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Today's News

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Students Compete Internationally to Build Biological Organisms From Standard Parts

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Cambridge, Mass.

Austin L. Day, a senior at the University of California at Berkeley, holds up an IV bag filled with a brown-red liquid resembling bloody-mary mix. The unsavory concoction is Berkeley's entry in a genetic-engineering competitionâ€”a blood substitute called "Bactoblood," made from modified bacteria.

Spurred by the worldwide shortage of human blood for transfusions, the Berkeley team developed a synthetic version by tinkering with the DNA of a common bacterium, *E. coli*. The young biologists added a collection of genes to produce hemoglobin, the molecule in red blood cells that carts oxygen around our bodies. They inserted more genes to make Bactoblood suitable for freeze-drying. And for safety, the students installed a "genetic kill switch" to destroy all the *E. coli* DNA, leaving essentially just a bag of hemoglobin. "It's disease-free, self-replicating, and universally compatible," says Mr. Day.

Not bad for 10 weeks of work by a bunch of undergraduates.

The Berkeley team was one of 56 teams from 20 countries that convened at the Massachusetts Institute of Technology's Ray and Maria Stata Center here in November for the International Genetically Engineered Machine Competition, known as iGEM. The underlying goal of the competition is to figure out whether biological organisms and devices can be built from a collection of standard, off-the-shelf parts, just as someone might build a kit plane or car.

For the undergrads involved, it's an opportunity to build whatever creature they can imagineâ€”living organisms that crank out biofuel, detect and remove pollutants, or even gauge the purity of olive oil. More importantly, the students are helping build the foundations of a nascent field, synthetic biology.

The founders of the iGEM competitionâ€”all MIT faculty membersâ€”take the view that living organisms are not just fuzzy, wet, ambiguous things, but machines. So they want to infuse synthetic biology with the principles and precision of engineering. Or at least try.

Biology is an opportunistic science, explains Randy Rettberg, principal research engineer in the institute's biological-engineering department. Scientists obtain their bits and pieces of DNA from labs scattered around the world, and assemble the molecules using whatever enzymes are convenient. It can take months to cut

and paste DNA together, and when it is assembled, it comes with no guarantee that it will actually function inside a living cell. Frequently what worked on paper doesn't work in the lab. And there are no global or national standards for manipulating DNA so that other researchers can easily use the building blocks.

To solve those problems, iGEM's founders are, via the efforts of hundreds of competitors, developing a library of DNA snippets, each with a specific function, that have been engineered to snap together with other library parts like genetic Legos. These "biobricks" are created according to strict guidelines so that each one is compatible with others in the collection, which is officially called the Registry of Standard Biological Parts. The registry contains about 2,000 biobricks.

With the biobricks, the competition's founders want to eliminate much of the drudgery and unpredictability of genetic engineering and "give students the freedom to do what they can imagine," says Mr. Rettberg, who is also iGEM's director.

Biofuels From Bacteria

The students certainly embraced that freedom. A group from the University of Alberta decided to go "green" with its entry by engineering *E. coli* to convert complex sugars into butanol, a biofuel. Their strategy was to pluck genes for manufacturing butanol from another microbe and tweak the system to crank out high levels of the fuel. Eventually they hope to insert the butanol-producing genes into another bacterium that will use light to convert carbon dioxide (instead of sugar) into butanolâ€”thereby creating a solar-powered biofuel generator that eats up a greenhouse gas.

"You just think up something and then you build it," says Sarah Hollingshead, a member of the University of Edinburgh team and the mind behind a project to make yogurt that flavors itself. "How cool is that?"

The teams of undergraduates are interdisciplinary mishmashes of biologists, biochemists, informaticists, engineers, and mathematicians. At the start of summer vacation, each group receives a genetic tool kit containing the current collection of biobricks. The teams use them to build an organism or biological system that can perform a certain task within one of five categories: energy, health and medicine, the environment, biological tools, or information processing. The teams are also encouraged to invent biobricks.

After finishing its work, each team mails its DNA creations and new biobricks directly to the registry. (The expanded tool kit of biobricks is sent out the following year.) In the name of open-source biology, each team constructs a "wiki" Web site describing the project and documents its progress in an online lab notebook. Then, in a frenetic two-day jamboree, some 550 students from around the globe descend on the cartoonish Stata building, a Frank O. Gehry creation, to describe their inventions. The teams are judged on their feats of DNA engineering and their presentations, posters, Web sites, and novel DNA biobricks.

MIT held the first synthetic-biology competition in 2004 with just five American institutions. The idea was a hit, and in 2005 the first official iGEM competition attracted 13 teams from four countries. In 2006, 37 teams from 15 countries joined the fray. A team from the University of Ljubljana, in Slovenia, took first place.

That high-profile win put synthetic biology on the fast track at the University of Ljubljana, says Anja Korencic, a fourth-year biochemistry major. To qualify for the 2007 team, students were asked to pitch ideas on how to stop HIV infection. Of 37 interested students, seven were chosen to participate in iGEM.

