News:

Posted by Jennifer Welsh
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A new virus-sized probe can look deeper into cells than ever before, and finally allows scientists to monitor intracellular activities without disrupting the cells' external membranes, according to a study published today in *Science*.

"This is a paper that can bring breakthrough and revolutionary insight into our understanding of intracellular structures," said Zhong Lin Wang, who develops nanotechnologies at the Georgia Institute of Technology but was not involved in the work.

Nano-size transistor penetrates cell membrane
Image: Charles Leiber

The new device is a type of sensor known as a transistor, which detects changes in electrical activity when touching or inserted into a cell. It differs from previous cellular-sized transistors in its unique three-dimensional shape and its tiny size -- smaller than a cell's own microtubules. Additionally, the new probe is coated with a lipid bilayer, which merges with the cell's membrane to allow the tip to penetrate into living cells and get an inside view of its molecular actions without affecting cellular structure or activity.

Previously, nano-scale transistors were limited to two dimensions, forcing cells to conform to a flat surface, possibly causing changes to the cells' intracellular activities and only allowing detection of the electrical changes outside of the cell. Alternative probes that could detect internal changes, such as glass pipets, were too big to penetrate cells without disrupting their membranes. Furthermore, pipets work by conducting the cell's electrical output to an external monitor through a highly-conductive liquid inside the pipet that carries the current. This fluid can leak into the cell and cause biochemical changes inside the cell.

The new transistor-probe, on the other hand, works by transmitting an electric signal through a tiny, semi-conductive nanowire, which can enter the cell without affecting its overall structure, said lead author Charles Leiber, who studies nanotechnology at Harvard University.

"This new transistor is so small and sharp that it can penetrate inside the wall of the cell," said Wang. "This is going to have a big impact from the technical point of view and the cellular biology point of view."

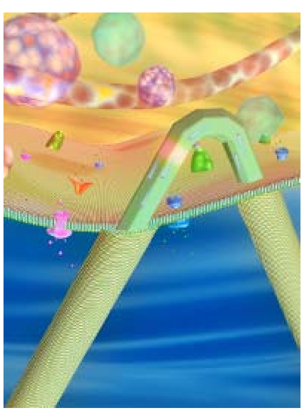

Diagram of nanoprobe in cell
Image: Charles Leiber

The nanoprobes are made from a 5nm think wire. Leiber's team bent the wire in two adjacent 120 degree angles, making a V shape. When it is inserted into the cell, the wire picks up changes in the electrical activity, like an action potential in a neuron or the beat of a heart cell. This signal is sent through the nanowire to the end, which sticks out of the cell membrane and connects to monitoring equipment that records the data.

Leiber and his team are currently using these probes to study neurons, but by adding special proteins or nucleic acids to the end of the probe, Leiber hopes to use these transistors as biosensors to monitor the activity of specific proteins within the cell in real time. Furthermore, the researchers are also looking to future applications of the technology, including looking at whole tissues in culture, and also possibly designing larger sensors that could be attached to whole tissues in living organisms to monitor widespread electrical changes of, for example, a beating heart.

While the probes are complex to make, Leiber believes that the device is not too far from being able to be developed as a tool for general researchers. Unlike other kinds of probes, they can be made in vast quantities -- "millions of billions at a time" he said -- and they're not too difficult that other nanoscientists wouldn't be able to make these for

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themselves and their colleagues. "Labs skilled in the nanoscience end of this certainly could make the probes, and take it back to other labs," he said.

Bozhi Tian, et al., "Three-dimensional, flexible nanoscale field-effect transistors as localized bioprobes," *Science***, 329: 830-4, 2010.**

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