

IGB NEWS

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Volume 15 Number 1

UPCOMING EVENTS

Spatial Omics Workshop

March 21, 2022, 10:30am—5:15pm
[Join via Zoom](#)

A half-day workshop to explore the development of cross-disciplinary interest and collaborations in the emerging field of “Spatial Omics.” More details and free registration [here](#).

IGB Seminar - MMG

From DNA to natural products via reverse genetics and synthetic biology
March 22, 2022, 12:00 p.m.
[Join via Zoom](#)

Alessandra Eustaquio, PhD
University of Illinois Chicago; Assistant Professor, College of Pharmacy

Lunch with the Core

High-dimensional characterization of phototroph-heterotroph interactions
March 23, 2022, 12:00 p.m.
[Join via Zoom](#)

Chandana Gopalakrishnappa,
Graduate Research Assistant, Physics

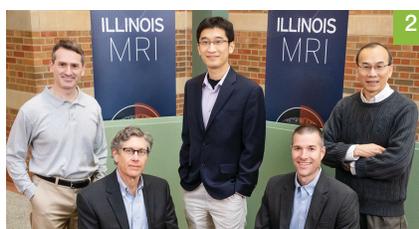
To go lunches will be provided.

IGB Faculty Spotlight Lecture

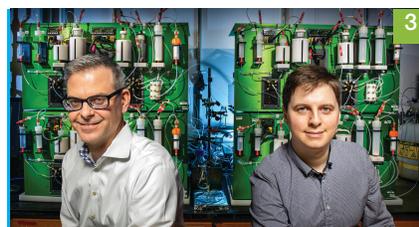
The intelligence of the (soft) body
March 29, 2022, 12:00 p.m.
[Join via Zoom](#)

Mattia Gazzola, PhD
University of Illinois; Assistant Professor, Mechanical Science and Engineering

FEATURED NEWS



Team uses MRI to image epigenetics in the brain



Chemical building blocks makes complex 3D molecules in a snap

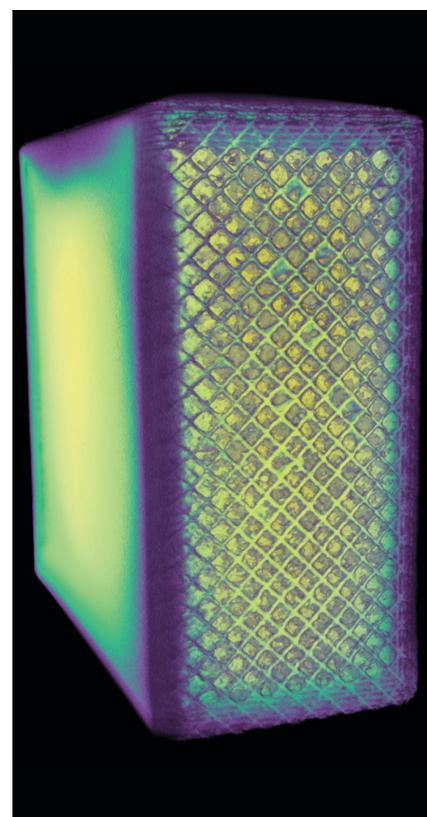


15 Years of IGB:
The RIPE Project



On the Grid:
Happenings at IGB

IMAGE OF THE MONTH



The image shows the density of 1x2x2 cm³ cube of a manufactured 316 stainless steel block using selective laser sintering (a 3D-printing process). The CT scan helps in determining defects produced in the material during the manufacturing process. This was scanned using the NSI X-5000 3D micro CT system and rendered using NSI eFX software, image courtesy of Charul Chadha and Iwona Jasiuk, Mechanical Science and Engineering Department.

IGB News

Share your news with the IGB. Send ideas on stories, articles, and features to nvasi@illinois.edu.

FEATURE



Team uses MRI to image epigenetics in the brain

A multidisciplinary team at the University of Illinois Urbana-Champaign has devised a new approach to 3D imaging that captures DNA methylation, a key epigenetic change associated with learning in the brain. The scientists say their proof-of-concept study in pigs will easily translate to humans, as the new method relies on standard MRI technology and biological markers already in use in human medicine.

