Cell

Engineering a Biological Revolution

The new field of synthetic biology promises to change health care, computer technology, the production of biofuels, and more. Students participating in the International Genetically Engineered Machine (iGEM) competition are on the front lines of this revolution.

A scientific revolution has begun, and it's being ushered in by groups of young people wearing matching T-shirts and hoodies. The International Genetically Engineered Machine (iGEM) competition invites college and high school students to design and build their own biological "machines." Students work throughout the summer and fall in labs all around the world designing and building cellular systems to address real-world problems. The most recent competition culminated in a four-day event in October in Boston, Massachusetts, where each of the nearly 300 teams presented its project. The colorful gathering with 3,000 participants (another 2,600 registered participants didn't make the trip) felt more like a celebration than a competition. Hundreds of six-foot banners lined the wide hallways of the Hynes Convention Center, each banner advertising a genetic engineering project. Groups of students wearing matching T-shirts or sweatshirts emblazoned with their team's name and project gathered in the huge poster exhibition area. A team from France wore red berets, and the students from Munich wore traditional Bavarian skirts or lederhosen while giving their presentation.

The iGEM competition, which originated as a course at the Massachusetts Institute of Technology and held its first competition in the summer of 2004, has fueled excitement and progress in synthetic biology around the world. Fundamentally different from research biology, the field of synthetic biology combines engineering and biology, applying design principles to the world of cells for the purpose of building a marketable product to solve a human problem. Synthetic biologists view cells as factories containing machines that manufacture "outputs." The goal is to genetically reprogram these machines in order to produce a desired output and to do it efficiently. Synthetic biologists often combine multiple functions in an engineered biological system, creating something new that doesn't exist in nature. For example, researchers have created targeted cancer treatments using a multifunction biological system, housed within *Salmonella* bacteria. The bacteria, which already thrive in the low-oxygen environment of a tumor, are perfect tools for drug delivery. The bacteria are engineered to produce tumor-killing drugs, and they are designed with a quorum sensing system—a system that allows each bacterial cell to sense how dense the bacterial population is. Once the population gets to a predetermined density, the bacterial cells self-destruct simultaneously, releasing a large dose of their toxic drugs directly to the tumor cells.

This type of cancer treatment isn't ready for humans yet, but synthetic biologists say the not-too-distant future will feature treatments like this, as well as yeast that produce jet fuels, synthetic anti-malarial drugs costing pennies per treatment, genetic data storage, microbes that manufacture alternatives to petroleum-based acrylics, and synthetic organs "printed" by 3D printers, ready for implantation. The students participating in iGEM are part of this revolutionary future.

