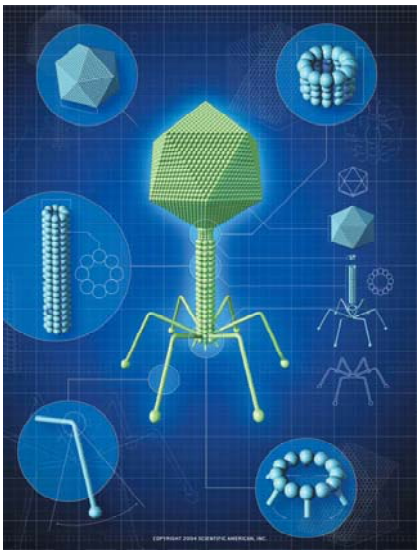
Synthetic Biology
The Portfolio

Every one is talking about it…

Biologists are crafting libraries of interchangeable DNA parts and assembling them inside microbes to create programmable, living machines

SYNTHETIC LIFE

By W. Wayt Gibbs



REDESIGNED VIRUSES will help biologists learn how to build reliable genetic machines. A group at the Massachusetts Institute of Technology has reorganized the genome of the T7 bacteriophage drawn here.

Evolution is a wellspring of creativity; 3.6 billion years of mutation and competition have endowed living things with an impressive range of useful skills. But there is still plenty of room for improvement. Certain microbes can digest the explosive and carcinogenic chemical TNT, for example—but wouldn't it be handy if they glowed as they did so, highlighting the location of buried land mines or contaminated soil? Wormwood shrubs generate a potent medicine against malaria but only in trace quantities that are expensive to extract. How many millions of lives could be saved if the compound, artemisinin, could instead be synthesized cheaply by vats of bacteria? And although many cancer researchers would trade their eyeteeth for a cell with a built-in, easy-to-read counter that ticks over reliably each time it divides, nature apparently has not deemed such a thing fit enough to survive in the wild.

It
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biological devices is far from easy. Biologists have been transplanting genes from one species to another for 30 years, yet genetic engineering is still more of a craft than a mature engineering discipline.

"Say I want to modify a plant so that it changes color in the presence of TNT," posits Drew Endy, a biologist at the Massachusetts Institute of Technology. "I can start tweaking genetic pathways in the plant to do that, and if I am lucky, then after a year or two I may get a 'device'—one system. But doing that once doesn't help me build a cell that swims around and eats plaque from artery walls. It doesn't help me grow a little microlens. Basically the current practice produces pieces of art."

Endy is one of a small but rapidly growing number of scientists who have set out in recent years to buttress the foundation of genetic engineering with what they call synthetic biology. They are designing and building living systems that behave in predictable ways, that use interchangeable parts, and in some cases

Scientific American , May 2004

it, rather than by tearing it apart. Two, make genetic engineering worthy of its

Synthetic Biology Remakes Small Genomes

Researchers are taking the first steps toward realizing the goal of building chromosomes by wholesale remodeling of organisms' genomes

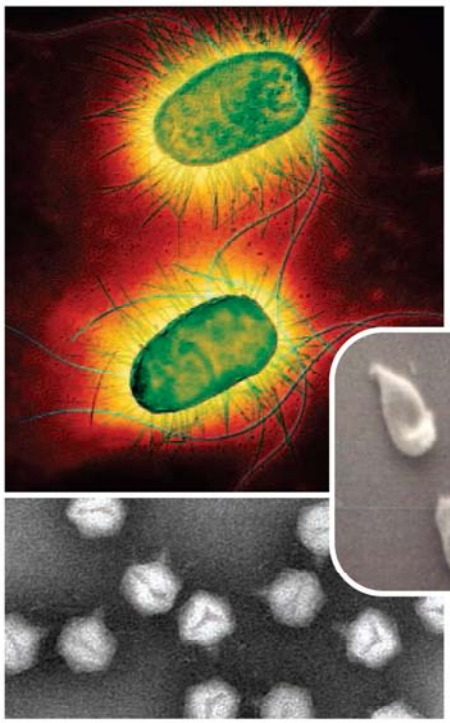
HILTON HEAD, SOUTH CAROLINA—People just can't leave nature alone. They have long stopped mighty rivers with dams, they are now breeding seedless watermelons, and they soon hope to customize microbes. Researchers from civil engineers to molecular biologists are developing ways to mold genomes like a potter does clay. These efforts to remake bacterial and viral DNA go far beyond adding or deleting a gene or two. Scientists are reducing, stretching, and recreating chromosomes as they lay the foundation for the emerging field of synthetic biology. "What we are most excited about are useful things we can make by messing around with the whole genome," says George Church, a technologist at Harvard University in Cambridge, Massachusetts.

Through their genome manipulations, synthetic biologists expect to learn more about how microorganisms function and also harness them to make complex proteins, get rid of toxic wastes, or carry out tasks not yet envisioned. Some of this new field's progress was on display at a genome meeting last month.* "You sensed a lot of excitement and stirring," says Ari Patrinos, chief of genome research at the U.S. Department of Energy. "It reminds me of the very early days of the Human Genome Project."

At this point, however, the field is more talk than reality, says J. Craig Venter, president of the J. Craig Venter Institute in Rockville, Maryland. "There's not a lot of data yet." It's difficult to separate the hype about synthetic biology from the hard results, agrees Patrinos. "This is the frontier" of biology, he notes.

