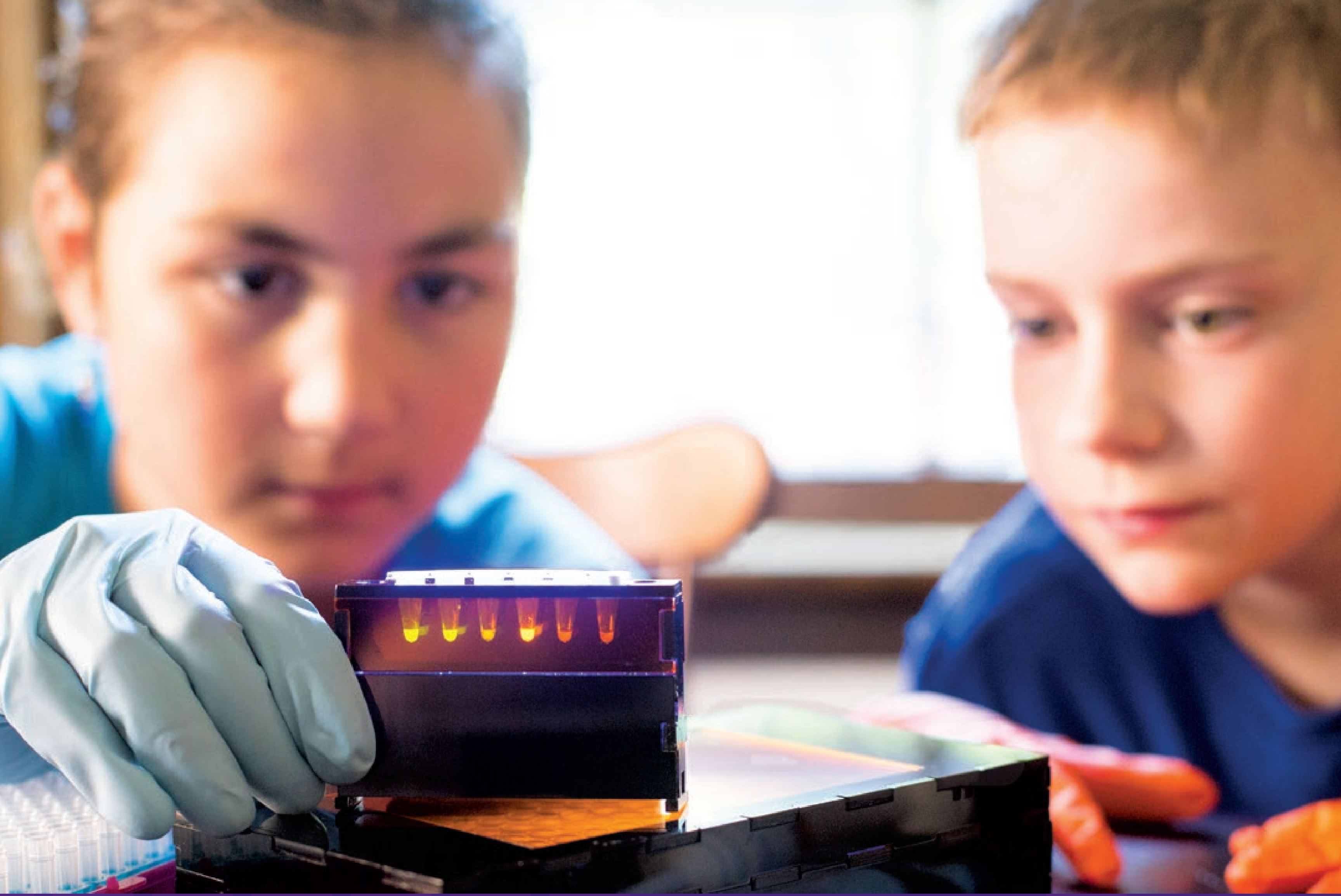

SYNTHETIC BIOLOGY BASICS, BIT BY BIT

New educational kits, BioBits, aim to inspire the next generation of synthetic biology researchers.

For teachers like Tom Martinez, the standard biology curriculum can feel a bit stale—teaching the same old units, recounting facts that have been passed down for decades. Yet science teachers often find incorporating cutting-edge concepts into their curriculum difficult because they feel isolated from the latest research.

"As a teacher, you're not part of what's going on in the real world of science," says Martinez, who teaches AP biology and biotechnology at Glenbard East High School in Lombard, Illinois. "You can get stuck in your same patterns. Teachers are a tough crowd. We like what we like, and change needs to be easy and convenient. You need to get some bang for your buck."

