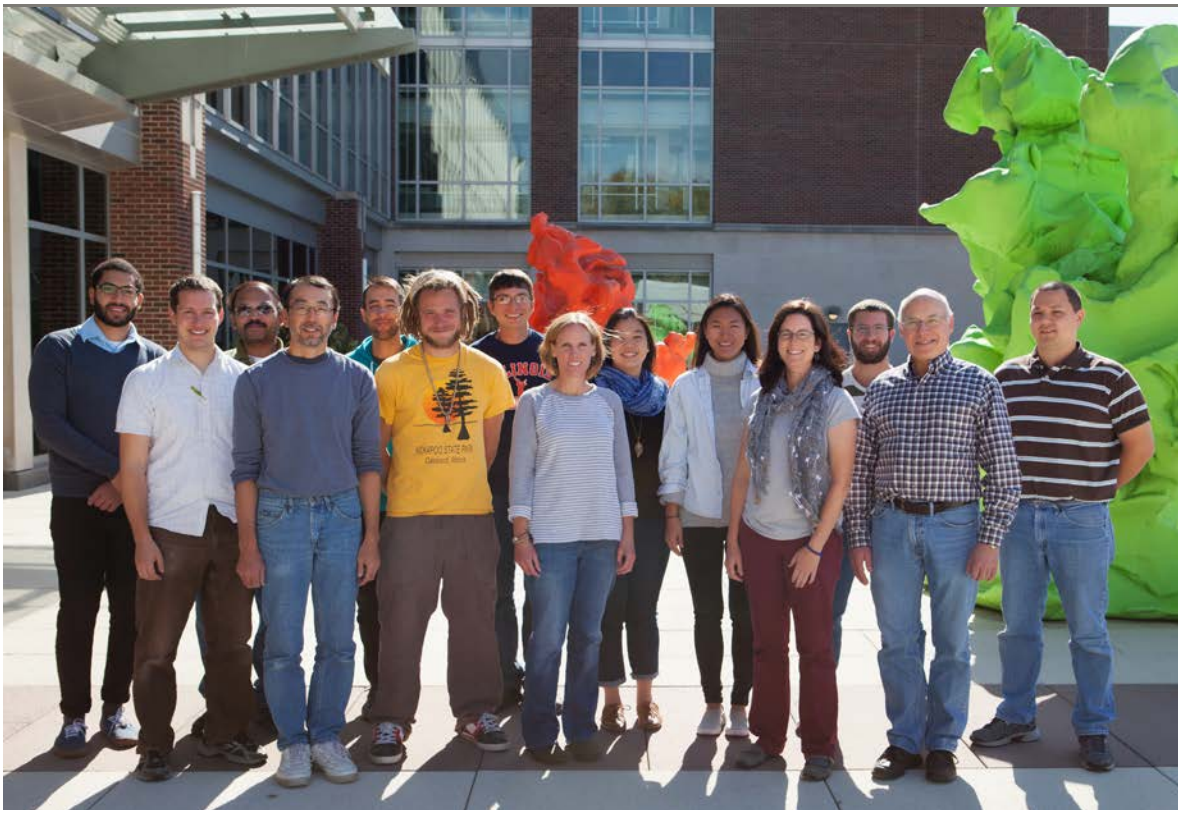
Long and Somerville predict that over time, acreage devoted to sugarcane and cellulosic biofuels will increase, while corn—which has relatively fewer GHG-related benefits—will be grown almost exclusively for food and livestock feed.

"The U.S. has many millions of acres of unused and marginal land that could support biofuel crop production to the economic and environmental benefit of those regions," Long said. "This cannot be done tomorrow, but with well-planned research and development, in 20 years these acres could provide a perpetual and sustainable source of fuels for the U.S."

"We cannot afford to ignore the effects of GHG emissions on our climate," said Long.

In time, biofuels will likely cost less than fossil fuels, which might one day be subject to carbon taxes for environmental damage from GHG emissions. But ultimately, it's the environmental costs we have to worry about, Long said.

"We cannot afford to ignore the effects of GHG emissions on our climate," said Long. "Failing to allocate acreage to produce these sustainable fuels will cost us much more in the long run. But to fully realize the potential of bioenergy, we need support for continued technical improvements, together with effective and enabling policies. Planned in an informed way, we can have both food and fuel from plants." ■



The Genomic Ecology of Global Change research theme, led by Donald Ort

INCREASING CROP PRODUCTIVITY BY MAKING CROP PLANTS MORE EFFICIENT & BETTER NEIGHBORS

How can we meet the accelerating food needs of the world's population without increasing the amount of land used for farming? By making plants better neighbors and borrowing molecular tricks from other species to make their use of light and carbon more efficient, researchers such as Robert Emerson Professor of Plant Biology Donald Ort (BSD/GEGC Theme Leader) hope to improve the photosynthetic efficiency of crops and give a much-needed boost to food production.

The Food and Agriculture Organization of the United Nations projects that the food supply must double by 2050 to meet global needs. Ort recently led an international team of researchers to coauthor a *Proceedings of the National Academy of Sciences* review that creates a roadmap for possible avenues of research to increase plant productivity. The article was based on the outcomes of a 2013 workshop held at the Banbury Center at the Cold Spring Harbor Laboratory.

"What I wanted to do in the workshop was to convene the people who understand photosynthesis," said Ort, "and get them in the same room with the people that had the background to know how to begin to develop the tools to implement some of these things."

Since the major improvements in crop yield that were achieved during the Green Revolution of the mid-twentieth century, yield potential of many of the world's most important crops has reached a plateau. One major avenue for increasing crop yield remains relatively unexplored: finding ways to make photosynthesis, the process by which plants convert captured light into energy, more efficient.

Plant photosynthesis can be surprisingly wasteful, in part because plants have been selected through evolution to outcompete their neighbors. Plants' upper leaves absorb more light than they can use, emitting unused energy as heat and leaving little light not only for surrounding plants but for their own lower leaves.

"In a green soybean field, most of the light is absorbed at the top of the canopy. Most of the day, those leaves are four to five times oversaturated. One leaf layer down, they are light starved," said Ort. "If we can get greater penetration by changing the plant architecture or changing the leaf pigment content, our models suggest the efficiency of that canopy goes up."

Ort and coauthors suggested multiple molecular strategies to realize increased photosynthetic efficiency, including inserting the photosystem of a photosynthetic bacterium that captures infrared wavelengths, decreasing the amount of pigment in upper leaves to allow a more even distribution of light to all levels of the plant canopy, and developing crops with "smart canopies" that respond adaptively to changing light levels.