Some of the hard results discussed at the meeting came from geneticist Frederick Blattner of the University of Wisconsin, Madison, who has gradually been shrinking the genome of *Escherichia coli*. The altered bacterium hardly notices, and it may offer advantages for genetic engineering, he reported.

Blattner began trimming the microbe's genome after sequencing various *E. coli* strains. He found that although the strains had 3.7 million bases in common, each also had about another million bases—cordoned off in specific "islands" of DNA—unique to each strain. His group has been deleting these genetic islands and other bits of DNA one by one, checking that the bacteria survive despite each loss. They perform these excisions using the natural process of homologous recombination. For example, they introduce into bacteria a stretch of DNA containing the sequences on either side of an island. A small number of the microbes will then swap out their similar stretch of DNA for the synthetic island-free version. The process is "scarless," as no extra DNA is left behind.



Designer bugs. *E. coli* (*above*), mycoplasma (*inset*), and bacterial virus (*lower*) studies are leading to customized chromosomes.

So far, the group has made 43 such deletions, whittling the core *E. coli* genome to less than 4 million bases and 3500 genes. That's far fewer than the 4444 genes now known to exist in the *E. coli* sequence. The researchers plan to trim even more, cutting another 3[illegible] then, we think we will have rem[illegible] the nonessential material," Blattn[illegible]

With its lean bacterial chro[illegible] streamlined *E. coli* strain created[illegible] group is 10 times better at absorbi[illegible] than one of the strains commonly used in genetic engineering. Now, "he can take this reduced genome and begin to add in [genes for] important industrial or pharmaceutical pathways," says Hamilton Smith, a molecular biologist at the Venter Institute. Moreover, notes Blattner, his new strain should be more resistant to certain undesirable genetic changes because it lacks the DNA islands, which tend to hop around the genome creating mutations.

Pump up the genome

In contrast to those who would shrink microbial chromosomes, Drew Endy of the Massachusetts Institute of Technology (MIT) in Cambridge has been expanding one. A civil engineer, Endy is one of the most visible—and controversial—spokespersons for the synthetic biology field. He runs a yearly contest in synthetic biology that has grown beyond MIT to include international teams (*Science*, 9 January 2004, p. 158). One of the most innovative entries thus far has been a bacterial camera, in which researchers endowed bacteria with genes for light-sensing proteins and other components for generating an image on culture media.

On his lab's synthetic biology Web site, Endy has set up a virtual bulletin board of research ideas, results, and protocols in the field; it draws 15,000 visitors a day. Some of his peers privately complain that Endy is a larger-than-life self-promoter—he's got his own synthetic biology company, gives scores of talks worldwide each year, and has helped create an upcoming comic strip with a main character called Device Dude who is a synthetic biologist. Others argue that he's driving the field forward. "He's injecting a lot of rigor in a field that is still somewhat soft," says Patrinos.

At the meeting, Endy described his lab's unusual work on T7, a virus that infects bacteria. He had been bothered by genes in T7's genome that were embedded or partially embedded in other genes and therefore shared some of the same DNA, as they complicated his ability to predict how infection and the resulting incorporation of viral DNA into the host genome are affected by different host environments. His model treated all the genes as separate entities and didn't take into consideration what happens if genes overlap. So he and his colleagues pulled apart T7's overlapping genes by inserting an extra copy [illegible]

[illegible] 40,000-base genome in this initial round of experiments, hoping that removing the overlaps didn't disrupt the genes' regulation or

* Genomes, Medicine, and the Environment 2005, 16–19 October, Hilton Head, South Carolina.

T. HOROWITZ/CORBIS

Starting from scratch

Genetic engineering is old hat. Biologists are now synthesizing genomes, altering the genetic code and contemplating new life forms. Is it time to think about the risks? Philip Ball asks the experts.

Redesigning Life. That was what Steven Benner wanted to call his 1988 conference in Interlaken, Switzerland. A chemist now at the University of Florida in Gainesville, Benner was organizing the meeting to explore the possibilities for making artificial chemical systems that mimic essential features of living things.

But his title caused such a furore among prospective attendees that Benner had to tone it down to Redesigning the Molecules of Life. "Individuals as distinguished as Nobel laureates were convinced that the title would incite anti-recombinant-DNA riots in Switzerland," Benner explains.

Benner's conference helped to define one strand of the emerging discipline known as synthetic biology, a field that is now raising worries that won't be deflected simply by semantics. The expanding toolbox of ways to re-engineer microbes — and even construct new ones — has opened up extraordinary possibilities for biomedical discovery and environmental engineering. But it also carries potential dangers that could eclipse the concerns already raised about genetic engineering and nanotechnology. If biologists are indeed on the threshold of synthesizing new life forms, the scope for abuse or inadvertent disaster could be huge.

In a dramatic demonstration of the potential risks, virologist Eckard Wimmer at the State University of New York at Stony Brook announced in 2002 that his team had built live poliovirus from scratch using mail-order segments of DNA and a viral genome map that is freely available on the Internet[1]. The feat put a spotlight on the possibility that bioterrorists could create even more dangerous organisms — including Ebola, smallpox and anthrax — perhaps endowing them with resistance to antibiotics.