Martinez and his like-minded peers are exactly the crowd Michael Jewett and his graduate student Jessica Stark had in mind when they and their collaborators developed BioBits, new educational biology kits that teach the basics of synthetic biology through simple, hands-on experiments.

Even better, the kits provide a cheap and easy way to show how basic biological reactions work by engaging students' sight, smell, and touch. For example, BioBits can easily produce fluorescent reactions that dazzle the eye or olfactory reactions that create a banana smell without the technical machinery usually required to achieve such effects.

"As scientists and engineers, we all had that one teacher in high school who got us excited about science," says Jewett, Northwestern Engineering professor of chemical and biological engineering. "We had hands-on experiential, visual experiences that made us think, 'I need to learn more about that.' My students and I are dedicated to finding ways to inspire others to get excited about science in that same way."

TRANSLATING THE LAB TO THE CLASSROOM

The idea for the kits came together from several avenues. Jewett's lab has been developing cell-free translational systems that take the cells' inner systems involved in protein synthesis and metabolism and repurpose them for applications in medicine and energy. The process essentially uses the machinery inside the cell without having to fight the cell's natural evolutionary objective.

Research like this and other studies being conducted in Northwestern's Center for Synthetic Biology, where Jewett serves as co-director, has the potential to create new targeted therapeutics and sustainable chemicals and next-generation materials. But conducting synthetic biology experiments typically requires expensive incubators, freezers, and specialized tools like spectrometers, which makes such experimentation infeasible in a high school classroom.

Stark saw this disconnect first hand. For years she helped with the Jewett lab's annual National Science Foundation-sponsored Research Experience for Teachers, which brings Chicagoland middle and high school science teachers to the Evanston campus each summer to learn about the latest research in the field.

"While the teachers really enjoyed the experience in our lab, they said it wasn't translating well into the classroom, where they didn't have the same access to experimental resources that we do at a university," she says. "I made it my goal to develop a hands-on experience that could be run by anyone, anywhere."

CREATING A KIT FOR LESS THAN $100

Meanwhile, at the Massachusetts Institute of Technology, James Collins's lab had been taking those cell-free systems and freeze-drying them for use in molecular diagnostics. That process makes the system stable, eliminating the need for freezers.

Seizing an opportunity for collaboration, Jewett connected with Collins, the Termeer Professor of Medical Engineering and Science and member of the core faculty at Harvard University's Wyss Institute; the two combined their technology and developed freeze-dried cell-free pellets for educational kits. As a result, to initiate a basic reaction of biology—the transcription of DNA into RNA, and then the translation of that RNA into a protein—a high school student would just need to add DNA and water and let the mixture incubate.

Together, the professors and graduate students at both schools asked themselves two questions: "Can we take this technique and create educational kits to teach students the basics of synthetic biology?" And, "Can we make it available for less than $100, a price point affordable for school systems?"

The answer was "yes," and the result was BioBits Bright, a kit that contains six different freeze-dried templates. When students add water to create the reactions and let the reactions incubate, they come back to find that each template fluoresces a different color.

"When we tested it with students, they just had so much fun seeing that visual output," Stark says. "You get this glowing result that both validates you did everything right and makes abstract biology concepts more concrete."

Photographs by Megan Beltran

High school students watch Northwestern Engineering's Jessica Stark (center) and Michael Jewett demonstrate BioBits.

The team then expanded on the idea to create BioBits Explorer, which includes experiments to engage other senses. One experiment creates a compound that smells like bananas; another creates a hydrogel that students can touch and squish. "With these kits, students can carry out, in a day, the most core process of living systems," says Jewett, Charles Deering McCormick Professor of Teaching Excellence.

"IT KIND OF BLOWS THEM AWAY."

Stark worked with the Office of Community Education Partnerships at Northwestern to test the kits with local students and teachers and worked with teachers to develop a supporting curriculum. "Teachers helped us understand what would be feasible in the classroom," Stark says. "We wondered if it was even going to work in their hands. It was really nice to see the teachers and students get the intended result the very first time."

Martinez, a former Research Experience for Teachers participant, was an early tester of the kits. Right away, he saw them as a "fresh and new and interesting" element he could fit within his genetics curriculum.

"It's a really nice melding of classroom experience with bench experience," he says. "It's going to make molecular engineering more accessible and easier for students and teachers to do."

Martinez even tested the kits with students in an after-school club. He says they loved it.

"When you're 16 or 18 years old, you have no idea about any of this stuff," he explains. "When they first see it, it kind of blows them away because it's so foreign. It allows them to be creative with the genetic constructs they want to see. We spend all our time deconstructing living things to see how they work, and until now, we didn't spend any time trying to influence a cell to do what we want it to do."

