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Better Way to Wire Up Cells

Nanowire arrays could be used for future medical implants.

By Katherine Bourzac

Understanding how brain and heart cells process and generate electrical signals could lead to a new understanding of neurological and heart disease. Until a few years ago, however, it simply wasn't possible to make electrical recordings at the level of single cells. In 2006, Harvard researchers used nanowire transistors to measure electrical signals at 50 points along a single neuron. Now the same research group has developed a new nanowire recording system and have used it to capture some of the most precise, high-quality electrical recordings ever made from heart cells.

The Harvard work, led by chemistry and chemical-biology professor Charles Lieber, is "at the forefront of research in integrating nanowire nanotechnology and bioscience," says Zhong Lin Wang, Regents Professor at the Center for Nanostructure Characterization, at Georgia Tech.

Nanoscale devices that interface electrically with cells could lead not only to a better understanding of the origins of disease, but also to better neural prostheses and other medical devices.

Lieber says that the goal of his lab is to make electrical devices that interface with biological tissues on a biologically meaningful scale--in other words, on the nanoscale. Cells process electrical signals as those signals travel down the length of a cell; the subcellular electrical processing that takes place in neurons, for example, plays an important role in normal and abnormal learning and memory. "If one wants to understand how signals propagate and why it doesn't happen in the way it should" in diseases such as epilepsy or heart arrhythmias, "you need to measure at a fine scale," Lieber says.

To create such fine-scale recordings, Lieber uses transistors made of silicon wires just tens of nanometers in diameter. The nanowires are grown in a reaction chamber, then aligned on a silicon wafer and supplied with metal electrodes and interconnects. Until now, researchers have grown cells on top of a chip in order to interface nanowires with cells.

"We recognized that one doesn't necessarily have to grow the cells on the substrate," says Lieber. Instead, in research described online this week in the *Proceedings of the National Academy of Sciences*, the Harvard group grows cells on sheets of flexible polymer. Nanowires themselves are cell friendly, but a rigid silicon wafer is not the friendliest place for biological tissues to grow. By growing the tissues separately on plastic substrates, the Harvard researchers can make better tissue samples to work with. Better samples means that more meaningful measurements. And because the Harvard researchers can position the tissue over the nanowires under a microscope, they can choose particular tissue areas or particular cells from which to record. Being able to bring an already growing group of cells in contact with a recording array will also be critical for making future implants.

"The modular approach is quite elegant," says Peidong Yang, a professor of chemistry at the University of California, Berkeley. Yang has used nanowire arrays to study the effects of electrical inputs on stem-cell development.

So far, the Harvard group has used the modular system to record electrical activity in beating heart tissues. In one experiment, says Lieber, they were able to orient the tissue over the nanowire arrays to make detailed recordings of the electrical connections between three heart cells. "The propagation speeds are not uniform and depend on the details of their connectivity," he says. For example, the connection between two of the cells showed more electrical resistance than between others.

To understand what these detailed biophysical measurements mean in terms of health and disease, many more of them will need to be made and analyzed. But, says Yang, Lieber's work shows that making complex, high spatial and temporal resolution measurements is feasible.

"This study extends the application of nanotechnology for cell interfacing, which is probably one of the most promising biological applications of nanowires," adds Nicholas Kotov, a professor of chemical engineering at the University of Michigan. "Development of nanomaterials for this purpose can help a lot of people with devastating diseases related to the breakdown of signal transmission between cells."

Lieber is now using the modular system to make recordings from neural tissue, which is more fragile, and he's developing new ways of arranging the nanowires. One reason that these tiny wires can make such good electrical connections with cells is that a large amount of surface area comes into contact with the surrounding tissue. By making nanowire arrays with different configurations, Lieber hopes to expose even more of the wires' surfaces for interaction with cells.

The group is also working on nanowire devices that can simultaneously record both electrical and chemical signals. Lieber's previous work has shown that nanowire transistors decorated with binding molecules can act as extremely sensitive chemical sensors: their conductivity changes in a predictable way when they bind to a molecule of interest, such as a neurotransmitter. Simultaneously recording the effects of electrical signals, hormones, neurotransmitters, and other chemicals would give a more integrated picture of biological functions.