The authors also discussed how key genetic and genomic technologies may be improved to achieve these and other modifications.

The paper was coauthored by Sabeeha Merchant, a professor of biochemistry and a member of the Molecular Biology Institute at the University of California, Los Angeles, and 23 other coauthors from around the world, including Gutgsell Endowed Chair of Plant Biology and Crop Sciences Stephen Long (BSD/GEGC). ■

RESEARCH EFFORTS NEED PEOPLE WHO CAN HANDLE BOTH COMPUTATIONAL PROBLEMS & BIOLOGY PROBLEMS

INTERDISCIPLINARY PROBLEM SOLVING

HPCBio (High-Performance Biological Computing) led by Victor Jongeneel

When Victor Jongeneel (GNDP), a senior research scientist at the National Center for Supercomputing Applications (NCSA) and IGB Director of Bioinformatics, was an undergraduate studying biology in Switzerland, his advisor told him that biologists had no need for computers.

Today, Jongeneel directs HPCBio (High-Performance Biological Computing) at the IGB. HPCBio was created to address the need for a facility to supply infrastructure, user support and training, and research and development capability in computational genomics in the Illinois research community.

"Biologists need computer scientists to help them understand and analyze their data, and computer scientists need to understand what the problems are that biologists are working on," Jongeneel said.

WHY DO BIOLOGISTS NEED COMPUTERS?

In an article published in *PLOS Biology*, researchers, including Swanlund Chair Professor of Entomology and IGB Director Gene Robinson, Professor of Computer Science Chengxiang Zhai (BSD), and Willett Faculty Scholar and Associate Professor of Computer Science Saurabh Sinha (BSD/GNDP), noted that dramatic drops in DNA sequencing costs have led to a second genomic revolution. Over the last decade, the total amount of sequence data produced has been doubling approximately every seven months. Within ten years, the genomes for millions of species of plants, animals, and microbes, plus millions of human genomes, will be sequenced.

To handle these data, research efforts need people who can handle both computational problems and biology problems. One such "bilingual" researcher is functional genomics bioinformatics specialist and HPCBio staff member Jenny Drnevich.

"Before they actually collect their samples or do the analysis, we can talk to them about what they want to test and what kind of experimental design, what treatments they want to do, how many replicates pre-treatment they need to do, and then also fit within their budget," she explained. Samples are sequenced at the Roy J. Carver Biotechnology Center. When they come back, Drnevich or one of her colleagues checks the sequencing quality and normalizes the samples to take into account any inconsistencies.

"Biologists need computer scientists to help them understand & analyze their data & computer scientists need to understand what the problems are that biologists are working on," Jongeneel said.

They then use Biocluster, the campus hub for biocomputing, to analyze the results.

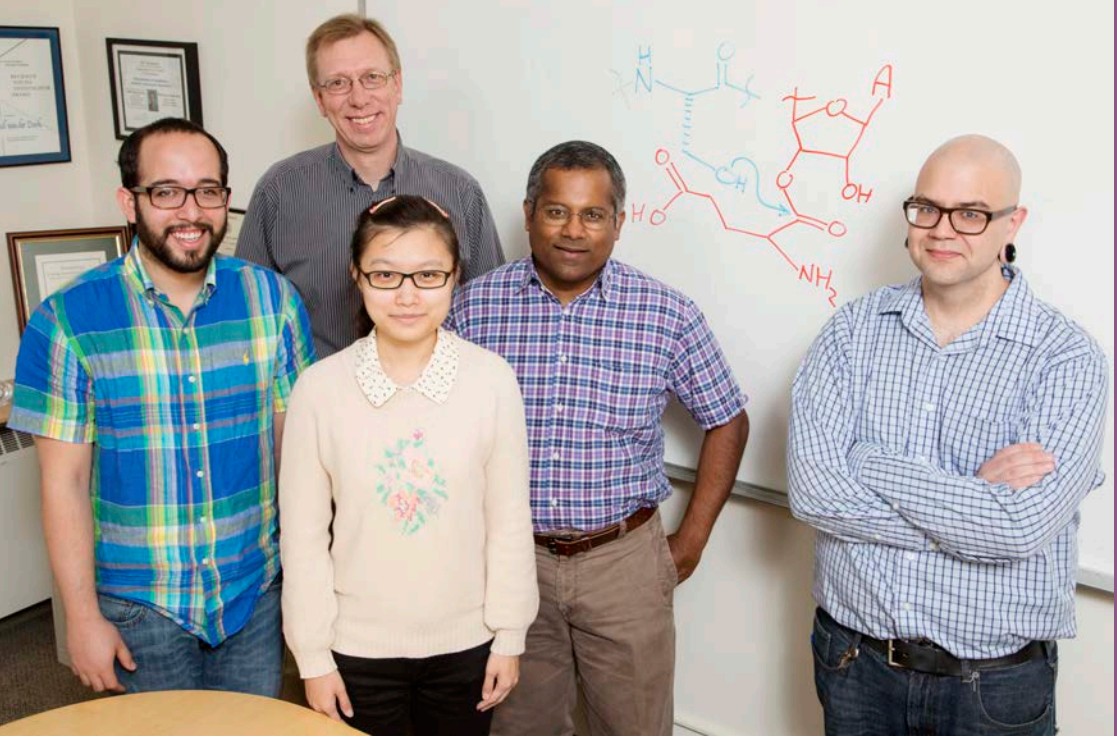
As research scientist Chris Fields noted, the group has worked on many different projects, "and there are not many projects we turn down." These have included research on samples from hot springs in Yellowstone National Park, the rat genome, bacterial genomes, and honey bees.

"Your data is usually on the order of billions, even tens of billions of pieces of sequence and you have to analyze all of this and make something out of it," he said. "Most conventional computers . . . don't have enough speed, memory, or processing power to actually deal with this in a meaningful way. They don't even have the ability to store the data."

Biocluster, said Fields, has these capabilities. "It has the ability to store tons of data, to process tons of data, and it does so by spreading the work out. You can split it up, process all of those in chunks, and then bring it back together again."

To date, HPCBio has taken on over 130 projects. It has helped to attract new research funding to campus; support researchers with ongoing projects; train graduate students, postdocs and faculty members; develop relationships with industrial partners; and catalyze new interdisciplinary projects involving biologists and computational scientists.

HPCBio has become a well-known and appreciated participant in the campus research enterprise and an indispensable partner for the many researchers generating high-throughput sequencing data. ■



TEAM DISCOVERS HOW MICROBES BUILD A POWERFUL ANTIBIOTIC

From left, Manuel A. Ortega, Wilfred van der Donk, Yue Hao, Satish Nair, & Mark Walker

IGB researchers have solved a decades-old mystery about how a powerful antibiotic is made in nature and opened up new avenues of research into thousands of similar molecules, many of which could be medically useful.