Epigenetics is a key mechanism by which gene expression is regulated. The new approach – called epigenetic MRI, or eMRI – will open up new avenues of research into how such changes mold the brain, allowing it to grow, learn and respond to stress, the researchers said. The technique also may be useful in the study of neurodegenerative processes like Alzheimer’s disease.

The findings are reported in the Proceedings of the National Academy of Sciences.

DNA methylation is one mechanism that cells use to regulate which genes are actively expressed, said Dr. King Li, a professor in the Carle Illinois College of Medicine at the U. of I. who led the research with U. of I. bioengineering professor Fan Lam (GNBP) and IGB Director Gene Robinson (GNBP).

“Our DNA is the same from cell to cell and it doesn’t change,” Li said. “But tiny molecules, like methyl groups, are attached to the DNA backbone to regulate which genes are actively being

transcribed into RNAs and translated into proteins. DNA methylation is a very important part of the control of gene functions.”

Previous research showed that DNA methylation is one of several epigenetic changes that occur in the brain when an animal responds to its environ-

Pictured above, from left, chemistry professor Scott Silverman; entomology professor and IGB Director Gene Robinson, bioengineering professor Fan Lam; animal sciences professor Ryan Dilger; and electrical and computer engineering professor Zhi-Pei Liang.

ment, said Robinson, a professor of entomology at Illinois who studies the interplay of genomics, experience and behavior in honey bees. His studies have shown that many genes in the brain are upregulated or downregulated in bees as they mature, change roles in the hive, encounter new food sources or respond to threats.

There are two control systems in the brain, operating at different time scales, Robinson said. Neurons and other brain cells respond to environmental cues within seconds or milliseconds, while changes

in gene expression take longer. For example, when a honey bee experiences a threat, it must take action immediately. It relies on neurons to rapidly fire and allow it to act defensively. But the bee’s brain continues to respond even after the threat has lapsed, preparing itself for a potential future threat with changes in gene expression.

“We’re focusing on this second control system, the molecular control system, which relies on gene expression,” Robinson said. “These changes can take minutes to occur, but can last for hours, days or even longer.”

Scientists have been unable to precisely capture the molecular changes that take place in the living brain over time. Earlier epigenetic studies of honey bees and other organisms required the removal of brain tissue or that the animal be dissected for analysis. A previous research effort in the human brain imaged an enzyme involved in regulating one epigenetic change but did not target the epigenetic change directly. The Illinois team wanted to use the power of MRI to directly image epigenetic changes in live subjects.

For the new approach, the team relied on a key insight: Li realized that an essential amino acid, methionine, could carry an atomic marker known as carbon-13 into the brain, where it could donate the carbon-13-labeled methyl group needed for DNA methylation. This process would mark the DNA with a rare isotope of carbon. Carbon-13 occurs naturally in the body, but its sister isotope,

carbon-12, is much more abundant, Li said. About 99% of the carbon in living tissues is carbon-12, he said.

Methionine must be obtained through the diet, so the team decided to test the idea that feeding the carbon-13-labeled methionine to study subjects would allow it to pass into the brain and label those regions undergoing methylation.

“When we started this project, we thought it might fail,” said Lam, who worked with Illinois chemistry professor Scott Silverman to develop a method to distinguish between methylated DNA and other methylated molecules in the brain. “But the potential was so exciting that we had to try.”

Previous studies had already shown that MRI can image carbon-13, and orally administered carbon-13 has been in use in human subjects for decades. But the carbon-13 signal from living animals is weak, so Lam and U. of I. electrical and computer engineering professor Zhi-Pei Liang relied on their expertise in MRI and MR spectroscopy to significantly enhance the eMRI signal.

The team first tried the method in rodents, then switched to working in piglets, whose larger brains are more like human brains. For this, they relied on the expertise of co-author Ryan Dilger (GNDDP), a professor of animal sciences at Illinois who studies the factors that influence neurodevelopment in pigs.

“This project is highly multidisciplinary,” Lam said. “We have on the team engineers, imaging and radiology experts, and people with very strong backgrounds in clinical applications. We also have scientists with expertise in nutrition science, animal science, chemistry and genomics.”

