Crossing computers, cells

Scientist works to create engineering discipline: microbial engineering / **Simson L. Garfinkel**

CAMBRIDGE – TOM Knight is working toward the day when a computer can reproduce itself. That's right: a cross between a microprocessor and microbiology.

Knight's work is taking shape on the ninth floor of the Artificial Intelligence Lab at the Massachusetts Institute of Technology. Instead of computer terminals, this office has flasks, beakers, and test tubes. Instead of printers and modems, the lab has a gene amplification device based on the polymerase chain reaction. Instead of computer manuals, there are microbiology journals.

Here on the ninth floor, senior research scientist Knight is fusing the tools of computer science and biology to create a engineering discipline: microbial engineering.

Computer scientists have a lot to learn from the way that mother nature has constructed cells, says Knight. Take a memory chip out of a typical desktop computer, and the computer is likely to crash. Take a few cells out a human brain, and it's impossible to tell the difference. That's because biological systems are much more redundant, resilient, and flexible than manmade ones.

On the other hand, adds Knight, biologists have a lot to learn from the way that computer scientists build technology and control complexity. "Biologists are motivated to understand what naturally occurs. They revel in the complexity. Engineers want to simplify to the point that they can completely understand something," he says.

Biology has another huge advantage over traditional computer science. A typical computer chip factory costs a billion dollars and every wafer has to be individually manufactured. A biologist, however, can grow a trillion organisms overnight in a laboratory for just a few dollars in material costs.

That's why Knight, who has worked at MIT since he got his first job there as a 10th grader in 1963, has spent much of the past five years sitting in on MIT's doctorate-level biology classes. His goal is to combine elements from both fields to help develop a new generation of hybrid computer systems that are fast, flexible, and incredibly cheap to manufacture.

Knight's ultimate goal is to be able to program bacteria the way that an engineer might program a microprocessor today. The Microbial Engineering Lab's first project, starting up now, is to genetically modify E. coli bacteria and add a few logic gates – the building blocks from which all digital computers are created. One idea that Knight is toying with is to build a simple oscillator – a circuit that repeatedly turns on and off – and to combine it with the genes that create photoluminescence proteins. The result would be a bacteria that flashes on and off at a regular interval.

Another project that Knight's group is considering is a simple flip-flop, the basic building-block of a computer memory chip, that can be set or reset from outside the cell. Such a system could be used for storing data or for controlling the expression of other proteins. "We want a cell where we can say turn on this gene, turn off that gene," he says.

But Knight is the first person to admit that there are fundamental gaps between what's possible in a test tube and what's possible on a desktop PC. "You'll never run Microsoft Word on one of these bacteria," he says.

One reason is the clock speed. Most of today's computers operate on a clock that switches on and off a hundred million times every second; genes inside a bacteria cycle on and off roughly once every 10 minutes. Bacterial computers, as a result, will be very slow. But because it will be possible to create trillions of them quickly and cheaply, Knight says, they might be ideally suited to large problems that can be broken up into many tiny pieces – such as breaking cryptographic codes or solving complex mathematical equations.

Another limitation on the ultimate complexity of a bacterial computer is size. Every gene and messenger protein inside a cell takes up a finite amount of space. Knight estimates that the typical bacteria only has room for 200 or so additional signals or logic gates. That means that computational microbes will probably be limited to performing relatively simple functions – things that are done today with small microcontrollers.

But a microbial microcontroller would have the advantage of being able to reproduce and manufacture proteins, thanks to its cellular machinery.

Even if Knight doesn't pull off his grand schemes, there are likely to be big payoffs from this basic research. For example, one thing that's complicated about biology today is the basic mechanics of conducting experiments and recording results. Despite the fact that laboratories are filled with computers, most biologists record their results with a pen in spiral-bound notebooks.

To Knight, one of the architects of the information age, such manual manipulations are pitifully primitive. So one of the side projects that the Knight Lab is considering is the creation of a self-documenting laboratory – a smart room in which to conduct experiments, where a computer can sense the readouts of every laboratory instrument and record the results itself.

GLOBE STAFF PHOTO / DAVID L. RYAN

Senior research scientist Tom Knight at MIT's Artificial Intelligence Lab.

If you think that Knight is just some crackpot computer hacker who has gotten tired of stamping out code, think again. Working with MIT professors Gerald Sussman and Harold Abelson, the Amorphous and Cellular Computing project at MIT has received a multiyear, multimillion-dollar grant from the UltraScale Computing Project at the Department of Defense Advanced Research Projects Agency.

That's the same organization that kickstarted the Internet and much of the microelectronics revolution with funding back in the 1960s and early '70s. Perhaps in another 30 years, computers that are based, in part, on biology will be as common as systems with network connections today.

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