Miniaturized biosensors for minimally invasive implants

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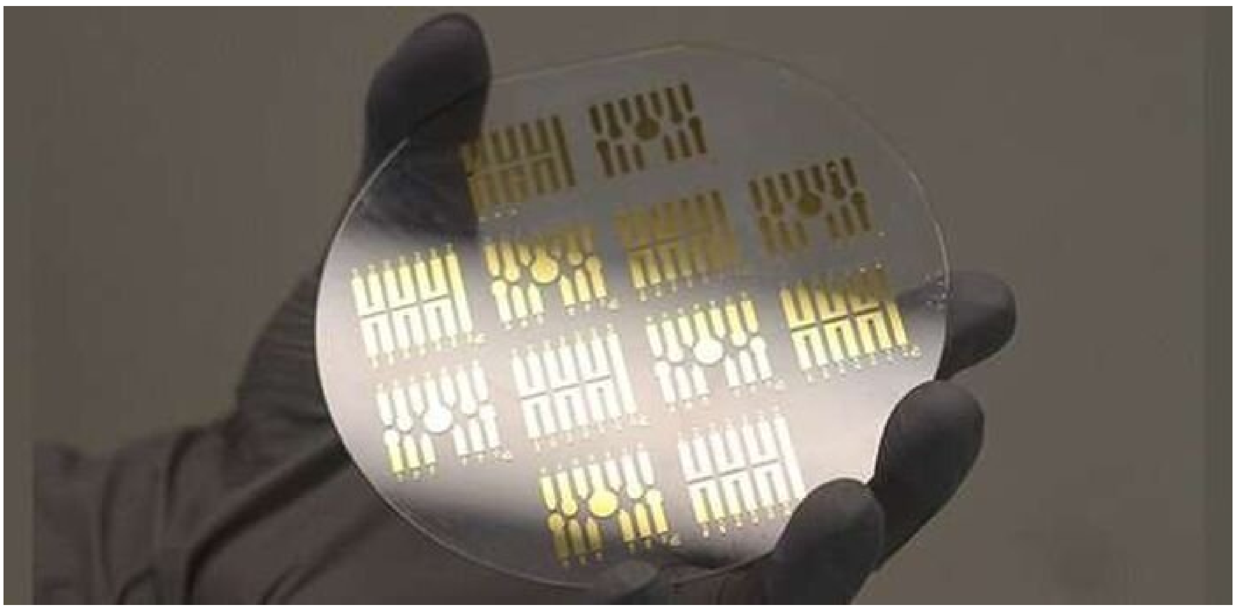
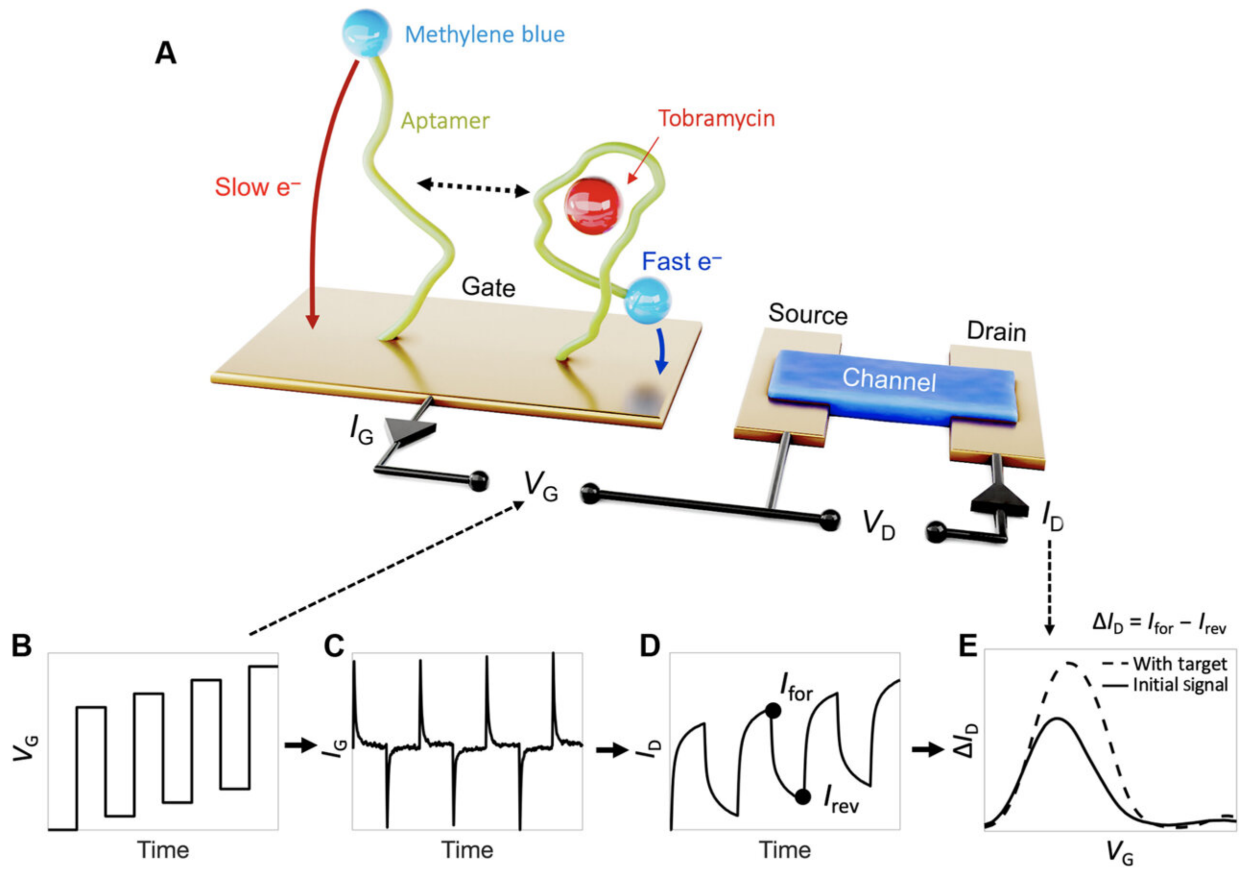