In the experiments in piglets fed a diet that included carbon-13-labeled methionine, the researchers found that MRI could detect an increasing signal from carbon-13-labeled methyl groups in the brain. Further analyses allowed them to differentiate methyl groups on DNA from other methylated molecules.

The piglets had more new DNA methylation in the brain a few weeks after birth than they did at birth,

and the increase was much greater than expected based on changes in size alone.

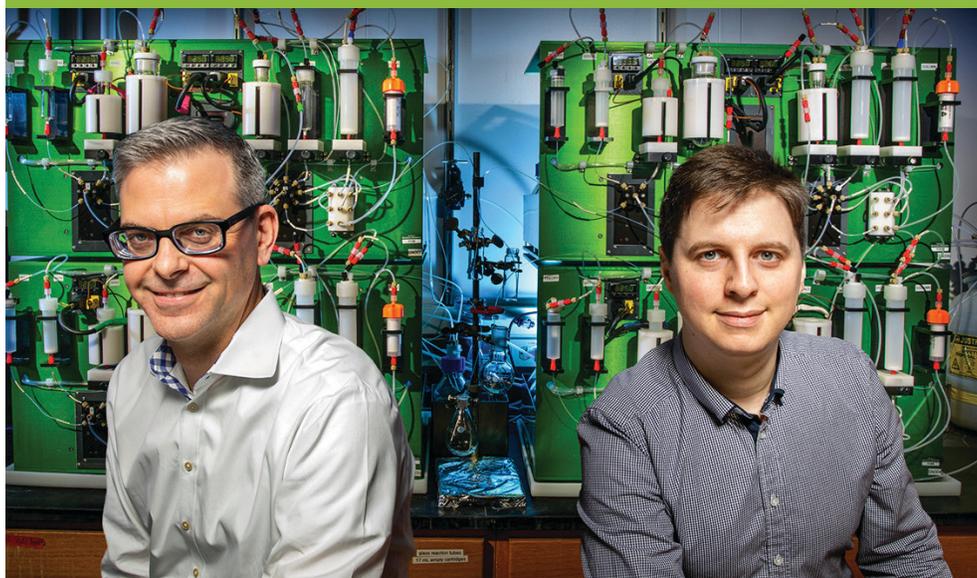
“This finding is very encouraging because it reflects what we expect to see if this signal is environmentally responsive,” Li said. “It is known from animal studies that brain regions that are most involved in learning and memory experience more epigenetic changes. There also were regional differences in DNA methylation across the pig brain, just like there are regional differences in classical MRI studies.

“We now expect to apply this technique in humans. Getting this label into the brain is easy and does no harm to the body. We’ll give it to people through the diet and then we can detect the signal.”

Their first application of the approach will likely occur in studies comparing the brains of people with and without neurodegenerative disease, he said. ■

Written by Diana Yates. Photo by L. Brian Stauffer.

RESEARCH



New set of chemical building blocks makes complex 3D molecules in a snap

A new set of molecular building blocks aims to make complex chemistry as simple and accessible as a toy construction kit.

Researchers at the University of Illinois Urbana-Champaign and collaborators at Revolution Medicines Inc. developed a new class of chemical

building blocks that simply snap together to form 3D molecules with complex twists and turns, and an automated machine to assemble the blocks like a 3D printer for molecules.

This automation could allow chemists and nonchemists alike to develop new pharmaceuticals,

materials, diagnostic probes, catalysts, perfumes, sweeteners and more, said study leader Dr. Martin D. Burke (MMG), a professor of chemistry at Illinois and a member of the Carle Illinois College of Medicine, as well as a medical doctor. The researchers reported their findings in the journal *Nature*.

RESEARCH CONT.

“It makes very complex 3D molecules in a very simple way,” Burke said. “This has been the secret chamber that only card-carrying chemists with decades of experience can enter. This new advance blows that door wide open. Now everyone can come in and play in the sandbox, because these very complex molecules become very accessible.”

For more than 15 years, Burke’s group has pioneered the development of simple chemical building blocks called MIDA boronates, which snap together sequentially using one simple reaction to build small molecules. His lab and collaborators at Revolution Medicines developed a molecule-making machine that automates chemical synthesis using these building blocks. However, the MIDA blocks are largely limited to making flat, 2D molecules.