The team focused on a class of compounds that includes dozens with antibiotic properties. The most famous of these is nisin, a natural product in milk that can be synthesized in the lab and is added to foods as a preservative. Nisin has been used to combat foodborne pathogens since the late 1960s.

Researchers have long known the sequence of the nisin gene, and they can assemble the chain of amino acids (called a peptide) that it encodes. But the peptide undergoes several modifications in the cell after it is made that give it its final form and function. Researchers have tried for more than 25 years to understand how these changes occur.

"Peptides are a little bit like spaghetti; they're too flexible to do their jobs," said chemist and Howard Hughes Medical Institute investigator Wilfred van der Donk (MMG), who led the research with biochemist Satish Nair. "So what nature does is it starts putting knobs in, or starts making the peptide cyclical."

For nisin, an enzyme called a dehydratase removes water to help give the antibiotic its final, three-dimensional shape, which is the first step in converting it into a five-ringed structure.

The rings are essential to nisin's antibiotic function: two of them disrupt the construction of bacterial cell walls; the other three punch holes in bacterial membranes. This dual action makes it much more difficult for microbes to evolve resistance to the antibiotic.

Previous studies showed that the dehydratase was involved in making these modifications, but researchers have been unable to determine how it did so. This has prevented the discovery, production, and study of dozens of similar compounds that also could be useful in fighting foodborne diseases or dangerous microbial infections.

Manuel Ortega, a graduate student in van der Donk's lab, established that the amino acid glutamate was essential to nisin's transformation.

"[He] discovered that the dehydratase did two things," Nair said. "One is that it added glutamate [to the nisin peptide], and the second thing it did was it eliminated glutamate. But how does one enzyme have two different activities?"

To help answer this question, Yue Hao, a graduate student in Nair's lab, used X-ray crystallography to visualize how the dehydratase bound to the nisin peptide. She found that the enzyme interacted with the peptide in two ways: It grasped one part of the peptide and held it fast, while a different part of the dehydratase helped install the ring structures.

"There's a part of the nisin precursor peptide that is held steady, and there's a part that is flexible. And the flexible part is actually where the chemistry is carried out," Nair said.

Ortega also discovered that transfer RNA, a molecule best known for its role in protein production, supplies the glutamate that allows the dehydratase to help shape the nisin into its final, active form.

"In this study, we solve a lot of questions that people have had about how dehydration works on a chemical level," van der Donk said. "And it turns out that in nature a fairly large number of natural products—many of them with therapeutic potential—are made in a similar fashion."

The National Institute of General Medical Sciences at the National Institutes of Health and the Ford Foundation supported this work, which was reported in *Nature*. ■

HONORING CARL R. WOESE

THE INSTITUTE FOR GENOMIC BIOLOGY HAS BEEN RENAMED IN HONOR OF MICROBIOLOGY PROFESSOR CARL R. WOESE

INSTITUTE FOR GENOMIC BIOLOGY RENAMED FOR PROFESSOR CARL R. WOESE

The University of Illinois' Institute for Genomic Biology has been renamed in honor of a microbiology professor, Carl R. Woese, who changed the course of science with his discovery of a third major branch of the tree of life. Woese died in 2012.

"We are now the Carl R. Woese Institute for Genomic Biology," said Swanlund Chair of Entomology and IGB Director Gene Robinson. "By changing our name, we honor an individual who has made legendary contributions to science, who served as an Illinois microbiology faculty member for nearly 50 years, and who, as a founding member of the IGB, paved the way for us to emerge as a leader in advancing life sciences."

Woese was also honored in October 2015 when the American Society for Microbiology named the university as a Milestone in Microbiology site, a designation that recognizes institutions that have substantially advanced the science of microbiology.

In 1977, Woese and his colleagues discovered that there were three distinct branches, or "domains," of life, not two as had been previously thought. The new class of organisms, known as Archaea (are-KEY-uh), look superficially like bacteria but are genetically and evolutionarily as distinct from bacteria as are plants and animals.

Woese made his discovery by comparing the molecular sequences associated with the cellular machinery that translates the genes of individual organisms into proteins. In doing so, he pioneered the practice of using molecular sequences to gain insights into biology, an approach that is the precursor of today's genomics.

EMERGENCE OF LIFE MOOC

Although Carl Woese's concepts have revolutionized our understanding of the fundamental structure and evolutionary relatedness of all living entities on Earth and are central to cutting-edge genomic research, they are taught in very few classrooms. The Emergence of Life Massive Online Open Course (MOOC), led by microbiologist and geologist Bruce Fouke (BCXT/EBI), looks at the four-billion-year history of life on Earth through the lens of the modern Tree of Life.

Woese pioneered the practice of using molecular sequences to gain insights into biology, an approach that is the precursor of today's genomics.

Over 15,000 people participated in the eight-week course. Topics discussed included primordial life before the first cell had evolved, the approximately four-billion-year development of single- and multi-celled life, and the influence of earth system processes (meteor impacts, volcanoes, ice sheets) on shaping and structuring the tree. This synthesis emphasizes the universality of the emergence of life as a prelude for the search for extraterrestrial life.

The College of Liberal Arts and Sciences, the NASA Institute for Universal Biology, and the IGB partnered to present this educational opportunity, made possible with the contributions of scientific experts from around the world.

SYMPOSIUM HONORS CARL R. WOESE, DISCOVERER OF LIFE'S THIRD DOMAIN

To commemorate its renaming and celebrate Carl Woese's influence on some exciting advances in biology, the IGB held the symposium *Looking in the Right Direction: Carl Woese and the New Biology* on September 19-20, 2015.

This symposium highlighted modern research directions in genomic biology that have been inspired or impacted by Woese's work and ideas, encompassing microbiology, evolution, and synthetic biology. Penny Chisholm, Lee and Geraldine Martin Professor of Environmental Studies from the Massachusetts Institute of Technology and one of the world's foremost experts on marine microbiology, delivered the opening public lecture.

"Carl Woese once quipped that he saw further than others because he was looking in the right direction. He taught us how to look backwards in time, to see the earliest life on this planet. But he never stopped looking forwards either, to the future of biology," said Swanlund Professor of Physics Nigel Goldenfeld (BCXT). ■

CARL R. WOESE RESEARCH FUND

The Carl R. Woese Institute for Genomic Biology and Department of Microbiology are pleased to announce the "Carl R. Woese Research Fund" to provide support for research on evolution, systems biology, and ecosystem dynamics. Carl Woese approved this fund 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.