Creative thoughts

Since then, biologists' abilities to engineer life have bounded ahead. Wimmer took three years to build his poliov… November genome sequencer … and his colleagues at the Insti… logical Energy Alternatives i… Maryland, announced that th… just three weeks to assemble … infects bacteria[2]. At the same time, bacterial cells are being rewired to perform functions they can't fulfil in nature. And researchers are getting close to determining the smallest set of genes necessary to support a living cell, which might make it possible to cook up new life forms.

Almost 30 years ago, concerns that recombinant DNA technology could pose risks to human health and the environment prompted leading molecular biologists to call an unprecedented summit. They gathered at the Asilomar Conference Center in Pacific Grove, California, in February 1975, where they decided to voluntarily forego some kinds of research and to instigate safety measures to prevent abuses of the new techniques.

Is it now time for another Asilomar? Researchers involved in synthetic biology generally agree that more discussion of how to avoid risks is urgently needed, but have yet to take the formal step of calling for a sum-

Nature, Oct 2004

The reason we face the question of risk at all is that the potential rewards of pursuing synthetic biology are so great. Protein engi-

Scientific American, April 2005

In the Business of Synthetic Life

Synthetic biology might someday lead to artificial organisms. To James J. Collins, it already offers pharmaceutical promise, like turning a person's cells into custom drug factories By SAM JAFFE

JAMES J. COLLINS: MAKING LIFE

- Practices synthetic biology, in which researchers tinker with genetic networks, rather than single genes of conventional genetic engineering.
- Found in previous work that a vibrating insole can improve the elderly's sense of balance, sparking interest from athletic shoe companies.
- On why engineering is easier than science: "All you have to do to succeed at engineering is to build something bigger, cheaper or faster. Science is creating new knowledge. That takes a lot more sweat and pain."

At first glance, the bacterial colonies that dot a petri dish in the Boston University laboratory of James J. Collins do not seem all that special. Each *Escherichia coli* bacterium has been genetically altered to manufacture a specific protein once the population density of the colony around it reaches a predefined level.

A skeptic might yawn. After all, genetic engineering isn't new. But these cells haven't just had a foreign gene spliced into them. Collins inserted a whole genetic network—he put in many genes that interact together as well as with the natural genetic machinery of the cell. In this case, he dropped in a quorum-sensing network from a *Vibrio fischerii* bacterium. If conventional genetic engineering is like changing the blade on a screwdriver, then Collins's approach is akin to altering the contents of the entire toolbox at once.

The 39-year-old Collins is a member of an emerging field called synthetic biology. Practitioners create novel ingredients for the recipe of life, including nucleic acids, amino acids and peptides. Some of them even hope to manufacture an artificial organism [see "Synthetic Life," by W. Wayt Gibbs; SCIENTIFIC AMERICAN, May 2004]. It is still considered a seed-stage discipline, where brilliant young scientists wow one another with proof-of-concept experiments and publish papers filled with pages of mathematical formulas. Collins, on the other hand, is the first to generate commercial technologies that are in the advanced stages of development. More than any other, he is proving that synthetic biology is ready for the marketplace, much more quickly than others expected it could be.

The most promising of those technologies is an RNA ribo-regulator, which Collins first described in 2004. It consists of a sequence of DNA that, with the help of a genetically engineered virus, integrates into a host bacterium's genome. The DNA then creates a loop of messenger RNA that binds to a site on the ribosome (the cell's protein factory), thereby blocking the production of a specified protein. The regulator

TRACY POWELL

Designs on life

Earlier this month, students from around the world locked horns in competition. Their challenge was to build functioning devices out of biological parts. **Erika Check** finds out how they got on.

Even if you're thinking big, you usually have to start small. Especially, as a group of Swiss students found, when big means counting to infinity. The team was drawing up a blueprint for the world's first counting machine made entirely of biological parts. Although they had their sights on loftier numbers, they opted to go no higher than two. If the plan worked, it would be a proof-of-principle for a much larger tallying device.

The group, from the Federal Institute of Technology (ETH) in Zurich, was one of 17 teams unveiling their projects at the first international Intercollegiate Genetically Engineered Machine (iGEM) competition, held at the Massachusetts Institute of Technology (MIT) in Cambridge on 5 and 6 November. The event attracted students from all over the world to design and build machines made entirely from biological components such as genes and proteins. They drew up grand designs for bacterial Etch-a-Sketches, photosensitive t-shirts, thermometers and sensors. And if none of the designs succeeded completely, that was more because of the limitations of the nascent science of synthetic biology than any lack of enthusiasm, creativity or hard work.

Synthetic biology aims to merge engineering approaches with biology. Researchers working at the most basic level are copying simple biological processes, such as the production of a protein from a gene. They break the process down into its component elements, such as a gene and the pieces of DNA and other molecules that control its activity. They then string these elements together to build a module they know will behave in a particular way — say, oscillate between producing and not producing a protein, or produce a protein that can switch another module on or off.

It is these kinds of components — oscillators and switches — that engineers order from suppliers and link together to build more complex electronic circuits and machines. Synthetic biologists are trying to develop a similar armoury of biological components, dubbed BioBricks, that can be inserted into any genetic circuit to carry out a particular function. Scientists at MIT have established a Registry of Standard Biological Parts, a catalogue of BioBricks that theoretically can be ordered and plugged into a cell, just as resistors and transistors can be ordered and plugged into electronic circuitry[1–3].