The new set of building blocks, called TIDA boronates, unlock the missing third dimension, incorporating specific twists and 3D structures directly into the blocks.

“It’s all about function. Three dimensionality equals function,” Burke said. “The first generation was like those square and rectangular children’s bricks that can click together to build a nice, simple toy house. These are like the cool, complex brick kits for adults that let you build the Batmobile.”

To demonstrate the capacity of the TIDA blocks and the new second-generation molecule-making machine, the researchers synthesized two antimicrobial natural products with specific 3D features including a cyclical structure, as well as an array of smaller representative structures found in different types of molecules.

“Nature is very good at making three dimensional things a very precise way,” said postdoctoral researcher Daniel Blair, the first and co-corresponding author of the paper. “A lot of the molecules we use as inspiration for making many of our medicines are natural products, and those with these 3D structures tend to perform better in clinical applications. Yet until this point it has been very difficult to capture these structures within modular building blocks. The whole goal is to help more people make more molecules as simply as possible.”

The building-block approach to making molecules holds many advantages for chemists and nonchemists alike, the researchers said. Typically, chemists put a lot of time and effort into making a single target molecule, Blair said.

“Three-dimensionality hampers the preparation of different derivatives of a molecule to explore its function,” Blair said. “By capturing a lot of that three-dimensionality up front in modular building blocks, we can easily construct a target molecule. Next, we can exchange single building blocks to directly access derivatives and then see how that affects molecular functions.”

In addition to incorporating more function, TIDA boronate building blocks are up to 1,000 times more stable than MIDA boronate blocks in important reaction settings. They are also very stable in water, enabling simple synthesis of even more classes of chemicals under a wider array of conditions.

“MIDA had this loose spot where the connector piece was. When we switched to TIDA, that connector part twisted like a screw, and it’s like tighten-

ing down a bolt and a nut. And now it’s surprisingly stable,” Burke said.

The researchers are working to expand the library of TIDA boronate building blocks and plan to make them as widely commercially available as possible, using the success of MIDA boronates as a road map. MIDA boronates are now widely used: Around 270 are commercially available, and more than 250 academic and industrial labs have used them to make discoveries leading to more than 750 publications and 200 patent applications, Burke said.

“One of the things we’re so excited about now is we can make molecular building kits for really complex molecules. Like a plastic block kit has all the specialized pieces and you snap them together, now we can imagine kits for complex, important molecules, and make them accessible to nonchemists. I think it’s a chance for us to shatter some of those barriers that have traditionally limited who gets to innovate at the molecular scale.”

The National Institutes of Health, the National Science Foundation, the Damon-Runyon Cancer Research Foundation, the Henry Luce Foundation, the ACS Division of Organic Chemistry and the Austrian Science Fund supported this work. The U. of I. has filed patent applications for both MIDA and TIDA boronates. Burke is a founder, shareholder and consultant for Revolution Medicines Inc., which provided additional support for this research in the form of TIDA reagent. ■

*Written by Liz Ahlberg Touchstone.
Photos by Fred Zwicky*

DEPARTMENT ANNOUNCEMENTS

CNRG

DEGAUSSER

CNRG has recently purchased a degausser to aid in getting rid of failed drives and older hardware that may have important data still on the hard drive. It is a very quick process to run drives through our degausser. If you have any broken drives or older magnetic media around that you need to dispose of, bring it down to us in 131 and we can permanently delete the data with the degausser.

What is degaussing, you ask? “Degaussing is a unique technique of the permanent deletion of data applicable to memory devices based on a magnetic media (hard disk, floppy disk, magnetic tapes on open reels or cassette). It can ensure the rapid sanitization of information from media where it is not possible to apply overwriting erasure software due to hardware failure.” <https://www.ontrack.com/en-us/blog/what-is-degaussing-and-how-does-it-work> ■

MONTHLY PROFILE



RIPE

Realizing Increased Photosynthetic Efficiency (RIPE) is an international research project that is engineering crops to be more productive by improving photosynthesis, the natural process all plants use to convert sunlight into energy and yields. By equipping farmers with higher-yielding crops, we can ensure that everyone has enough food to lead a healthy, productive life.

