TECHNOLOGY UPDATE

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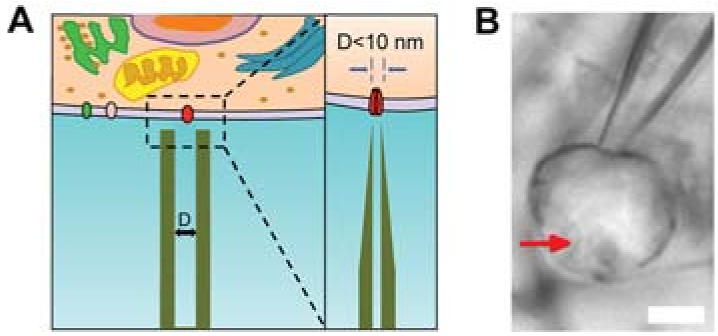
Tiniest bioprobe breaks new size record

Researchers at the Universities of Harvard in the US and Peking University in China say they have made the smallest bioelectronic probe ever. The device, fabricated from a 3D nanowire-nanotube heterostructure measuring less than 10 nm in diameter, could be used to explore miniscule subcellular assemblies, such as synapses and dendritic spines. Such organelles are difficult, if not impossible, to study using existing such probes.



(http://images.iop.org/objects/ntw/news/13/1/12/image1.jpg)

Intracellular bioelectronic probe (http://images.iop.org/objects/ntw/news/13/1/12/image1.jpg)

"The extremely tiny size of our device (which is 10 times smaller than the smallest bioprobes made to date) also means that it is non-invasive," team member Xiaojie Duan told *nanotechweb.org*.

The researchers, led by Charles Lieber (http://cmliris.harvard.edu/) of Harvard, made their probe by first fabricating silicon nanowire (SiNW) field–effect transistors (FETs) on a substrate. Next, they grew germanium nanowires (GeNWs), which serve as sacrificial templates for the nanotube probes, atop the SiNW FETs and etched the ensemble using hydrogen peroxide to reduce the size of the upper regions of the GeNWs while keeping the lower portions the same size. To form the nanotube structure, a thin layer of silicon dioxide (SiO_2) was then deposited on the entire structure, followed by a two-step selective buffered hydrofluoric acid etch to reduce the thickness of the SiO_2 shell on the GeNWs and expose the tip of the GeNW core. Finally, the GeNWs were etched with hydrogen peroxide to form the 3D SiO_2 nanotube-SiNW structure.

SEM images revealed that the upper portion of the SiO_2 nanotube has an internal diameter of around 8 nm and a wall thickness of about 10 nm. The tip of the nanotube is tapered so that it is sharp but the lower part has much larger internal diameter of about 80 nm and is 30 nm thick thanks to the hydrogen peroxide etching step.

Recording fast electrical signals in neurons and other cells

The device could be used to record fast electrical signals in neurons and other cells, says team member Xiaojie Duan. But how exactly? When the nanotube tip penetrates the cell membrane, the cell cytosol fills the nanotube and acts as a liquid gate (or electrode) for the underlying SiNW-FET, she explains. “Directly monitoring the conductance change of the SiNW-FET thus allows us to determine the transmembrane potential change of the cell and record action potentials. Indeed, we have already used our device to monitor the transmembrane resting potentials of HL-1 cells.”

The researchers say that they have also measured the bandwidth of the probes themselves and have found that it remains high (at around 3 kHz), even for probes as small as 5 nm in diameter. A frequency of 3 kHz is high enough to record fast intracellular action potentials of neurons and other biological cells, which typically take several milliseconds to measure.

Large-scale arrays could map electrical activity of neural networks

“Our probe will be very useful for future electrophysiological studies, such as investigating intracellular activity in organelles like dendrites, dendritic spines and cell nuclei,” says Lieber. “Such measurements are generally difficult, if not impossible, with existing biological probes,” he stresses. “We would also like to integrate our probes into large-scale arrays, since this would allow us to map the electrical activity of neural networks with unprecedented spatial resolution and minimal invasiveness.”

All is not plain sailing, however, and one major challenge will be to accurately position the ultrasmall probes on subcellular structures. “To do this, we might, for instance, label the probe with a florescence dye or use other biocompatible materials to mark the nanotube. Another option could be to add specific biochemical surface targeting groups to the probe.” says team member Tian-Ming Fu, a graduate student in the Lieber group.

The current work is detailed in *PNAS* doi: 10.1073/pnas.1323389111 (http://www.pnas.org/content/early/2014/01/08/1323389111.abstract).

Further reading

Tiny probe looks good on camera (Sep 2008) (http://nanotechweb.org/cws/article/tech/35566)
Nanodiamond probe detects individual target atoms (Jul 2013) (http://nanotechweb.org/cws/article/tech/53953)
Simple EBID process delivers robust nanoneedle AFM probe (May 2011) (http://nanotechweb.org/cws/article/lab/45904)