

Programmable cells: Engineer turns bacteria into living computers

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In a step toward making living cells function as if they were tiny computers, engineers at Princeton have programmed bacteria to communicate with each other and produce color-coded patterns. The feat, accomplished in a biology lab within the Department of Electrical Engineering, represents an important proof-of-principle in an emerging field known as "synthetic biology," which aims to harness living cells as workhorses that detect hazards, build structures or repair tissues and organs within the body.

"We are really moving beyond the ability to program individual cells to programming a large collection -- millions or billions -- of cells to do interesting things," said Ron Weiss, an assistant professor of electrical engineering and molecular biology.

Collaborating with researchers at the California Institute of Technology, Weiss and graduate student Subhayu Basu programmed *E. coli* bacteria to emit red or green fluorescent light in response to a signal emitted from another set of *E. coli*. In one experiment, the cells glowed green when they sensed a higher concentration of the signal chemical and red when they sensed a lower concentration. In a Petri dish, they formed a bull's-eye pattern -- a green circle inside a red one -- surrounding the sender cells.

In addition to demonstrating that the genetic programming techniques work, this sensing system could be useful for the detection of chemicals or organisms in laboratory tests. "The bull's-eye could tell you: This is where the anthrax is," said Weiss.

The researchers published their results in the April 28 issue of *Nature*. In addition to Weiss and Basu, authors of the paper are postdoctoral researcher Yoram Gerchman at Princeton and professor of chemical engineering Frances Arnold and graduate student Cynthia Collins at Caltech. It was funded by a grant from the U.S. Defense Advanced

Research Projects Agency.

In previous work, including a paper published March 8 in the *Proceedings of the National Academy of Sciences* along with Sara Hooshangi and Stephan Thiberge, Weiss showed the feasibility of inserting engineered pieces of DNA into cells to make them behave in the same manner as digital circuits. The cells, for example, could be made to perform basic mathematical logic and produce crisp, reliable readouts that are more commonly associated with silicon chips than biological organisms. The new paper applies similar techniques to a large population of cells.

"Here we're showing an integrated package where the cells have an ability to send messages and other cells have the ability to act on these messages," said Weiss.

The creation of patterns, such as the bull's-eye effect, is a key step in one of Weiss' eventual goals, which is to have the cells secrete materials that build physical devices such as antennas or transmitters in places that are hard for humans to reach. Programmed cells also could be used to control the repair or construction of tissues within the body, possibly guiding stem cells to the locations where they are needed for the growth of new nerve or bone cells in a process Weiss called "programmed tissue engineering."

Even the early step of creating patterns in a Petri dish, however, may be useful as a tool for other scientists, particularly developmental biologists who are trying to understand how the cells of an embryo arrange themselves into patterns that become the various body parts of a mature organism. In fruit fly embryos, for example, the first cells are thought to differentiate into the head, abdomen and other parts based on the concentration of chemical signals that are emitted from the ends of the embryo.

In addition to conducting laboratory experiments, Weiss and colleagues are creating computer models of their engineered systems, which allow them to study how small modifications would affect the ultimate behavior of the organisms. So far, said Weiss, the experimental results have matched the computer models fairly closely, but the goal is to have a mathematically exact description of how each component works.

"One of the nice things about synthetic biology is that because we built the network from scratch, we should be able to model all the important details," he said. At some point in the future, he said, scientists will be able to choose a behavior they want from cells, and a computer program will create a genetic circuit to accomplish the task. "Then we can do an experiment to see if the community of cells is behaving as we desire. That is going to have a tremendous number of applications."

Source: Princeton University

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