More than perhaps any other scientist, Woese focused attention on the invisible but pervasive microbial world, a realm that extends far beyond the pathogenic bacteria that are studied in medical science. He overturned one of the major dogmas of biology in 1977 when he discovered a third domain of life, the Archaea, microorganisms that are able to live in extreme environments without oxygen in conditions thought to be reminiscent of Earth's early environment.

Woese's notable awards included: election to the U.S. National Academy of Sciences; the Crafoord Prize in Biosciences; the National Medal of Science; the Leeuwenhoek Medal; and the MacArthur Foundation Fellowship (nicknamed the "Genius Grant").

The IGB organized a symposium *Looking in the Right Direction: Carl Woese and the New Biology* from September 19-20, 2015, to mark the renaming of the Institute. The symposium highlighted some of the historical aspects of work on microbiology, evolution, and molecular biology as researched by Carl Woese and colleagues and also some of the most exciting modern research directions that have been inspired or impacted by his work and ideas.

Please make a gift to recognize Prof. Woese and support new scientists. The IGB and Microbiology plan to recruit a cadre of Woese Fellows who will earn their degrees in microbiology while performing their research at the IGB. Woese Fellows will be specially selected for their creativity and interest in interdisciplinary research. We believe we will be able to attract some of the best and brightest students, who will find it quite an honor to be a Woese Fellow.

The Woese Research Fund can impact science, just as Carl Woese's insights have profoundly changed our basic understanding of biological classification and transformed our knowledge of life's diversity. Woese helped solidify the University of Illinois as a world leader in the use of genomics to answer some of the most challenging questions confronting us today. With your help, the "Carl R. Woese Research Fund" will help ensure that Illinois remains a world leader for generations to come. ■

PLEASE MAKE A GIFT TO RECOGNIZE PROF. WOESE AND SUPPORT NEW SCIENTISTS.

GENE E. ROBINSON
Director, Carl R. Woese Institute for Genomic Biology
Swanlund Chair
Center for Advanced Study Professor
in Entomology and Neuroscience

JOHN E. CRONAN
Head, Department of Microbiology
Professor of Microbiology and Biochemistry
Microbiology Alumni Professor

http://www.igb.illinois.edu/content/carl-r-woese-research-fund

$3.1 MILLION AWARDED TO DEVELOP ALL-TERRAIN ROVERS FOR FIELD PHENOTYPING

The University of Illinois announced that it has been awarded a 2-year, $3.1 million grant from the Department of Energy Advanced Research Projects Agency-Energy (ARPA-E). Illinois will lead the Mobile Energy-crop Phenotyping Platform (MEPP), working in partnership with researchers from Cornell University and Signetron Inc.

The researchers will develop all-terrain automated ground rovers that travel between rows in the crop fields, viewing each plant from below and above. These platforms will measure crop growth via 3D reconstruction of plants and stands and use reflectance of many different wavelengths of light and infra-red radiation, along with LiDAR (laser light detection and ranging) sensors, to assess physiological indicators of performance. Advanced biophysical computational models of crop growth and DNA-sequencing technologies will allow researchers to associate genes with improved crop performance to accelerate breeding of energy sorghum. Once established, these techniques will be applicable to all crops.

Illinois received this competitive award from ARPA-E's Transportation Energy Resources from Renewable Agriculture (TERRA) program.

TERRA

MEPP

MOBILE ENERGY-CROP PHENOTYPING PLATFORM

ILLINOIS & AAAS CO-SPONSOR BIOENGINEERING PANEL

Bioengineers are developing integrated devices for diagnosing and treating diseases and improving health. Researchers are testing implantable, flexible electrodes that can monitor biological function or stimulate cell growth; "lab-on-a-chip" devices that can cheaply diagnose diseases; and better brain-computer interfaces that allow people to use brain impulses to control prosthetics.

Development of biomedical engineering devices holds great potential for collaborative research, but making the technology available for public use is challenging. The interdisciplinary nature of the field, which relies on experts in engineering, biology, medicine, and physical and materials science, can create challenges for those trying to apply that research and technology as they navigate funding and regulatory agencies.

A panel consisting of Swanlund Chair Professor of Entomology and IGB Director Gene Robinson, Swanlund Chair Professor of Materials Science and Engineering John Rogers, Professor of Bioengineering Rashid Bashir (RBTE), and University of California, San Diego, Professor of Bioengineering Todd Coleman addressed these and other challenges at an event entitled "Visionary Frontiers at the Convergence of Biology, Medicine, and Engineering" held in Washington, D.C. on January 14, 2015.

RUBY MENDENHALL FEATURED ON SPOTLIGHT ON POVERTY & OPPORTUNITY WEBCAST

Ruby Mendenhall (GNDP), an associate professor of sociology, African American studies, urban and regional planning, and social work, was featured in a webcast on the *Spotlight on Poverty and Opportunity* site.

Mendenhall uses sociogenomics, which highlights the dynamic nature of the genome and how environmental factors can influence gene expression, to explore how aspects of stress in urban environments "get under the skin" to affect health and wellness. She is examining how the stress of living in neighborhoods with high levels of violence may affect expression of genes that regulate the immune system and inflammation. *Spotlight's* Jodie Levin-Epstein also talked with Mendenhall about the Earned Income Tax Credit and the impact of Black Women's Network on economic trajectories.

Ruby Mendenhall is an affiliate of the Institute for Computing in Humanities, Arts and Social Sciences.

Spotlight on Poverty and Opportunity: The Source for News, Ideas and Action is a non-partisan initiative that brings together diverse perspectives from the political, policy, advocacy, and foundation communities to find solutions to the economic hardship confronting millions of Americans.

IGB TRAVELS TO SHENZEN, CHINA, FOR BGI WORKSHOP

As part of an international exchange of knowledge and ideas, IGB members once again traveled to BGI (formerly known as the Beijing Genomics Institute) for a week-long learning and discussion workshop. They arrived in Hong Kong and journeyed via bus across the border to China to their destination, the Yantian District of Shenzhen.

Founded in Beijing with a mission to support science and technology development, build strong research teams, and promote the development of scientific partnership in genomics, BGI's headquarters were later relocated to Shenzhen as the first citizen-managed, non-profit research institution in China. BGI engages in large-scale, high-accuracy projects, sequencing over 50 plant and animal genomes and over 1,000 bacterial genomes.

