The twain finally meet: Nanowires and nanotubes combined to form intracellular bioelectronic probes

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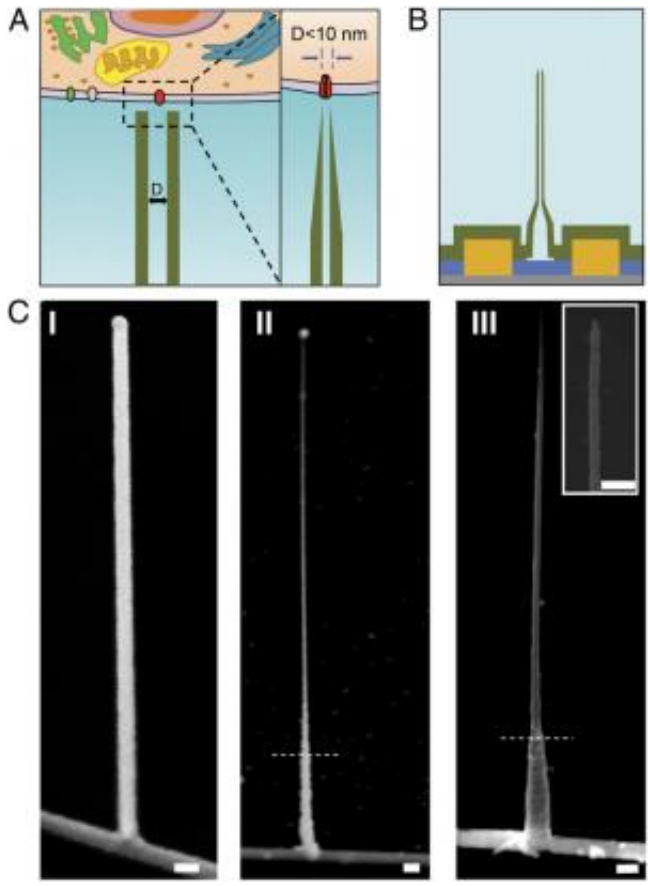


Schematics and SEM images of the ultrasmall BIT-FET. (*A*) Schematic illustration of an intracellular bioelectronic probe. (*Left*) General scheme of a probe for intracellular electrophysiology recording. (*Right*) A magnified view of the tip of a sub-10-nm bioelectronic probe and its related size to single ion channel. (*B*) Schematic structure of the ultrasmall BIT-FET. Green, yellow, blue, and gray colors represent SiO_2 layer, metal contact, SiNW, and silicon nitride

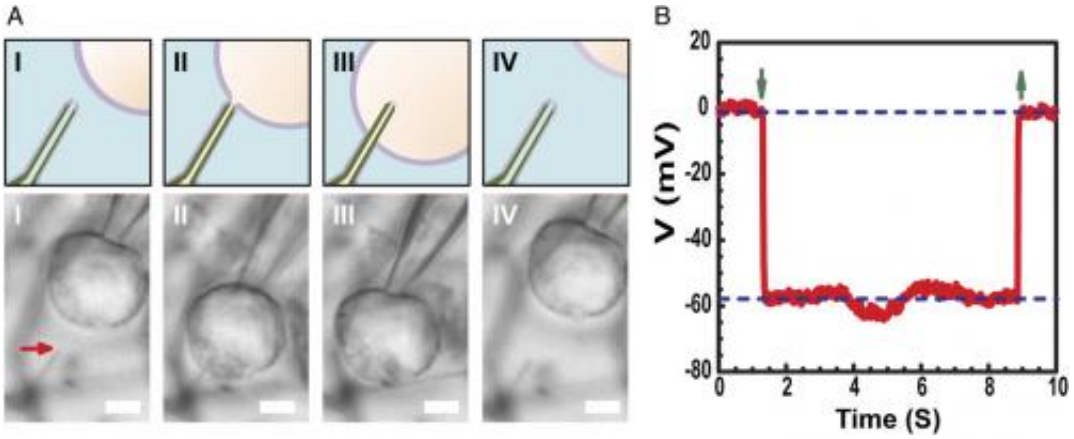
substrate, respectively. (*C*) SEM images of the ultrasmall BITFET at different fabrication steps. A GeNW branch was first grown on top of SiNW (*I*), followed by a subsequent H_2O_2 etching of top part of GeNW to shrink its diameter down to sub-10-nm regime (*II*). A final view of an ultrasmall BIT-FET with nanotube ID ~8 nm, and SiO_2 wall thickness ~10 nm is presented in (*III*). Inset of *III* is the closeup of the tip of the ultrasmall SiO_2 nanotube. White dashed lines in *II* and *III* indicate the point below which the GeNW and SiO_2 is protected by photoresist during H_2O_2 and BHF etching, respectively. All scale bars: 100 nm. Credit: Copyright © PNAS, doi:10.1073/pnas.1323389111