But it is hard to find scientists who are trained and interested in both biology and engineering to fuel the development of this new science. So, like true engineers, the founding synthetic biologists are trying to build their future colleagues from the ground up. To do so, they have commandeered a time-honoured engineering tradition: the student competition. The iGEM event began life as a project class for MIT students in 2003. Last year, it was thrown open to other US universities, and this year it went international. The organizers hope to attract 30 to 50 teams next year, including some from Asia.

Bidding for glory: teams from the ETH in Zurich (top), Cambridge, UK, (bottom right) and Massachusetts at the first international Intercollegiate Genetically Engineered Machine competition.

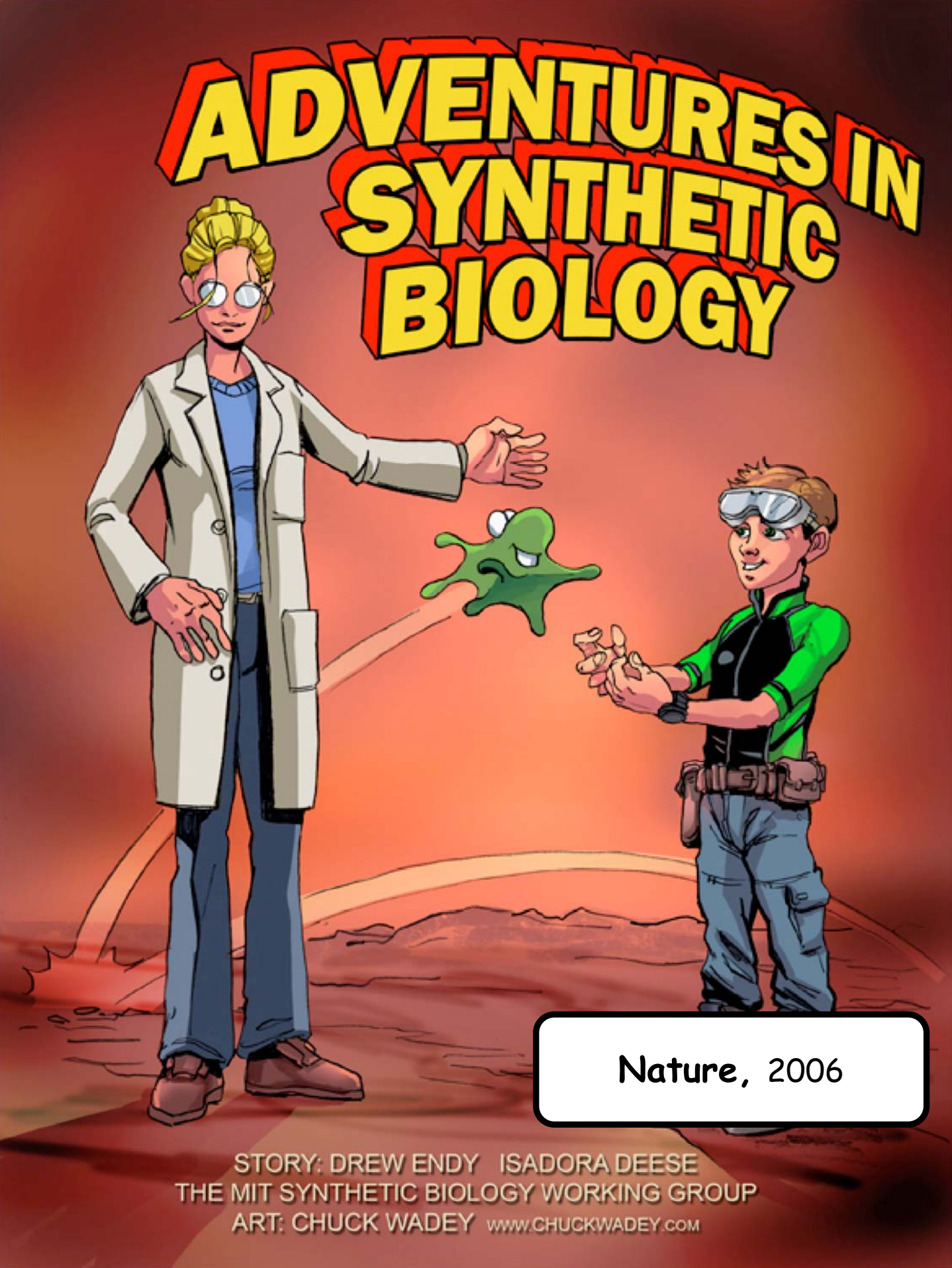
Competitive culture

Much like the robot competitions that tap into students' desire to build something cool, the iGEM jamborees fire the participants' natural curiosity — hopefully encoura… to learn something from engi… versa. "If you want to make so… field, you can't just get some gl… two cells together," says Ran… MIT, who organized the com… have to learn some biology to do it, and it's easy to do that during the competition because you know exactly why you're doing it."