NEIL SHUBIN, HOST OF PBS SHOW "YOUR INNER FISH," SPEAKS AT ILLINOIS

Have you ever wondered why the human body looks the way it does? Why our hands have five fingers instead of six? Why we walk on two legs instead of four? It took more than 350 million years for the human body to take shape. How did it become the complicated, quirky, amazing machine it is today? The truth is, hidden within the human body is a story of life on Earth.

Neil Shubin, the Robert R. Bensley Distinguished Service Professor of Organismal Biology and Anatomy at University of Chicago and host of the PBS show "Your Inner Fish," addressed some of these questions when he spoke as part of IGB's Genomics and Society lecture series on April 14.

Shubin is the associate dean for academic strategy of the University of Chicago's Biological Sciences Division. He is also the author of two popular science books: *The Universe Within: The Deep History of the Human Body* (2013) and the best-selling *Your Inner Fish: A Journey into the 3.5-Billion-Year History of the Human Body* (2008), which was named best book of the year by the National Academy of Sciences.

Shubin's research focus is on the evolution of new organs, especially limbs. He has conducted fieldwork in Greenland, China, Canada, and much of North America and Africa and has discovered some of the earliest mammals, crocodiles, dinosaurs, frogs, and salamanders in the fossil record. One of his most significant discoveries, the 375-million-year-old *Tiktaalik roseae* fossil, is considered an important transitional form between fish and land animals.

Shubin earned his doctorate in organismic and evolutionary biology at Harvard and was elected to the National Academy of Sciences in 2011.

POLLEN POWER CAMP PARTICIPANTS FORECAST A BRIGHT FUTURE FOR WOMEN IN PLANT SCIENCE

Cloudy skies and frequent rain contributed to an unusually wet central Illinois summer but could not dampen the enthusiasm for science displayed by 24 middle school girls who converged on IGB to learn about plants, pollination, and technology.

The attendees of Pollen Power, a week-long science day camp, participated in laboratories, presentations, and activities at the IGB as well as other Illinois science and technology facilities, including Champaign-Urbana Community FabLab, the Plant Biology greenhouse, and the Pollinatarium. Campers learned about the science of plant response to global climate change by engaging directly with scientists and the tools and methods they use.

Girls who attended the camp used microscopes to identify pollen from hundreds of plant species; scripted, designed, and recorded television "forecasts" to describe the past and future of Earth's climate and its ecological impact; and collected images, constructed a computer model, and built 3D-printed replicas of real pollen grains.

An important goal of the program is to help girls feel comfortable in the academic research environment and with the scientific process. Participants were encouraged to talk with female scientists—graduate students who acted as camp counselors, and faculty members who gave presentations and attended lunch groups—about research, life goals, and experiences in science.

Pollen Power Camp, offered last summer for the third year, is funded in part by the National Science Foundation. The camp was co-organized by plant biologists Andrew Leakey (EBI/GEGC), Lisa Ainsworth (GEGC), IGB Core Facilities, and IGB Outreach staff. Many other IGB members contributed their time and efforts.

LIFELONG LEARNING MEETS LIFE-CHANGING RESEARCH

A course offered by the University of Illinois Osher Lifelong Learning Institute (OLLI) this spring, "How Genomics is Changing Everything," garnered overwhelmingly positive reviews from its participants. OLLI is a member-driven learning community for people over the age of 50.

Animal biologist Alison Bell (GNDP) organized the course. Its aims are closely aligned with a central focus of the IGB's outreach mission–to make knowledge of genomics more accessible and relatable to all members of the public.

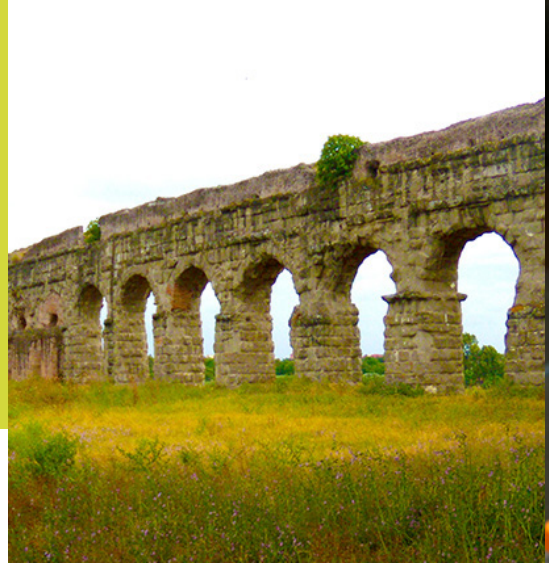
Topics covered in the course included the biological influences that shape animal and human behavior, the development of more resilient and productive food crops, regeneration of organs and tissues, and the genomics of cancer. In addition to Bell, anthropologist Ripan Malhi (CGRH/RBTE), plant biologists Lisa Ainsworth (GEGC) and Andrew Leakey (GEGC/EBI), animal biologist Karen Sears (GNDP/RBTE), cell and developmental biologists Lisa Stubbs (GNDP Theme Leader) and David Stocum (RBTE), and bioengineer Jian Ma (BSD/CDMC/GNDP) were course instructors.

IGB CONTRIBUTES EXHIBITS TO A NEW CARIBBEAN MARINE EDUCATION CENTER

Roy J. Carver Biotechnology Center director Bruce Fouke (BCXT), professor of geology and microbiology, and members of the IGB Communications Group contributed two posters to a new Marine Education Center (MEC) in Curaçao. The Center is part of the Caribbean Research and Management of Biodiversity Foundation (CARMABI), which is responsible for managing Curaçao's national parks, conducting marine and terrestrial ecological research, educating the public about nature and environment, and advising the government and others on nature-related issues.

The MEC, which the island's governor inaugurated on June 26, 2015, is a small but high-quality museum exhibiting information on the local marine life, particularly the coral reef surrounding the island, where Fouke is conducting research. It is part of a broader education program aimed at teaching schoolchildren about the importance of the coral reef, which is the base for diving tourism and fishing and protects the coast against storms.

IGB RESEARCH BRIEFS



GLACIAL MORAINES INFLUENCE NEW TECHNIQUES IN BIOMEDICINE

To find ways to deliver micro-therapies with more precision by controlling both the speed with which a drug is released and the spatial pattern it takes inside the body, IGB researchers look to glaciers for inspiration. Hyunjoon Kong (RBTE), a professor of chemical and biomedical engineering, and his team suggested using a microparticle-loaded hydrogel to deliver vascular endothelial growth factor (VEGF) at precise locations at the cellular level to stimulate cell growth to regenerate blood vessels.