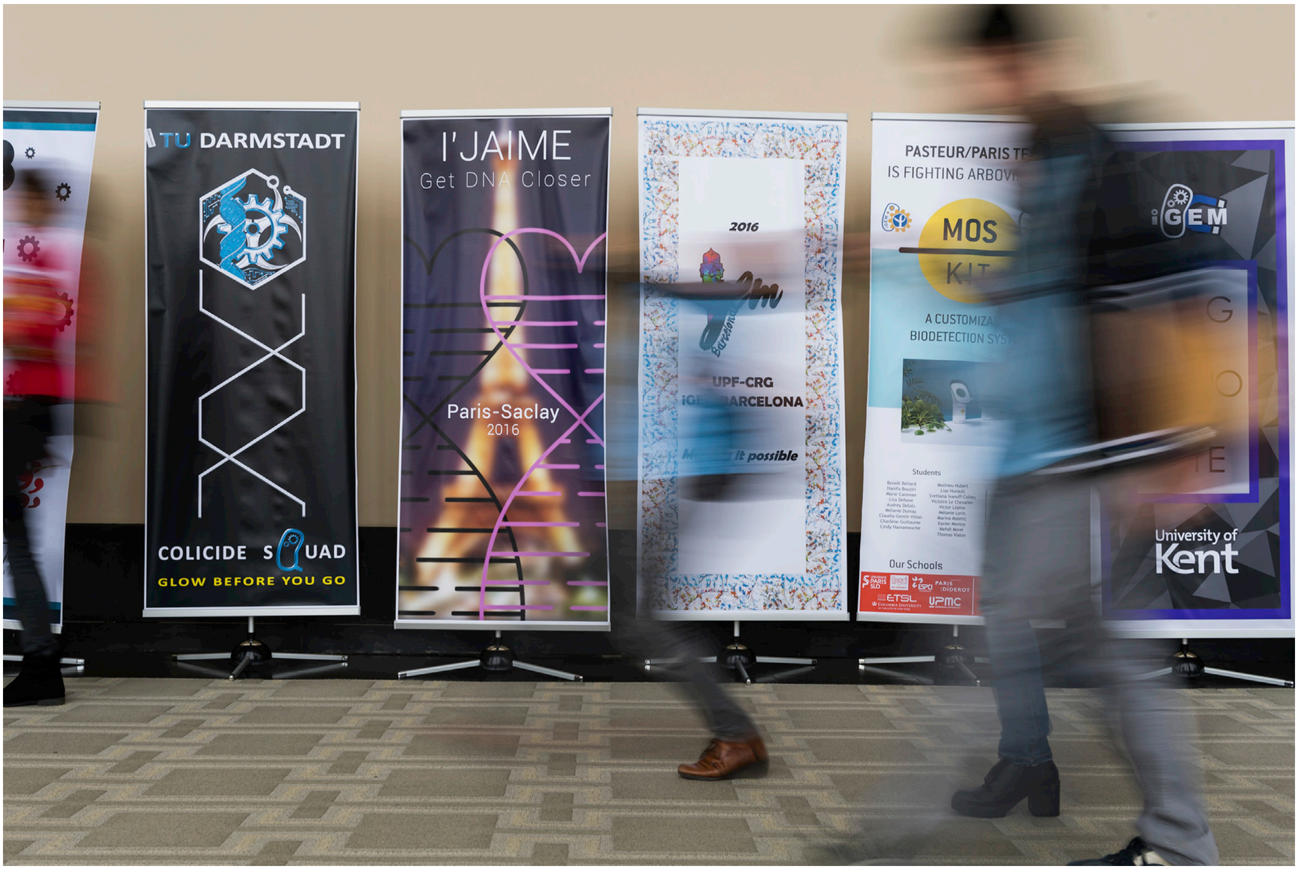
To be clear, this is a technical revolution more than a scientific revolution. The iGEM students see themselves less as traditional scientists and more as transformative designers who, like Steve Jobs, will invent entirely new product categories. In fact, one iGEM presentation concluded with a student unveiling his team's prototype device, a portable meter that measures alcohol content in the blood, and he did it exactly like Jobs announced the iPhone. Dressed in jeans and a long-sleeved black T-shirt, Jobs' iconic outfit, the student presented the device by pulling it from his pocket, just like Jobs did. The name of the device? The iMeter, of course.

Based on his first-hand experience in the computer industry, Randy Rettberg, president of the iGEM Foundation, believes synthetic biology will revolutionize our world. "The computer revolution—the information revolution—is an honest-to-god, for-real revolution that has changed everything." While the field of synthetic biology is only in its infancy and while "we don't yet have billion-dollar companies," says Rettberg, "revolutions come bit by bit by bit by bit" and tend to develop more slowly than expected.

Right now, synthetic biology is still at the part-building stage, and iGEM teams are helping to create new parts. Building parts involves applying engineering principles, such as modularity and standardization, to genetic material. *Modularity* refers to separating complex, natural biological systems into simpler components that each handle one task or function, such as detecting a toxic substance, binding to a particular target molecule, turning a gene on, or expressing green fluorescent protein. *Standardization* refers to creating component parts that all possess similar input and output interfaces so that parts can be combined easily, like in an electric circuit, and can be used interchangeably in different projects. A synthetic biologist with a new idea and a stockpile of different parts that work together could quickly bring that idea into reality. Each iGEM team creates at least one new biological part and then uses that part in conjunction with other parts they have created, or with parts created by previous iGEM teams, to design a multifunction biological machine. Individual parts are submitted to the Registry of Standard Biological Parts, an online registry and physical repository hosted by the iGEM Foundation and available for all iGEM teams to use. The registry currently contains some 20,000 parts.

