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WIRED

Life, Reinvented

A group of MIT engineers wanted to model the biological world. But, damn, some of nature's designs were complicated! So they started rebuilding from the ground up - and gave birth to synthetic biology.

By Oliver Morton

In January, students at M.I.T. are let off the leash to follow their fancies. The annual monthlong Independent Activities Period is a playground for the mind, offering courses, seminars, and special events devoted to everything from energy-dispersive x-ray spectroscopy to poetry reading. There's glassblowing, building spacecraft for mice, and the all-important coolest-stuff-made-of-duct-tape competition. "I wish I didn't teach an IAP," says Drew Endy, an assistant professor in biological engineering. "I'd take a whole bunch of the courses."

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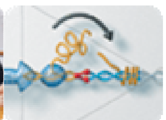

But Endy does teach an IAP. This year his class is devoted to building counters - devices that count from, say, 1 to 32. That may not sound like much of a challenge for students at the world's most prestigious engineering school; in fact, it's the sort of thing a nerdy middle school kid would solder together. But here's the rub: The counters his students design won't be electronic, but biological. They won't be made of transistors, but DNA. And they won't be inserted into breadboards, but living bacteria.

While Endy is keen on counters at the moment (they might have practical uses; for example, indicating how many times a given cell has divided since the counter was last reset), they're just stepping-stones to a new era in biology. Last year, his students programmed bacteria to form polka-dotted colonies. The year before, they designed microorganisms that blinked like Christmas lights. But the real purpose of the course isn't making a particular biological circuit; it's figuring out what it takes to make any biological circuit.

Endy is the newest recruit to a cabal of MIT engineers gathered around one of the university's computer science gurus, Tom Knight. Their aim is to create a field of engineering that will do for biological molecules what electronics has done for electrons. They call it synthetic biology.

"I think this will likely be the most important thing I've done," says Knight, whose track record already includes designing some of the earliest network interfaces, bitmapped displays, and workstations. "We're at the cusp of some dramatic changes."

If the notion of hacking DNA sounds like genetic engineering, think again. Genetic engineering generally involves moving a preexisting gene from one organism to another, an activity Endy calls DNA bashing. For all its impressive and profitable results, DNA bashing is hardly creative. Proper engineering, by contrast, means designing what you want to make, analyzing the design to be sure it will work, and then building it from the ground up. And that's what synthetic biology is about: specifying every bit of DNA that goes into an organism to determine its form and function in a controlled, predictable way, like etching a microprocessor or building a bridge. The goal, as Endy puts it, is nothing less than to "reimplement life in a manner of our choosing."

And what might the practitioners of this emerging science do with such godlike capability? Within a decade, some hope to create bacteria able to mass-produce drugs that currently have to be painstakingly harvested from rare plants. Others talk about making viruses encased in protein sheaths that can be used to produce fabric with molecular circuitry woven into its warp and weft. In the more distant future, synthetic biologists envision building more complex organisms, like supercoral that sucks carbon out of the biosphere and puts it into building materials, or an acorn programmed to grow into an oak tree - complete with a nifty tree house. And there's the opportunity to add new chromosomes to the human genome, ushering in a panoply of human augmentations and enhancements.

Synthetic biology has a long way to go before such wonders become possible, but each year's IAP course brings them closer as the MIT team learns by trial and error. As the course enters its third year, Endy and his students are closing in on an approach that will let them design systems considerably more elaborate than the simple projects they've attempted so far. And if getting there doesn't go smoothly, that's OK. "Engineers work best by flailing about," Endy says, "and we've been doing as much of that as anybody."

Drew Endy has a rapid-fire delivery and a high-intensity gaze. As an undergraduate at Pennsylvania's Lehigh University in the early '90s, he studied civil engineering. "I like to build stuff," he says. "I'm a kid in that regard." But he was also fascinated by biology, which led him to environmental engineering and molecular biology.

For his PhD project at Dartmouth, Endy developed a computer model of T7, a virus that infects the bacterium *E. coli*. His model's description of what happens as T7 attacks its prey - for example, which genes are turned on, and when - "wasn't complete bullshit," he says. In the uncertain business of simulating biological systems, that counts as success.

But the real test of a model is how well it predicts the outcome of circumstances never seen before. So Endy rearranged T7's DNA to make mutant strains in which the virus synthesized its proteins in a different order. Then he used his model to predict what the new guys would do when presented with some *E. coli* to infect. The results weren't good. "For all the interesting predictions, whenever I went into the lab the opposite thing would happen," he recalls. "It was really disappointing."

In the late '90s, Endy joined the Molecular Sciences Institute, an independent research outfit in Berkeley, California. There he realized there were two different ways forward. He could "go back and understand a whole bunch more about the science of the organism in order to model it better," which, Endy concedes, is "a fine and valid traditional path," not to mention the one MSI was devoted to. Or he could take a more radical approach: tear apart nature's work and reconstitute it in a more logical, malleable form. "I thought, Screw it," he says. "Let's build new biological systems - systems that are easier to understand because we made them that way.'"

At any other time, Endy's idea would have been deeply impractical. Custom-building biological systems meant writing DNA sequences from scratch, and the ability to write sequences trailed far behind the ability to read them. In the 1990s, though, the rate at which DNA could be read revved into high gear, and in 2000 it was becoming clear that DNA synthesis - stringing together pairs of nucleotide bases, the letters of the genetic code - would follow.