Scalable thin film transistor-based biosensors. Credit: Ben Woodington, University of Cambridge

A new method for the miniaturization of biosensors will enable new possibilities for minimally invasive implants. The miniaturized transistors are fabricated on thin, flexible substrates, and amplify biosignals, producing currents more than 200 times larger than analogous alternatives.

Diagnosing and monitoring diseases often rely on the detection of molecules called "biomarkers." However, the detection of such biomarkers need periodic blood draws, which are expensive, time consuming, require specialized equipment, and provide no continuous data. To avoid this, and provide real-time biomarker detection, Professor Kevin Plaxco's team at the University of California Santa Barbara pioneered the development of implantable aptamer-based sensors. These devices are electrochemical sensors based on DNA and they successfully track small molecules in real time.

A key step to translate these sensors to real-life applications in the clinic is to make them as small and minimally invasive as possible. To solve this miniaturization challenge, researchers at Cambridge teamed up with the Plaxco Lab to discover a way to combine aptamer-based sensors with an amplifying transistor platform. Together, they developed biosensors based on organic electrochemical transistors (OECT), which maintain high performances of the aptamer sensors even when shrunk to quite small dimensions. The results are reported in the journal *Science Advances*.



Square-wave gate potential profiles support high-gain aptamer-based OECT sensing.(**A**) Schematic of the aptamer-based OECT, which includes methylene blue–modified aptamers immobilized on the gate electrode. This functionalized planar gold gate and the PEDOT:PSS channel are designed to match capacitance allowing for voltage drop at both the channel and gate sides. (**B**) A pulse square wave superimposed over a voltage sweep is input as V_G, yielding (**C**) I_G current decays from the oxidation of the methylene blue. (**D**) The resulting I_D is proportional to integrated I_G. (**E**) Measuring the difference between each forward and reverse pulse current then yields a distinct methylene blue redox peak. Upon target addition, the charge transfer rate increases, yielding a larger integrated current and leading to a higher ΔI_D redox peak. Credit: *Science Advances* (2022). DOI: 10.1126/sciadv.add4111

Research student Sophia Bidinger, lead author of the paper, said, "This work is an important step towards creating better tools for health care providers. With this type of sensor, physicians will be able to gain unprecedented real-time data for tracking their patients' health."

Previous aptamer sensors were made of thin, millimeters-long wires. In contrast, the new transistor biosensors are so small that they are barely visible to the naked eye. This technology will be useful for medical applications that require sensors in delicate areas. For example, such a minimally invasive sensor could enable implantation in the brain—an ideal region to track biomarkers linked with mental disorders, such as depression.

Paper co-author Professor Tawfique Hasan said, "There is a huge market opportunity for continuous molecular monitoring. Besides glucose, there are not very many commercially available sensors. More tools for supporting continuous, in vivo sensing will save lives."

The cross-disciplinary research team will now explore possible next directions of this work. For example, another benefit of signal amplification is improved lifetime, so the sensor can operate for longer without being replaced. Each of these improvements is one step closer to deployment in humans for tracking anything from drugs to hormones to neurotransmitters.

Paper co-author Professor George Malliaras added, "The most exciting aspect of this work is that it could be used to detect virtually any small molecule. This will help doctors gain much more patient specific insight than ever before."

More information: Sophia L. Bidinger et al, Pulsed transistor operation enables miniaturization of electrochemical aptamer-based sensors, *Science Advances* (2022). DOI: 10.1126/sciadv.add4111