In moraines, shear tension builds in the ice as the glacier grows, driving minerals and sediment trapped inside and next to it outward to create a pile of soil, rock, and debris that becomes oriented in a specific way relative to the glacier's movement. The researchers tried to replicate that behavior inside their hydrogel.

Freezing the hydrogel with the VEGF inside it allowed them to orient the drug into uniform channels. They tested it in mice and found the host's blood cells more easily migrated into the gel, where they came into contact with the VEGF and grew more blood vessels.

This is encouraging news for biomedicine, and medicine in general, because it moves us closer to new procedures that might promote more rapid blood vessel generation in damaged tissues in humans.

TRAVERTINE REVEALS ANCIENT ROMAN AQUEDUCT SUPPLY

For hundreds of years, the Anio Novus aqueduct carried water 54 miles from the Aniene River of the Apennine Mountains down into Rome. Since it was built—somewhere between AD 38 and 52—scholars have struggled to determine how much water is to supplied the Eternal City, until now.

By studying the buildup of limestone deposits, called travertine, that formed as the water flowed within the aqueduct, researchers estimated the flow rate: 1.4 m^3/s (± 0.4), as reported in the *Journal of Archaeological Science*.

"At this rate, the aqueduct would have supplied the city with 370 gallons of water each second," said lead author Bruce Fouke (BCXT), a professor of geology and microbiology. "That's enough water per second to take a three-hour shower or to take seven baths."

This estimate is significantly lower than previous estimates, which did not account for travertine deposits. The authors found that even a small amount of travertine reduced the water flow by 25 percent.

MICROBES SCARED TO DEATH BY VIRUS PRESENCE

Some microbes could surrender to a harmless virus, but instead freeze in place, dormant, ceasing to grow and reproduce, waiting for the virus to go away. If it does not, they will die within 24 to 48 hours.

"The microbe is hedging its bet," said microbiologist Rachel Whitaker (BCXT), who led the study published in *mBio*. "If they go dormant, they might die, but we think this must be better than getting infected and passing it on."

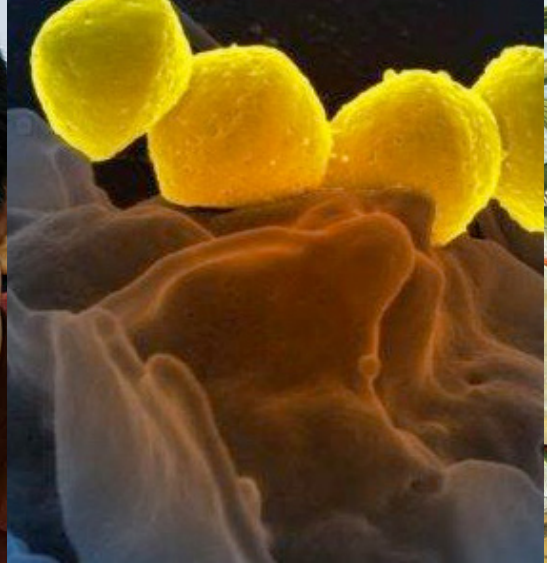
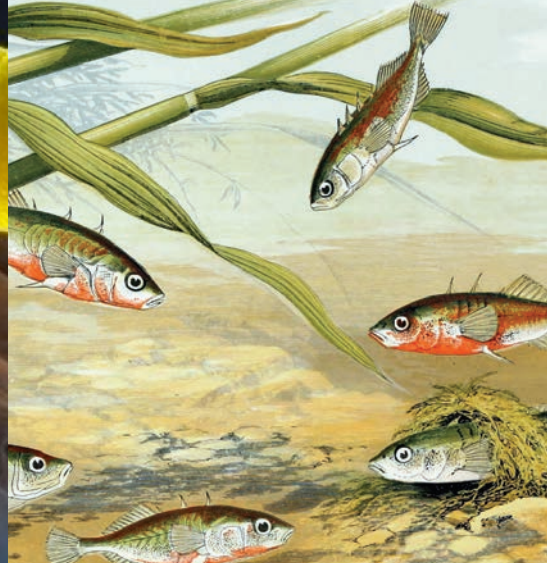
These microbes will go dormant in the presence of just a few viruses, whether active or inactive. While inactivated virus particles cannot infect a host, Whitaker's lab found they could still cause dormancy and ultimately death in the microbes, called *Sulfolobus islandicus*.

"People thought these inactivated viruses were just an accident, that they were just mispackaged," Whitaker said. "Now we know they are being sensed by the host so they are having an effect. People are starting to think that it is adaptive for the virus to produce inactivated virus particles."

CULTIVATED PAPAYA OWES A LOT TO THE ANCIENT MAYA

A genetic study of papaya sex chromosomes reveals that the hermaphrodite version of the plant, which is of most use to growers, arose as a result of human selection, most likely by the ancient Maya some 4,000 years ago.

Papaya plants are either male, female, or hermaphrodite. The hermaphrodites produce the desirable fruit that is sold commercially. Growing them is costly and inefficient because one-third of hermaphrodite fruit seeds and one-half of female seeds generate female plants, which are useless to growers. Farmers cannot tell which seeds will produce hermaphrodites until the plant has flowered, so they plant multiple seeds, identify the plants they want, and cut the others down.

From left, Roman aqueduct, Rachel Whitaker, Ray Ming, Streptococcus pyogenes, and stickleback fish

Researchers are trying to develop "true-breeding" hermaphrodite papaya that will produce only hermaphrodite offspring.

Plant biologist Ray Ming (EBI/GEGC) and his team sequenced and compared the "male-specific" and "hermaphrodite-specific" regions of the sex chromosomes in 24 wild male papaya and 12 cultivated hermaphrodite plants. They found less than half of one percent difference between the male and hermaphrodite sequences, suggesting that the evolutionary event that caused them to diverge occurred in the not-too-distant past.

Among the male papaya plants, the team identified three distinct wild populations: MSY1, MSY2, and MSY3, all from the northwest Pacific coast of Costa Rica. Their analysis revealed that the MSY3 population was most closely related to the hermaphrodite sex chromosome.

Given that no wild hermaphrodite papayas have been found in Central America, this suggests that the hermaphrodite papaya resulted from papaya domestication by the Maya or other indigenous groups.

This research, which was supported by the National Science Foundation, was reported in *Genome Research*.

RESEARCHERS LOOK TO HIV DRUG TO POTENTIALLY FIGHT BACTERIAL INFECTIONS

With antibiotic resistance on the rise, scientists are looking for innovative ways to combat harmful bacteria. Associate Professor of Chemistry Douglas Mitchell (MMG) and colleagues have now found a tool that could help them fight the pathogen that causes conditions from strep throat to flesh-eating disease: a drug approved to treat HIV. Their work, published in the journal *ACS Chemical Biology*, could lead to new treatments.