(Phys.org) —Miniaturized bioelectronic probes stand to transform biology and medicine by allowing measurement of intracellular components *in vivo*. Recently, scientists at Harvard University and Peking University designed, fabricated and demonstrated bioelectronic probes as small as 5 nanometers using a unique three-dimension nanowire-nanotube heterostructure. (A heterostructure combines multiple heterojunctions – interfaces between two layers or regions of dissimilar crystalline semiconductor – in a single device.) Through experimental measurements and numerical simulations, the researchers showed that these devices have sufficient time resolution to record the fastest electrical signals in neurons and other cells, with integration into larger chip arrays potentially providing ultra-high-resolution mapping of activity in neural networks and other biocellular systems.

Prof. Xiaojie Duan discussed the paper that she, Graduate Researcher Tian-Ming Fu, Prof. Charles M. Lieber and their co-authors published in *Proceedings of the National Academy of Sciences*. She first points out that nanotube probes and their heterojunction with silicon nanowire field-effect transistors (SiNW FETs) become mechanically less stable as diameter is reduced. "When the nanotube gets smaller and smaller," Duan tells Phys.org, "it gets easier to break the nanotube at the junction area with the SiNW. In the application of using the probe for

intracellular bioelectronic detection, there will be various forces, such as the capillary force from the liquid, as well as interaction between the probe and the cell membrane. These forces may break the probe if we have a weak junction between it and the SiNW."

Another issue is that electrical sensitivity is also reduced as nanotube diameter decreases, because the nanotube inner diameter (ID) defines the effective device gate area. "In the recording of intracellular transmembrane potential using our probe," Duan explains, "cytosol fills the nanotube and acts as the gate electrode for the underlying SiNW FET." *Cytosol* (also termed *intracellular fluid* or *cytoplasmic matrix*) is the liquid found inside cells, excluding organelles and other cytoplasmic components. "The cytosol potential change modulates the carrier density of the SiNW FET, thereby changing its conductance," Duan continues. "This is how our probe works for bioelectronics recording." The contact area between the cytosol and the SiNW – defined by the inner diameter of the nanotube – determines conductance modulation effectiveness. In other words, if the nanotube inner diameter is too small, the SiNW FET gate area will be too small as well.



Intracellular resting membrane potential recording. (*A*) Schematics (Upper) and differential interference contrast optical microscopy images (*Lower*) of an HL-1 cell manipulated by a glass micropipette to approach (*I*), contact (*II*), penetrate

(*III*), and retract (*IV*) from a phospholipid-modified ultrasmall BITFET probe. The red arrow indicates the position of the ultrasmall nanotube tip. Because pure SiO_2 nanotube is optically transparent, the GeNW template of this device was not etched for imaging. Scale bar: 2 μm. (*B*) Representative electrical recording results from a ~10 nm ID ultrasmall BIT-FET device; in this case, the GeNW was etched to yield the ultrasmall SiO_2 nanotube. Down- and up-pointing green arrows mark the beginning of cell penetration and withdrawal, respectively. The upper and lower horizontal dashed lines indicate the extracellular and intracellular potentials. Quasi-static water-gate measurements made before/after cell measurements show