15 Years of IGB The RIPE Project

Scientists have been breeding plants for over a century with the goal of feeding hungry people across the world. To that end, the Green Revolution in the 1960s used new technologies to increase food production in scale with the population growth. Unfortunately, these increases will not be enough in a few decades.

“The UN Food and Agricultural Organization predicts that the world will need to increase staple crop yields 70 percent by 2050,” said Stephen Long (BSD/CABBI/GEGC), the Ikenberry Endowed University Chair of Crop Sciences and Plant Biology. “The rapid advances that were achieved during the Green Revolution have slowed and will not meet this target.”

To catch up, the international Realizing Increased Photosynthetic Efficiency (RIPE) project was started in 2012 and the Illinois research efforts are based at the IGB. The goal of the project is to produce staple food crops that can efficiently convert sunlight into food and have increased productivity with fewer inputs.

RIPE primarily focuses on five crops: cassava, cowpea, maize, rice, and soybean, which are vital for sustaining the livelihood of people all over the world. “This project represents a huge effort to determine and apply the mechanisms of photosynthesis that can contribute to the challenge of this century - food security for all,” said Long.

Even though significant progress has been made, it is likely that RIPE’s technologies will not reach farmers until 2030, at which point the world’s population will have grown by more than a billion people. To expedite the scientific process, the project has nine research objectives that broadly fall into three categories: understanding the nuances of photosynthesis, improving its efficiency by manipulating a model crop, and transforming the target food crops to boost their yields.

“Our rich knowledge from a half-century of pho-

tosynthesis research, coupled with modeling, has enabled us to re-engineer this complex process in staple food crops. Our models predict that we could

*RIPE primarily focuses
on five crops: cassava, cowpea,
maize, rice, and soybean,
which are vital for sustaining
the livelihood of people
all over the world.*

achieve a 50 percent yield increase, which will go a long way to meeting the demands of this century,” Long said.

The researcher’s efforts have resulted in more than 80 research papers in the last 10 years and cover a wide range of topics including figuring out which of the 170 steps in photosynthesis can be tweaked to make the process more efficient; helping plants photosynthesize more efficiently even though sunlight intensity fluctuates throughout the day; modifying Rubisco—the main enzyme that captures carbon dioxide and converts it to sugars; optimizing crop canopies to allow better light penetration; and ensuring the modified crops are safe for the environment and consumption.

RIPE and its sponsors are also focused on making the technologies available to the farmers who need them the most. “We are committed to ensuring that the literal fruits of our labor are globally available and royalty free for smallholder farmers, particularly in sub-Saharan Africa and Southeast Asia, to help meet the huge challenge of feeding the future,” Long said. “While no single strategy will overcome the hurdles facing the industry, our success in RIPE and

our sponsors’ continued support give me hope that the future of agriculture is bright.”

RIPE was established with the help of a five-year, \$25-million grant from the Bill & Melinda Gates Foundation. In 2017, the project received another five-year grant for \$45 million from the Gates Foundation, the Foundation for Food and Agricultural Research, and the Foreign, Commonwealth & Development Office (formerly the U.K. Government’s Department for International Development). Additionally, the Gates foundation funded a \$13 million supplemental investment in 2018 to accelerate the translation of the project’s successes into food crops.

The RIPE project is led by the University of Illinois in partnership with the Australian National University, the University of Cambridge, the Chinese Academy of Sciences, the Commonwealth Scientific and Industrial Research Organization, Lancaster University, Louisiana State University, the University of California Berkeley, the University of Essex, and the USDA Agricultural Research Service. ■

Written by Ananya Sen.



Follow all the latest news from the RIPE project on Twitter, Facebook, Instagram, LinkedIn, and YouTube.

ON THE GRID HAPPENINGS AT THE IGB

AWARDS



CARLA CÁCERES

Carla Cáceres, Professor of Evolution, Ecology and Behavior (IGOH) was named by the University of Illinois as G. William Arends Professor.



ANDREW SMITH

Andrew Smith, Professor of Bioengineering (CGD) was elected Fellow of the American Institute for Medical and Biological Engineering (AIMBE) for outstanding contributions to the development of semiconductor quantum dots, ultrasensitive medical diagnostics, and bioengineering education.