Streptococcus pyogenes is responsible for more than 600 million illnesses and 500,000 deaths globally every year. The pathogen produces a toxin called streptolysin S, or SLS.

To jam the bacterial machinery that makes the toxin, the researchers turned to nelfinavir, an HIV drug. Although the drug targets an HIV protein, it is also known to incidentally block a key enzyme in strep-infected patients. That enzyme is related to one in *S. pyogenes* that is critical for producing SLS. The scientists made several nelfinavir-like compounds that stopped the bacteria from making the toxin in lab tests. They concluded that the drug and its variants could help future efforts to understand how the deadly bacteria works and how to stop it.

The National Institutes of Health funded the research.

IN STICKLEBACK FISH, DADS INFLUENCE OFFSPRING BEHAVIOR AND GENE EXPRESSION

Researchers reported that attentive stickleback fish fathers influence their offspring to behave in a way that makes them less susceptible to predators. The offspring of these fathers also show changes in brain gene expression.

"There is lots of evidence that moms are very important for their offspring," said animal biologist Alison Bell (GNDP), who led the study with researcher Katie McGhee. "But we know much less about fathers."

Bell and McGhee evaluated fatherly influence on fry behavior by separating half of the fry from their dads before they hatched. When a predator fish was near, the orphaned sticklebacks made frantic attempts to escape, making them easier targets for the predator. Siblings reared by attentive fathers exhibited less of this frantic behavior. In contrast, there were no behavioral differences between orphaned or parented fry of less attentive fathers.

These findings suggest that fathers can help to compensate for inherent vulnerabilities by changing their behavior in ways that affect offspring behavior, Bell said. The team also looked at gene expression in the fish and found that the variation in parental care was associated with changes in an enzyme that promotes DNA methylation, a chemical modification of the genome that alters expression of specific genes by changing the way that DNA near those genes is packaged.

This work, supported by the National Science Foundation and the National Institutes of Health, was published in the *Proceedings of the Royal Society B: Biological Sciences*. ■

IGB GRANTS

JIAWEI HAN
SAURABH SINHA
JUN SONG
ADITYA PARAMESWARAN
UMBERTO RAVAIOLI
CHENGXIANG ZHAI
VICTOR JONGENEEL
NATIONAL INSTITUTES OF HEALTH
KnowEng, a Scalable Knowledge Engine for Large-Scale Genomic Data

GENE ROBINSON
MOLLY SHOOK
NATIONAL INSTITUTES OF HEALTH
Dynamic and Stable Regulation of Aggression through DNA Methylation

REBECCA STUMPF
NATIONAL SCIENCE FOUNDATION
Female Sociality Dispersal and Comparative Microbial Community Composition in Pan troglodytes

TIM GERNAT
GENE ROBINSON
NATIONAL ACADEMIES KECK FUTURES INITIATIVE
Trade-offs between Group Function and Disease Spread in an Animal Society

DIPTI NAYAK
LIFE SCIENCE RESEARCH FOUNDATION
Synthetic Biology and Lab-based Evolution for Methanogenesis from Non-natural Substrates ■

IGB AWARDS

ALEKSEI AKSIMENTIEV, Associate Professor of Physics (CDMC), was selected as a 2015-16 NCSA Faculty Fellow.

RASHID BASHIR, Bioengineering Professor and Department Head (RBTE), was elected a Fellow of the International Academy of Medical and Biological Engineering (IAMBE).

JIANJUN CHENG, Associate Professor of Materials Science and Engineering (RBTE), was chosen as an American Institute for Medical and Biological Engineering (AIMBE) Fellow.

BRIAN T. CUNNINGHAM, Professor of Electrical and Computer Engineering (MMG), was named a Donald Biggar Willett Professor in the College of Engineering.

EVAN DELUCIA, Professor of Plant Biology (GEGC), was named a fellow of the Ecological Society of America.

LEE DEVILLE, Professor of Mathematics (BCXT), received the Distinguished Teaching Award in Mathematics for Tenured Faculty from the College of Liberal Arts and Sciences.

A. BRYAN ENDRES, Associate Professor of Agriculture and Consumer Economics (EBI), received an American Agricultural Economics Association Distinguished Extension/Outreach Program Group Award from the College of ACES.

JIAWEI HAN, Abel Bliss Professor of Engineering (GNDP), received the Engineering Council Award for Outstanding Advising.

BRENDAN HARLEY, Assistant Professor of Chemical & Biomolecular Engineering (RBTE), received the Everitt Award for Teaching Excellence, was named a 2015-16 Center for Advanced Study Fellow, and was elected a 2014 fellow of the American Association for the Advancement of Science.

PRINCESS IMOUKHUEDE, Assistant Professor of Bioengineering (RBTE), was named a 2015 Young Innovator of Cellular and Molecular Bioengineering.

KRISTOPHER KILIAN, Assistant Professor of Materials Science and Engineering (RBTE), received a National Science Foundation CAREER Award.

DOKYOUNG LEE, Professor of Crop Sciences (EBI), received the North American Colleges and Teachers of Agriculture Educator Award from the College of ACES.

WEN-TSO LIU, Professor of Civil and Environmental Engineering (BCXT), was appointed the Arthur C. Nauman Endowed Professor in the Department of Civil and Environmental Engineering.

STEPHEN LONG, Gutgsell Endowed Professor of Crop Sciences and Plant Biology (GEGC/BSD), was presented with a Thomson Reuters Highly Cited Researcher award, and was named one of the World's Most Influential Scientific Minds for 2014 by Thomson-Reuters.

DOUGLAS MITCHELL, Assistant Professor of Chemistry (MMG), received a Camille Dreyfus Teacher-Scholar Award from the Camille & Henry Dreyfus Foundation, received the 2015 Pfizer Award in Enzyme Chemistry from the American Chemical Society Division of Biological Chemistry, and was named a 2015-2016 Helen Corley Petit Scholar.

JEFFREY S. MOORE, Murchison-Mallory Professor of Chemistry (BSD), was named the 2015 recipient of the Leete Award by the American Chemical Society Division of Organic Chemistry.

PHILLIP NEWMARK, Professor of Cell and Developmental Biology (RBTE), was elected a 2014 fellow of the American Association for the Advancement of Science.

JAMES O'DWYER, Assistant Professor of Plant Biology (BCXT), was selected for a Simons Foundation Investigator Award.

