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Tiny Probes Measure Signals Inside Cells

Nanowire transistors could make better connections between the body and electronic devices.

By Katherine Bourzac

Researchers at Harvard University have made biocompatible, nanometer-scaled transistors that can be used to take highly precise electrical and chemical readings inside cells. The bioprobes are much more sensitive than the passive electrodes that have been used to make intracellular measurements in the past.

The Harvard group, led by chemistry professor Charles Lieber, is now developing more sophisticated bioelectronics that will take advantage of transistors' ability to send as well as receive electrical signals. They're also working with a tissue-engineering group to develop implantable bioelectronics that could make better connections between the body and neural prosthetics such as those that control some artificial limbs. The probes, which are based on silicon nanowires, can be grouped in large arrays, so the researchers also hope to use them to get a picture of biochemical and electrical networks in the large groups of cells that make up tissues. Such measurements are difficult to make today.

Conventional metal electrodes have been used to take electrical and chemical readings in single cells, but they are invasive, and they can't achieve good electrical performance unless they are relatively large compared to the cells themselves. They irritate tissues, and they can't amplify or process signals. They limit the sophistication of neural prosthetics because they don't have a very good connection to the nervous system at the single-cell level--the level at which the body processes information.

The Harvard cell probes, described today in the journal *Science*, are three-dimensional, V-shaped silicon nanowires with transistors at their tips. They're flexible and coated with two layers of lipid molecules, just as a cell is. When the transistor tip, which is about the size of a virus, encounters a cell, the cell pulls it inside. Lieber's group found that the tips can also be removed gently, with no ill effects to the cell. They've used the transistor probes to take electrical measurements in single cells and are now using them to measure electrical activity in the groups of adjacent cells that form tissues.

"They've demonstrated very impressive intracellular signal detection," says Yi Cui, a professor of materials science and engineering at Stanford University and a former member of Lieber's lab. What makes this possible, says Cui, is the innovative structure of the bioprobe. Lieber makes millions of the free-standing nanowires at once using a three-step growth process. First he grows one arm of the V from a silicon-containing gas. Then he creates a kink in the wire using a technique he developed last year. Next, he chemically treats the kink to create a transistor and then induces the nanowire to start growing again. The completed wire turns back 60 degrees at the kink. Electrical contacts on a variety of substrates can be connected to the arms of the V, turning the nanowires into three-dimensional electronic probes.

"These could be used for electrophysiology experiments to study the nervous system in a detailed way over long periods of time, or for cell-based drug screens, especially for cardiac drugs," says Lieber. Silicon-nanowire transistors have also been used as chemical sensors: their resistance changes measurably when a biomolecule such as mRNA or a protein attaches to a binding molecule at the surface. Lieber is interested in extending this capability to the probes.

The Harvard researchers are now collaborating with a group at MIT to incorporate the nanoprobes into medical devices, including scaffolds used to make artificial tissues. Circuits of nanowires could "innervate" an artificial tissue so that it could measure and respond to electrical signals propagating through the heart or brain. These bioelectronics might enable better communication between the brain and an artificial limb, for example.

Upcoming Events

2010 IEEE Conference on Innovative Technologies for an Efficient and Reliable Electricity Supply (http://www.ieee-energy.org/)
Waltham, Massachusetts
Sunday, September 27, 2009 - Tuesday, September 28, 2010
http://www.ieee-energy.org/ (http://www.ieee-energy.org/)

FutureM (http://www.futurem.org/Default.aspx)
Boston, MA
Monday, October 04, 2010 - Friday, October 08, 2010
http://www.futurem.org/Default.aspx (http://www.futurem.org/Default.aspx)

USA Science & Engineering Festival Expo (http://www.usasciencefestival.org)
Washington, D.C.
Saturday, October 23, 2010 - Friday, October 29, 2010
http://www.usasciencefestival.org (http://www.usasciencefestival.org)

15th Annual MITX Interactive Awards
(http://www.mitxawards.org/interactive/default.aspx)
Boston, Massachusetts
Thursday, November 18, 2010
http://www.mitxawards.org/interactive/default.aspx
(http://www.mitxawards.org/interactive/default.aspx)