In latest generation of tiny biosensors, size isn't everything

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(Phys.org) —When it comes to nanomedicine, smaller is—surprisingly—not always better.

UCLA Henry Samueli School of Engineering and Applied Science researchers have determined that the diminutive size of nanowire-based biosensors—which healthcare workers use to detect proteins that mark the onset of heart failure, cancer and other health risks—is not what makes them more sensitive than other diagnostic devices. Rather, what matters most is the interplay between the charged ions in the biological sample being tested and the charged proteins captured on the sensors' surface.

The finding counters years of conventional wisdom that a biosensor can be made more sensitive simply by reducing the diameter of the nanowires that make up the device. This assumption has driven hundreds of costly research-and-development efforts in the field of nanomedicine—in which tiny materials and devices are used to detect, diagnose and treat disease.

The research suggests new directions for designing biosensors to improve their sensitivity and make them more practical for doctors—and, eventually, patients themselves—to use.

"This is the first time the understanding of why nanowire biosensing works has been challenged," said Chi On Chui, an associate professor of electrical engineering and bioengineering at UCLA whose lab performed

the research. "The advantage is not from the fact that the wires are nanoscale, but rather how their geometry reduces the ability of the ions to inhibit protein detection. This research could be a step toward developing sophisticated, cost-efficient and portable devices to accurately detect a range of illnesses."

The research was published March 25 in the *Proceedings of the National Academy of Sciences*.

Nanowire biosensors are, in essence, electronic transistors with a diameter smaller than the width of a single red blood cell. When they are exposed to a sample of blood or another bodily fluid, the specific charged proteins being tested for are captured on the nanowires' surfaces. The charge of the captured proteins changes the rate of electric current flowing through the nanowire transistor. By monitoring the electrical current, researchers can quantify the concentration of proteins in the sample, which can give them an indication of heart health, diabetes and a number of other medical conditions.

A challenge to the practical use of the technology is that in addition to the charged proteins, many physiological fluids contain a large concentration of charged ions, such as sodium, potassium and chloride. These ions surround the proteins and mask the protein charge, which prevents the sensor from detecting the proteins.

Researchers in labs can circumvent this problem. But doctors performing tests on their patients or patients monitoring their own health at home cannot do so without the assistance of a technician. This has hampered the adoption of the technology.

The UCLA research advances understanding of nanowire efficiency in several ways. First, it proves that the small size of the nanowires is not inherently responsible for the fact that they outperform their planar

counterparts.

Second, it demonstrates that the improvement in performance results from the fact that ionic screening is reduced in tight spaces—such as the corners between a nanowire and the base it sits on—because ions have difficulty approaching proteins there. This corner effect exists in most biosensing structures, whether they are nanoscale or not; but the effect becomes more important at the nanoscale.

The research also shows that in general, devices with concave surfaces work more efficiently than those with convex surfaces.

"My hope is that researchers can use this understanding to do two things," said Kaveh Shoorideh, the UCLA Engineering graduate student who is first author of the research. "First, to make sensitive biosensors without resorting to expensive nanowires, and second, to come up with ways to reduce ionic screening without requiring a technician."

More information: Kaveh Shoorideh and Chi On Chui. "On the origin of enhanced sensitivity in nanoscale FET-based biosensors." *PNAS* 2014 111 (14) 5111-5116; published ahead of print March 25, 2014, DOI: 10.1073/pnas.1315485111

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