INSPIRING THE NEXT GENERATION OF SYNTHETIC BIOLOGISTS

The team published their work in August 2018. Since then, they have had more than 140 requests for kits. Right now, Stark serves as the sole manufacturer, creating and providing kits as she can. The team is working with Collins's graduate student Ally Huang and Wyss Technology Development Fellow Peter Nguyen to find a partner to distribute the kits. The goal is to create a nonprofit to scale up manufacturing and distribution.

The team is also developing more activities with the kits and envisions creating a one-stop database of open-source curricula, worksheets, and ideas for new experiments. The hope for both Stark and Jewett is that the kits will ultimately inspire high school students to pursue STEM careers.

"Over the next 50 to 100 years, the ability to engineer biological systems and program the living world will become much more commonplace," Jewett says. "To me, that's one of the reasons these kits are so important. We need to inspire a generation of biological engineers who can meet that need."

EMILY AYSHFORD

CENTER FOR SYNTHETIC BIOLOGY BUILDS ON SUCCESS

The creation of BioBits was just one achievement in a successful year for the Center for Synthetic Biology, which has experienced national recognition through high-profile awards and outreach programs, growth among new members and collaborators, and unprecedented success in garnering funding for next-generation research in building biological systems.

Among some of the achievements:

FUNDING

Faculty members within the Center have received millions of dollars in grant funding this year.

Josh Leonard and **Neda Bagheri** received the first-ever research project grant (R01) dedicated to synthetic biology from the National Institutes of Health (NIH).

Milan Mrksich and **Michael Jewett** received a $6.25 million Multidisciplinary University Research Initiative grant from the US Department of Defense to develop chemical methods for controlling the conformations and functions of proteins.

Danielle Tullman-Ercek, **Michael Jewett**, and **Keith Tyo** received a combined $15 million in funding to develop new technologies to engineer microorganisms to produce sustainable chemicals.

AWARDS

Michael Jewett received the 2018 Young Investigator Award from the

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Josh Leonard received a 2018 Charles Deering McCormick Professor of Teaching Excellence award. **Michael Jewett** received the award in 2017.

NEW MEMBERS

The Center added two new members:

Arthur Prindle, assistant professor of biochemistry and molecular genetics in the Feinberg School of Medicine, joined from a postdoctoral fellowship at University of California, San Diego, and is the first Center faculty member to be based in Feinberg. His research looks to understand how molecular and cellular interactions give rise to collective behaviors in microbial communities and to use that understanding to develop new synthetic biology approaches through microbiome engineering.

Neha Kamat, assistant professor of biomedical engineering, joined Northwestern from Harvard University, where she served as a NASA Postdoctoral Fellow. She integrates materials science and synthetic biology to design artificial cells to understand and recreate targeted cellular behaviors. These systems have potential to be used as targeted drug delivery and novel sensor systems, and as an approach to studying fundamental signaling processes within cells and systems of cells.

RESEARCH

Milan Mrksich and **Michael Jewett** developed new platforms for characterizing and optimizing sequences for making glycoproteins using cell-free protein synthesis and mass spectrometry. Their work was published in *Nature Communications* and *Nature Chemical Biology*.

Neda Bagheri designed a new machine-learning algorithm that can help connect the dots among the genes' interactions inside cellular networks. Called Sliding Window Inference for Network Generation, or SWING, the algorithm uses time-series data to reveal the underlying structure of cellular networks. The work was published in the *Proceedings of the National Academy of Sciences*.

Julius Lucks developed a powerful and versatile tool that achieves gene activation thousands of times better than nature. Lucks created the switch by molecularly programming an RNA molecule called Small Transcription Activating RNA, or STAR, that his group had previously discovered. He then used an algorithm to optimize STAR for specific applications. His NIH-funded work was published in

.

Danielle Tullman-Ercek developed a new way to manipulate a virus shell that self-assembles from proteins and holds promise as a carrier for disease detection, drug delivery, and vaccinations. She and her collaborators developed a new technique that separated out mutated scaffold proteins that remained intact from those that broke apart during mutation to understand how repurposed virus proteins could be used in medicine. The study appeared in *Nature Communications*.

OUTREACH

Joshua Leonard recently presented a TEDx talk on synthetic biology at the American School Foundation of Monterrey, Mexico, to inspire high school students to pursue STEM careers.

Danielle Tullman-Ercek and **Michael Jewett** led a new 10-week Research Experience for Undergraduates program, which brought in eight students from around the country this past summer to conduct research in synthetic biology laboratories.