This year, the teams presented an eclectic selection of designs. Students from the University of Cambridge, UK, tried to make a circuit that could control the movement of *Escherichia coli* bacteria. They aimed to engineer the bacteria to contain a switch governing their sensitivity to the sugar maltose. With the switch off, the microbes would ignore the sugar. Tripping the switch would make the bacteria sensitive to the sugar and induce them to move towards it. In the end, the group — like almost every other entrant — had trouble completing assembly of its genetic parts in time.

Many of the other students also tackled …on …ia …ce, …gy …at …the end of the competition.

A team from the University of Oklahoma's Advanced Center for Genome Technology in Norman tried to exploit the sugar arabinose as


ADVENTURES IN SYNTHETIC BIOLOGY
Nature, 2006
STORY: DREW ENDY ISADORA DEESE
THE MIT SYNTHETIC BIOLOGY WORKING GROUP
ART: CHUCK WADEY WWW.CHUCKWADEY.COM

Let us go forth and safely multiply

Synthetic biology, which involves the engineering of new biological components and organisms and the redesign of existing ones, will require community discipline and openness if it is to flourish safely, says **George Church**.

The developing field of 'synthetic biology' could be seen as yet another expression of scientific hubris. It has potential benefits, such as the development of low-cost drugs or the production of chemicals and energy by engineered bacteria. But it also carries risks: manufactured bioweapons[1] and dangerous organisms could be created, deliberately or by accident.

There is now a short window of opportunity during which the neologism can be attached to novel unions between the existing fields of genetic engineering, synthetic chemistry and metabolic engineering. Synthetic biology also needs to distinguish itself as a safe community effort that nurtures responsible practices and attitudes. For some, synthetic biology shares the potential, along with nanotechnology and artificial intelligence, to generate new entities that can reproduce and evolve at will[2,3]. Whether we believe that these are immediate, distant or imaginary threats, the concerns are real. For their part, biologists are excited by the potential for manufacturing precise, reliable and scalable synthetic components.

Safety first

A code of ethics and standards should emerge for biological engineering as it has done for other engineering disciplines. The community recognizes this need, but discussions are fragmentary. The next international meeting on synthetic biology (in May 2006 at the University of California, Berkeley) should make significant progress in that direction. What practical guidelines ought to be considered?

First, proper use of physical-isolation measures, as is already prescribed by levels 2 to 4 of the biosafety laboratory standards. Level 2 requires biological safety cabinets, lab coats, gloves and face protection; level 4 specifies a separate building, full-body suits and more.

Second, biological isolation — engineering biological systems to reduce their viability outside the lab and factory — should become standard practice. Genetic strains can be designed to require essential nutrients that are unavailable in the wild. The genome can also be engineered so that the genes cannot function in other cells. For example, a sufficiently novel genetic code for protein synthesis, not based on the standard amino-acid code, would not be expressed or function properly if taken up by natural cells or viruses. These safeguards should prevent genes for new toxins, allergens or pathogens from mixing and stably recombining with wild species.

The list of precautions is limited only by our creativity. Engineered cells could be programmed to self-destruct after a fixed time or on detecting an external signal. Similarly, engineered sequences can act as 'watermarks' for easier tracking. Genetic sequences that move around easily, such as transposons, can be removed from cells, thereby reducing undesirable genetic changes[4]. Other safety features we can imagine go beyond single-gene manipulations associated with conventional genetic engineering. For example, useful industrial microbes could be designed to have reduced mutation rates, except under specific lab conditions. Other microbes could be modified to detect the production of undesirable chemicals.

> "Learning from gene therapy, we should imagine worst-case scenarios and protect against them."

We should encourage young scientists to think constructively and build environments for sharing biological resources, with an emphasis on safety, as is happening in the International Genetically Engineered Machine (iGEM) programme. This event involves a growing number of universities (13 this year) sponsoring students to construct synthetic genetic systems (see page 417).

Above all, outreach is required. Genetically modified products, including crops and gene-therapy drugs, have been opposed for reasons that go beyond worries about scientific uncertainties. Citizens who will gladly take recombinant-DNA drugs (such as interferon, insulin and erythropoietin) are reluct
containing even trace amounts
DNA. Can synthetic biology ga
trust? We should learn from p
case of foods generated by synth
example, we need to recognize
ers include not just the farmers, but their neighbours and grocery shoppers also.

Learning from gene therapy, we should imagine worst-case scenarios and protect against them. For example, full physical isolation and confined lab experiments on human or agricultural pathogens should continue until we have data on a greater number of potential consequences — ecological and medical — of engineering such systems. Moving from closed-lab commercial projects to open-air systems will require appropriate experimental procedures and perhaps higher levels of biological isolation.

A watchful eye

In addition to a code of professional ethics for synthetic biologists, we need to watch for the rare cases when they transgress. This requires not just laws, but also monitoring compliance[5]. This could exploit government experience in the surveillance of illegal drugs and hazardous materials. In the commercial sector, monitoring systems could reveal suspect activities, such as labs requesting DNA that is related to potentially harmful biological agents. The purchase of precursor chemicals, nucleic acids, genes and designer cells could be screened against a pathogen database. However, automated monitoring will require cooperation by manufacturers[6] and international coordination. Discussions about this have begun, including one funded by the Sloan Foundation[7]. But any actions that penalize the legitimate manufacturer or user are likely to backfire, and having laws without government-mandated surveillance will be ineffective.

