Published online 12 August 2010 | Nature | doi:10.1038/news.2010.402

News

Nano-hairpin peeks into cells

An electrical probe in a fatty disguise could monitor neurons.

Zeeya Merali

A nanoprobe has been used to measure the electrical activity of a cell.

Science/AAAS

A nanometre-scale probe disguised as part of a biological membrane has successfully infiltrated and monitored a living cell. Researchers hope that the lipid-coated device will tell us more about the inner workings of cells.

The most common device currently used to record electrical signals within neurons and other cells is made from a micrometre-scale glass pipette containing an electrode. The pipette 'clamps' onto the cell's membrane and records electrical signals, but the technique is far from ideal, says Charles Lieber, a chemist at Harvard University in Cambridge, Massachusetts. The pipette is cumbersome, and often damages the cell it is meant to monitor.

Lieber and his colleagues wanted to make a nanometre-scale device incorporating a transistor that would be able to enter a cell and take electrical readings without causing too much harm. Today's best transistor probes can take measurements only from the outer surface of cells, like metal detectors hovering over the ground, giving only a "fuzzy" picture of what is happening inside, says Lieber. This is because transistors need two electrical contacts to measure voltage differences in the cell, and these contacts are usually positioned next to each other on a large, flat device — which would be too big to push into a cell without destroying it.

The team were able to build a more compact device by using a nanometre-scale wire shaped into a hairpin. The business end of the transistor sits on the pin's bent tip and penetrates the cell. The two arms of the hairpin, which serve as electrical contacts, do not penetrate the cell deeply so minimise damage.

In general, it is difficult to control the shape of nanowires, which are grown gradually on a substrate. But last year, Lieber's team reported that if you stop and restart this growth process, you can introduce a 120° kink[1]. By kinking their wire twice in quick succession, the team created the sharp hairpin bend that they required.

Undercover intruder

The smallest nanoprobe made by the team was less than 50 nanometres wide — smaller than the diameter of many virus particles. "This is literally the scale of the inner components of a cell," says Lieber. Unlike the pipette device, which required additional equipment to amplify the electrical signal, the transistor can scale-up signals that it measures, allowing "exquisite sensitivity", he says.

Most importantly, the nanoprobe does not have to be forceably jammed into the cell. The researchers coated its tip with phospholipids — the main constituents of cell membranes — tricking the membrane into accepting the tip and pulling it inwards. "We're really blurring the distinction between what's an electrical probe and what is biological matter," says Lieber.

The team demonstrated that the nanoprobe works by poking it into a single cultured embryonic chicken heart cell and recording a series of voltage peaks with a frequency of 2.3 Hertz, corresponding to the beating of the cell[2].

Zhong Lin Wang, who works on the use of nanotechnology in biological applications at the Georgia Institute of Technology in Atlanta, says that fabricating the device is an "outstanding" achievement. The device "could provide fundamental new information" about the movement of ions that give rise to the electrical signals produced by cells, he says.

The technology should also be fairly straightforward to reproduce, making it relatively easy to bring into widespread use quickly, says Mehmet Yanik, a neurotechnology expert at the Massachusetts Institute of Technology (MIT) in Cambridge.

Yanik says that the team should now test the device on neurons, cultured from tissue taken from brain slices. In particular, they should build an array of probes, which could detect the distribution and flow of information across complex neuronal circuits. "That would be a breakthrough technology for neuroscience," he says. Beyond that, the team could look into developing an *in vivo* probe for monitoring neuronal activity in animals' brains in a relatively non-invasive way, he says.

Lieber's group is already working on applying the device to neurons. Looking even further into the future, the team is collaborating with Robert Langer's tissue-engineering group at MIT, with an eye to growing tissue in which nanowire bridges are integrated. "The long-term idea is to make artificial tissue that is wired up and can be implanted to enhance medical monitoring," says Lieber. "But that's a dream for merging the digital and the biological that may take time to realize."

References

1. Tian, B. , Xie, P. , Kempa, T. J. , Bell, D. C. & Lieber, C. M. *Nature Nanotechnol.* **4**, 824-829 (2009).
2. Tian, B. *et al. Science* **329**, 830-834 (2010).

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