GENE ROBINSON (Director) was appointed to the Board of Scientific Advisors (BSA) of the National Courts and Sciences Institute (NCSI), and was conferred the degree of Doctor Philosophiae Honoris Causa of the Hebrew University of Jerusalem.

SANDRA RODRIGUEZ-ZAS, Professor of Animal Sciences (GNDP), received the Senior Faculty Award for excellence in research from the College of ACES.

CHARLES SCHROEDER, Associate Professor of Chemical & Biomolecular Engineering (BSD), was named a Dr. Ray and Beverly Mentzer Faculty Scholar.

KAREN SEARS, Assistant Professor of the School of Integrative Biology (RBTE), was named a 2015-2016 Helen Corley Petit Scholar.

SAURABH SINHA, Associate Professor of Computer Science (GNDP), was named a Donald Biggar Willett Professor in the College of Engineering.

VIJAY SINGH, Professor of Agricultural and Biological Engineering (GEGC), received the American Association of Cereal Chemists International Excellence in Teaching Award from the College of ACES.

BRYAN WHITE, Professor of Animal Sciences and Director, The Mayo Clinic/University of Illinois Strategic Alliance for Technology-Based Healthcare (BCXT), was elected to Fellowship in the American Academy of Microbiology.

DEREK WILDMAN, Professor of Molecular and Integrative Physiology (CGRH), received the International Federation of Placenta Associations (IFPA) Award in Placentology. ■

SHARING THE ART IN SCIENCE WITH THE WORLD

"ART OF SCIENCE: IMAGES FROM THE CARL R. WOESE INSTITUTE FOR GENOMIC BIOLOGY," NOW IN ITS FIFTH YEAR

The "Art of Science: Images from the Carl R. Woese Institute for Genomic Biology," is an exhibition of selected images produced in the IGB Core Facilities. Now in its fifth year, it is a meeting place between the university and our community as a whole and a celebration of common ground between science and art. The 2015 exhibition took place in April at the Indi-Go Artist Co-op in Champaign.

The exhibition comprises images from research addressing significant problems in the environment, medicine, and energy use and production. Images are selected to highlight the beauty and fascination encountered daily in scientific endeavors.

In June, the German Center for Research and Innovation (GCRI) in New York invited several members of the IGB to give them a special presentation on the exhibit. Kathryn Faith, managing artist for the Art of Science collection and senior multimedia design specialist at the IGB, along with director of IGB Core Facilities Glenn Fried, and cell and developmental biologist Lisa Stubbs (GNDP Theme Leader), spoke about genomic research and the relationship between art and science.

Images are selected to highlight the beauty and fascination encountered daily in scientific endeavors.

"Art of Science" images can be viewed at the Champaign Willard Airport and at the I Hotel and Conference Center in Champaign. ■

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.

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 and allows us to provide grants for daring, boundary-breaking research projects that more traditional funding agencies might be hesitant to support. 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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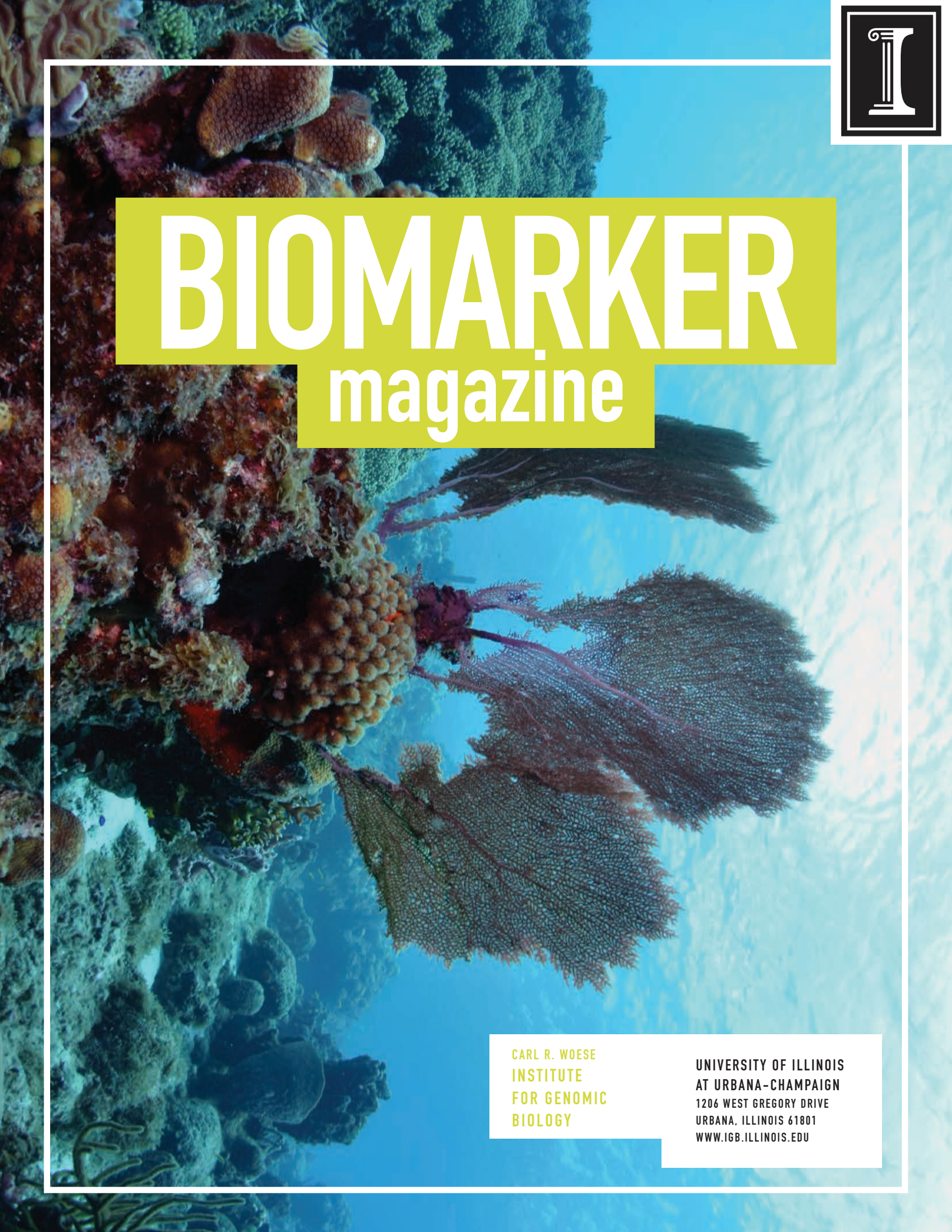

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CARL R. WOESE
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