Finally, the community needs to discuss the benefits of synthetic engineering to balance the necessary, but distracting, focus on risks. From now on, each small step towards engineering enzymatic pathways for cheaper pharmaceuticals, smart biomaterials and large-scale integrated genetic circuits should be celebrated. ■

George Church is in the Department of Genetics, Harvard Medical School, 77 Avenue Louis Pasteur, Boston, Massachusetts 02115, USA.

Nature, Nov 2005

http://arep.med.harvard.edu/SBP/ (2004).
6. Aldhous, P. *New Scientist* magazine **188** (2525), 8 (2005).
7. *Study to explore risks, benefits of synthetic genomics* http://web.mit.edu/newsoffice/2005/syntheticbio.html (2005).

Economist.com

Economist, Aug 2006

Synthetic biology

Playing demigods

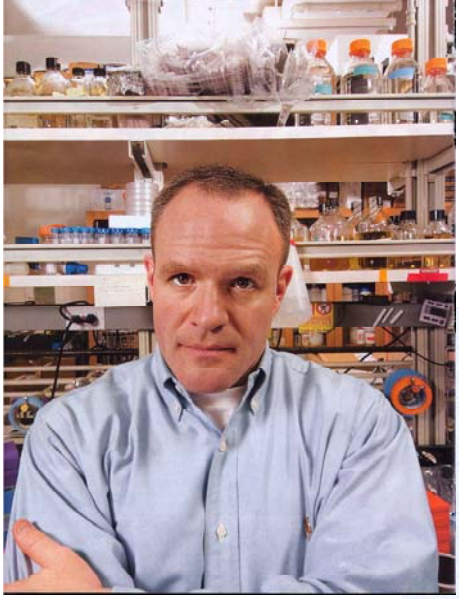
Aug 31st 2006
From The Economist print edition

Synthetic biology needs to be monitored, but not stifled

THERE will be no thunderstorm, no bolts of lightning channelled through giant switchgear, and definitely no hunchbacks called Igor. But sometime soon a line will be crossed in a laboratory somewhere and the first unarguably living thing created from scratch by the hand of man will divide itself in two and begin to reproduce. When it does so, it will abolish, once and for all, a distinction as old as human thought: that between animate and inanimate matter.

It is not considered polite, in the circles of synthetic biology as the subject is known, to mention the "F" word. Yet behind almost every discussion of the ethics of modern biology lurks the grinning spectre of Mary Shelley's novel, "Frankenstein", a parable on the unintended consequences of creating life. In truth, there is not much that is ethically dubious about making a bacterium from scratch. Making life is less worrying than modifying life—and modifying it in ways that are accidentally or deliberately harmful to mankind.

Synthetic biology is more than the mere tinkering of biotechnology. That just moves single genes around. Synthetic biologists plan to move lots of genes and to industrialise the process in a way that will let people order biological parts as routinely as they order electrical components. If this vision is realised (and there is still a long way to go) biotechnology will become a true branch of engineering, with benefits for industry, medicine and agriculture (see article and article). But biotechnology will also become a game that almost anyone can play—for fun or profit; recklessly or responsibly; for good or ill.



2006 SCIENTIST OF THE YEAR

JAY KEASLING

CHEMICAL ENGINEER AT THE UNIVERSITY OF CALIFORNIA AT BERKELEY

BY **CARL ZIMMER**

It's easy to be amazed by 21st-century feats of genetic engineering. Genes can be moved from one species to another, creating, say, goats that secrete drugs in their milk or bacteria that make human insulin. But that's not enough for Jay Keasling. Instead of the simple manipulation of single genes, he wants to engineer many genes to work together, like transistors wired in a circuit.

This new approach to manipulating life—along with explorations of artificial DNA, the creation of novel amino acids, and controlled evolution in the lab—has been dubbed synthetic biology, and Keasling, 42, is one of its chief engineers. As a nascent science, synthetic biology must prove itself through practical application, and Keasling is now close to providing just that: He is attempting to integrate genes from different species into a microbe to fabricate a drug for malaria. It is not just a technical tour de force but a humanitarian one. Keasling's microbes will churn out the drug for a fraction of its current cost, making it accessible to much more of the world. Properly harnessed, these microbes could save millions of lives.

Keasling spent his childhood immersed in the practical end of biology, chemistry, and engineering—he was raised on a farm. This background eventually led him to the burgeoning field of biotechnology. In the early 1980s, genetic engineering had just made the leap from the laboratory to the boardroom, as corporations made small fortunes inserting genes into *Escherichia coli* to produce insulin, growth hormones, and other valuable molecules. In Keasling's eyes, however, gen
neering hadn't harnessed the full power of c
tists had simply inserted a single gene into b
coaxed them into churning out as many co
same protein as possible.

Often the production of molecules isn't so s
quires a complex of several genes. One gene
protein, which then must be reworked by other proteins. Keasling wanted to invent the tools that would allow him to engineer these kinds of genetic assembly lines. So he pursued his Ph.D. not in biology but in chemical engineering. What goes on in a cell, Keasling surmised, is a lot like what goes on in a chemical plant: Petroleum goes in, and after a whole chain of reactions, plastic comes out.