Building a New Field

To the delight of the founders and the faculty judges, iGEM has become much more than a competition. It is a factory for the next generation of synthetic biologists.

"One of the most amazing things about the jamboree this year was how much I was able to learn," says Drew Endy, an assistant professor in MIT's biological-engineering department. One example, he explained, arose from the University of Melbourne team, which created a biobrick based on genes harvested from a marine organism. When the biobrick is active, it produces gas vesicles or "buoyancy chambers" that make bacteria float. "Part of me is embarrassed that I didn't know about that," he says.

The competition is sparking a long-overdue transformation in biology education, says J. Craig Venter, who led the private effort to sequence the human genome and is not involved in the iGEM competition.

"The way biology is normally taught, it comes across as pretty dismalâ€”you memorize lots of facts and then you regurgitate them to people," says Mr. Venter, who is now focusing much of his research on synthetic biology in an attempt to create the first synthetic species and build a microbe that will produce biofuel. The competition "approaches things from a problem-solving and design perspective. That, I think, is a huge leap forward."

The project-based approach requires the students to initiate the projects, rather than simply carrying out the requests from their advisers.

"Synthetic biology is new to the facultyâ€”they didn't grow up with it," says Tito Jankowski, a member of the Brown University team, who is majoring in biomedical engineering. "Collectively our team knows a lot more than our advisers."

That's not just youthful bravado, says Gary M. Wessel, a professor of biology at Brown, who is teaching a course in synthetic biology. "We are a different generation, and we were trained to compartmentalize our education to the point where we excluded anything that wasn't specifically in our domain."

Synthetic biology is liberating, he says, because instead of spending years learning from textbooks how cells and organisms work, one can basically start from a design perspective and build from the bottom up.

Howls and High-Fives

At 6 p.m. on the first day of the competition, the presentations are over and the student area throbs with excitement. Music blares, students heap food on their plates, and the conference morphs into a big party. The judges have fled the noise to pick out the finalists, to be announced at 8 p.m. A loud groan erupts from the crowd as the students are told the judges need more time to make their decisions. At 8:30 the finalists are announced: UC-Berkeley, a team from several institutions in Paris, Peking University, Slovenia, the University of California at San Francisco, and the University of Science and Technology of China.

Howls, high-fives, and group huddles erupt.

"It was very exciting to be chosen, but there was a lot of pressure because of last year," says Ms. Korencic.

"It was a lot of blood, sweat, and tears," laughs Mr. Day, adding that making the finals was particularly

sweet because Bactoblood had been his full-time job during the summer and much of the fall semester.

The next day at the Kresge Auditorium, the six finalists present their work to all the competitors. As the judges convene for a second time, students burn nervous energy by jumping onto the stage and line dancing.

The first-time competitor Peking University takes the grand prize for engineering a way to make cells cooperate. The team raises the iGEM trophyâ€"a giant silver Legoâ€"up in the air and poses for pictures. "It is a big surprise," says Yifan Yang, a fourth-year biology major at Peking.

Mr. Yang's team built a bacterial assembly line in which a task is divided among genetically identical cells that have specialized but are able to cooperate. This division of labor mimics the human body, where genetically identical cells differentiate into heart, liver, and muscle cells, for example, and complete different tasks. In fact, this divide-and-conquer strategy is a key characteristic of all multicellular organisms.

The iGEM judges view the Peking group's work as a conceptual breakthrough. "This is a very interesting project because it goes beyond the genetic engineering of single cells," says Lee M. Silver, professor of molecular biology and public policy at Princeton University, who served as one of 23 judges. "So Peking University has taken the first step to what happened a billion years ago when the first cell evolved the ability to differentiate itself."

As the competition ends and the Chinese students pack up their trophy, competitors depart thinking about next year. Many of the projects made for the 2007 contest are not geared for commercialization, and so the students will probably leave the Bactoblood and their other creations to focus on new ways to snap genetic parts together. The greatest legacy of their efforts will be the new biobricks they built. The newly formed BioBricks Foundation is drafting a public license that will ensure that the DNA bricks, which are freely available to researchers, remain open-source genetic parts.

Eventually the library of biobricks will reach a critical mass that will enable people to build sophisticated organisms that carry out useful functions, says Mr. Endy, of MIT.

The open-source ideology underlying iGEM makes this arm of synthetic biology much more egalitarian than fields like genomics, where researchers need significant grants and major laboratory equipment to do research, says A. Malcolm Campbell, a professor of biology at Davidson College, who advised a joint team from Davidson and Missouri Western State University. "Synthetic biology is so cheap and affordable that you can be a small school and still be a major playerâ€"all you need are bright, creative students."

Mr. Venter says the competition teaches originality, which he wishes would seep through the staid world of professional research. "I'm hoping," he says, "to hire a lot of these kids in a few years."