TING LU

Ting Lu, Professor of Bioengineering (BCXT/ BSD/CABBI//MME), was elected Fellow of the American Institute for Medical and Biological Engineering (AIMBE) for outstanding contributions to the design, analysis and engineering of gene circuits that control microbial cell functionalities.



AMY WAGONER JOHNSON

Amy Wagoner Johnson, Professor and Andersen Faculty Scholar, Mechanical Science and Engineering (EIRH/RBTE) was elected Fellow of the American Institute for Medical and Biological Engineering (AIMBE), in recognition of her work recruiting and advancing women and persons of color in academia and pioneering research in biomaterials and biomechanics.



GENE ROBINSON

Gene Robinson, IGB Director, Swanlund Chair, Professor of Entomology (GNDP) was elected one of 17 councilors, serving a three-year term, for National Academy of Sciences (NAS).



RACHEL WHITAKER

Rachel Whitaker, Professor of Microbiology (IGOH leader/BCXT) was appointed the Harry E. Preble Professorship.

SYMPOSIUM

IGB FELLOWS SYMPOSIUM

IGB FELLOWS SYMPOSIUM REGISTRATION NOW OPEN

Learn about IGB research, hear about current issues in the life sciences, and network with other students at the annual Fellows Symposium! Register for free to attend and present a poster at our in-person poster session. Lunch is provided.

Register at fellows.igb.illinois.edu.

EVENT



ART OF SCIENCE 12.0

Join us for the Art of Science 12.0 at Cafeteria & Company in Urbana. Opening night on May 6th from 4:00pm to 8:00pm, and an additional showing on May 7th from 10:00am to 4:00pm.

Sponsored by the IGB, BodyWork Associates, and the Catherine and Don Kleinmuntz Center for Genomics in Business and Society

Cafeteria & Company
208 W. Main Street, Urbana

RECENT PUBLICATIONS

Please include your connection to the IGB in your author byline when submitting publications, as it will greatly help track potential newsworthy items and increase the possibility of coverage.

Brown, M. D., Shinn, L. M., Reeser, G., Browning, M., Schwingel, A., Khan, N. A., & Holscher, H. D. (2022). Fecal and soil microbiota composition of gardening and non-gardening families. *Scientific reports*, 12(1), [1595]. <https://doi.org/10.1038/s41598-022-05387-5>

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Frye, K. A., Sendra, K. M., Waldron, K. J., & Kehl-Fie, T. E. (2022). Old dogs, new tricks: New insights into the iron/manganese superoxide dismutase family. *Journal of Inorganic Biochemistry*, 230, [111748]. <https://doi.org/10.1016/j.jinorgbio.2022.111748>

Lim, J., Stavins, R., Kindratenko, V., Baek, J., Wang, L., White, K., Kumar, J., Valera, E., King, W. P., & Bashir, R. (2022). Microfluidic point-of-care device for detection of early strains and B.1.1.7 variant of SARS-CoV-2 virus. *Lab on a chip*. <https://doi.org/10.1039/d2lc00021k>

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Clark, G. G., Pan, W., Giammar, D. E., & Nguyen, T. H. (2022). Influence of point-of-use filters and stagnation on water quality at a preschool and under laboratory conditions. *Water Research*, 211, [118034]. <https://doi.org/10.1016/j.watres.2021.118034>

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Deng, H., Konopka, C. J., Prabhu, S., Sarkar, S., Medina, N. G., Fayyaz, M., Arogundade, O. H., Vidana Gamage, H. E., Shahoei, S. H., Nall, D., Youn, Y., Dobrucka, I. T., Audu, C. O., Joshi, A., Melvin, W. J., Gallagher, K. A., Selvin, P. R., Nelson, E. R., Dobrucki, L. W., ... Smith, A. M. (2022). Dextran-Mimetic Quantum Dots for Multimodal Macrophage Imaging *In Vivo*, *Ex Vivo*, and *In Situ*. *ACS Nano*, 16(2), 1999-2012. <https://doi.org/10.1021/acsnano.1c07010>

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I ILLINOIS

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