Keasling spent his first decade at the University of California at Berkeley building the new tools he would need to turn cells into chemical plants. He studied plasmids, tiny ringlets of DNA that genetic engineers use to insert foreign genes into bacteria. He also found ways to coax microbes into producing abundant copies of a particular protein, and he invented powerful chemical switches that allowed him to trigger protein production.

Meanwhile, other scientists were similarly borrowing techniques from engineering and figuring out how to manipulate microbes, an effort they came to call synthetic biology. In 2003 the first synthetic biology conference took place at MIT, and by 2006 the field had become a media darling. *The Economist* heralded it as "Life 2.0"; *Forbes* wrote about the potential "regenesis" of life.

Behind the dazzle lies the tedious reality: Synthetic biology requires a lot of work to do relatively simple things. Take, for example, the bacterial camera. In 2005 scientists from the University of Texas and the University of California at San Francisco reported that they had created a strain of *E. coli* that could produce a photograph-like image. They inserted genes for sensing light and producing pigments into the bacteria and then engineered the

cent effective against the parasite that causes malaria and has few side effects (malaria kills some 3 million people a

Discover, Dec 2006

Economist.com

Synthetic biology

Gassed up

May 24th 2007
From The Economist print edition

Economist, May 2007

A new, green way to make hydrogen

THE problem with living things is that they do insist on growing. They also insist on metabolising. The reason this is a problem, at least from the point of view of the new science of synthetic biology, is that all this growing and metabolising is a dissipation of effort from the task you want your souped-up bug to do.

Synthetic biology works by taking enzymes from a range of organisms (and sometimes other enzymes that have been tweaked so much that they no longer resemble anything natural), and assembling them into novel biochemical pathways in tame microbes. That allows synthetic biologists to turn out things like drugs and precursor-molecules for plastics more efficiently than traditional chemists can.

But the process would be even more efficient if it separated the pathway from the microbe. And that is what Percival Zhang, of Virginia Tech, has managed. He and his colleagues have taken 13 enzymes, derived from five different organisms ranging from spinach to rabbits via yeast and bacteria, and assembled a pathway that converts starch into hydrogen. No living organism can perform that feat, but it is a trick that might, if commercialised, provide hydrogen for fuel cells cheaply and easily.

To do this sort of thing, you really have to know your enzymes. Most enzymes can perform only one chemical transformation. The art, therefore, is to create a chain in which the output of one provides the input of the next. It is rather like a puzzle in which one word is transformed into another by altering one letter at a time, while always making the result a legitimate word. Except, in this puzzle, the length of the word can change, too. To turn starch (a polymer composed of glucose molecules) into hydrogen (an elemental gas composed of two hydrogen atoms) in this way is no easy task. To complicate things still more, the enzymes in question all have to like the same conditions of temperature and acidity, otherwise they will not be able to work simultaneously.

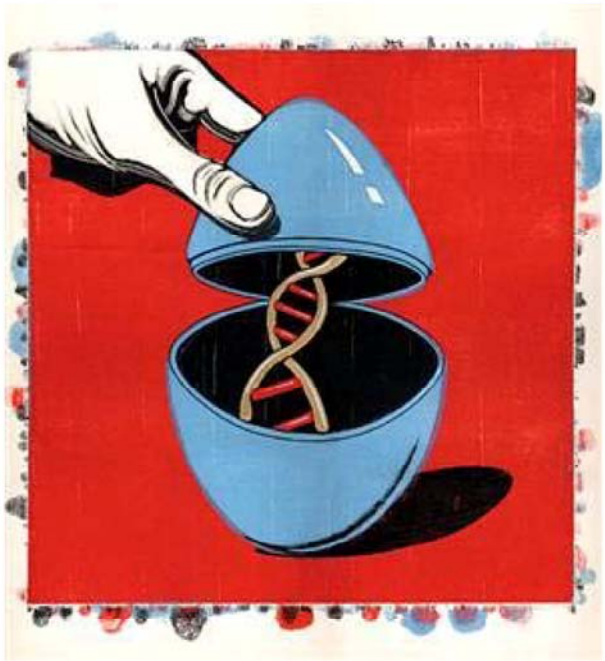
MSNBC.com Newsweek

Scientists Push the Boundaries of Human Life

A new generation of scientific mavericks is not content to merely tinker with life's genetic code. They want to rewrite it from scratch.

By Lee Silver

Newsweek International



June 4, 2007 issue - It last happened about 3.6 billion years ago. a tiny living cell emerged from the dust of the Earth. It replicated itself, and its progeny replicated themselves, and so on, with genetic twists and turns down through billions of generations. Today every living organism—every person, plant, animal and microbe—can trace its heritage back to that first cell. Earth's extended family is the only kind of life that we've observed, so far, in the universe.

This pantheon of living organisms is about to get some newcomers—and we're not talking about extraterrestrials. Scientists in the last couple of years have been trying to create novel forms of life from scratch. They've forged chemicals into synthetic DNA, the DNA into genes, genes into genomes, and built the molecular machinery of completely new organisms in the lab—organisms that are nothing like anything nature has produced.