Safety and Ethics

Because synthetic biologists alter the genetic code of living organisms—organisms



Banners describe each iGEM team's project, Hynes Convention Center, 2016. Photograph courtesy of iGEM Foundation and Justin Knight.

that reproduce quickly and whose genes could affect the environment or be affected by the environment—the field of synthetic biology is teeming with issues around safety and ethics. Critics are concerned about accidental harm to the environment, to workers in labs and manufacturing plants, to patients, and to wider communities, not to mention the intentional harm caused by people with evil motives. Critics ask how it is possible to even guess the environmental impacts of synthetic organisms. A collaboration of 117 environmental and social justice organizations published a document titled "The Principles for the Oversight of Synthetic Biology," and in it, they advise taking a precautionary approach, which requires exploring and developing alternatives to engineered biological machines, implementing transparent research and safety regulations, and engaging in "open, meaningful, and full public participation at every level." They insist on broader conversations with all stakeholders regarding ethical issues, specifically questions about the fundamental relationship between humans and nature and questions about economic justice.

While safety and ethics are huge areas that require larger conversations and decision-making processes, iGEM teams grapple with the safety and ethical issues associated with their projects. Even at the first iGEM competition, with just a handful of teams, students were already doing this, Rettberg says. "We brought in the topic: Is it safe? Is it moral? Is it okay to do this thing? Is it good to do this thing? … What would happen if this got loose?"

Today, all iGEM projects are closely reviewed by iGEM's own safety committee, which consists of experts from biotech companies, research institutions, and policy agencies. Teams fill out detailed forms about their project, biological materials to be used, equipment, resources, and safety training. The safety committee monitors projects throughout the competition and can disqualify any team over safety concerns.

Students engage in conversations with scientists and nonscientists, asking for input about their project. They specifically work to create two-way conversations with the public in a variety of ways: they conduct surveys, they arrange meetings with groups who would be affected by their product or application if it came to market, they present their work at local fairs and schools and invite questions, and they create games and activities that educate the public about the basics of synthetic biology. The iGEM judging rubric includes the question, "Did the [education and public engagement] work establish a dialogue?"

A team from Taiwan, China developed a biological part that creates a spider toxin

An iGEM team presents its project at the Hynes Convention Center, 2016. Photograph courtesy of iGEM Foundation and Justin Knight.

to be used by farmers as an alternative to pesticides, so they met with an agricultural expert, an entomologist, organic farmers, and the owner of an organic tea store to get their technical input, as well as discuss issues associated with food safety and pesticides.

The University of Calgary team, using a bacterial host, created a medical patch to be used by astronauts as protection from ionizing radiation, but they discovered that there were no Canadian policies addressing the use of engineered organisms in biotherapeutics. They worked with one of the directors of Canada's public health department and helped write a policy brief, addressing some of the regulatory gaps related to engineered organisms.

Diversity, Openness, and Mutual Support

The iGEM competition embodies the values of diversity, openness, and mutual support. Teams are comprised of students from a diversity of majors—biology, computer science, chemistry, genetics, biotechnology, biomedical engineering, mathematics, environmental engineering—in order to create innovative and effective projects. In addition, most teams have roughly an equal number of women and men (think about that for a moment).

The founders of iGEM believe that radical openness is one of the fastest ways to fuel innovative design. Therefore, all information about a team's project is published on the web, including a description of the project, what real-world problem it intends to solve, lab notes, diagrams, photographs, and videos, as well as the names of team members, funders, and mentors. Anyone can access this information. In addition, all the information in the extensive online Registry of Standard Biological Parts is available to the public.

Teams are encouraged to actively help and support each other. One team provided another team with bacterial growth data for its computer model. One team hosted a lab workshop to teach a couple of teams about the biological part assembly standard. One team shared its yeast strains with a team that did not have a yeast lab. One team tested another team's biological part. And one team helped another team develop their software application. In addition, many teams helped mentor new teams.

So, it is clear that the iGEM competition is not a competition in the traditional sense. In fact, it feels like the beginning of a revolution of a different sort: a revolution where students are excited about scientific discovery and design; where they are motived to solve local problems by including all stakeholders in the conversation; where they reflect deeply on their work and how it will affect others; where they work with diverse team members and help other teams; where they share their discoveries and inventions openly.

A revolution where they come together once a year to celebrate their work.

Asif Gil, a member of the team from Technion – Israel Institute of Technology, stated that the best part of iGEM's large gathering was "meeting so many people from different countries and different scientific backgrounds." He added, "A few times after I finished presenting our poster, I was caught up with other iGEMers in a conversation that started in biology, moved on to physics, and ended with a … discussion about nationalities. It was fascinating! I also found it very interesting how, in spite of technology and multiple platforms to transform knowledge, we as human beings still need the unmediated form of communication in order to learn new information. It made me hopeful."

The entire iGEM culture makes me hopeful, too.

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