The people who are defying Nature's monop
collection of engineers, computer scientists
look at life quite differently than traditiona
professor George Church wants "to do for b

Newsweek, June 2007

bio-era
BIO-ECONOMIC RESEARCH ASSOCIATES

Genome Synthesis and Design Futures: Implications for the U.S. Economy

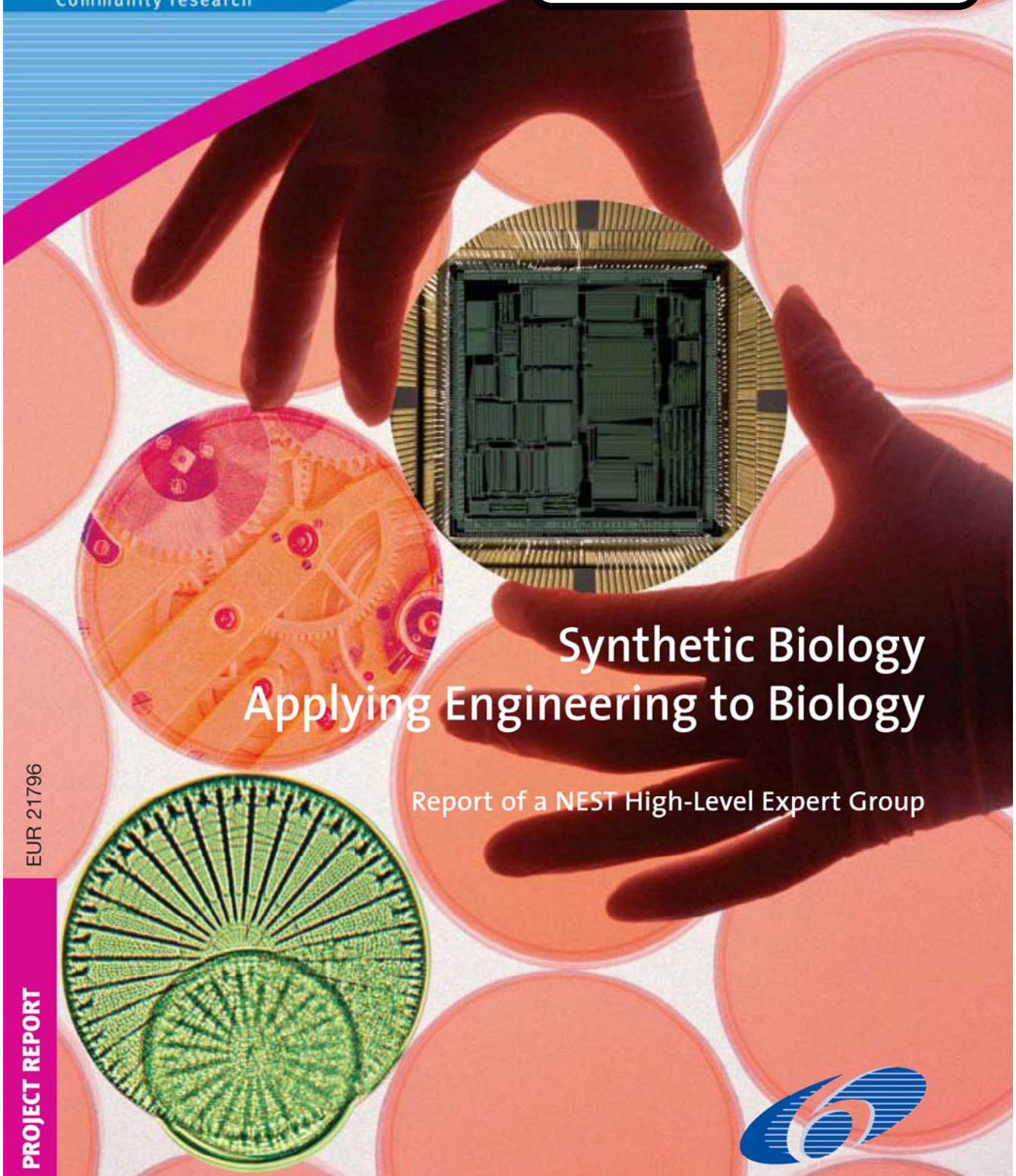
A Special Bio-era Report
Sponsored by U.S. Department of Energy
February 2007

US DOE, Feb 2007

EUROPEAN COMMISSION

Community research

EU Commission, 2005



Synthetic Biology
Applying Engineering to Biology

Report of a NEST High-Level Expert Group

EUR 21796

PROJECT REPORT

SPECIFIC ACTIVITIES COVERING A WIDER FIELD OF RESEARCH

EUROPEAN COMMISSION

Community Research

Call for Proposals on Synthetic Biology

Planned Deadline – 15 February 2006

NEST (New and Emerging Science and Technology)

NEST announces a Call for Proposals on *Synthetic Biology*, one of its PATHFINDER initiatives for 2006.

The objective of this call is to bring together high level research groups in Europe with the long term goal of creating artificial systems based on biological engineering principles. These systems could foster unprecedented benefits in applications such as health, energy, environment or materials.

Further information, including the official work programme, reference document, and submission requirements, can be obtained via the NEST web site : www.cordis.lu/nest

Information can also be obtained through ... Point (NCP). For contact details please consult: www.cordis.lu/nest/ncp.htm

NEST - PATHFINDER

EU Commission, 2005

The Academy of Medical Sciences

The Royal Academy of Engineering

Systems Biology: a vision for engineering and medicine

A report from the Academy of Medical Sciences
and The Royal Academy of Engineering

Academy of Medical Sciences, Feb 2007