PUBLISHED: 9 MARCH 2017 | VOLUME: 1 | ARTICLE NUMBER: 0048

BIOELECTRONIC DEVICES

Long-lived recordings

A silicon dioxide passivation layer dramatically lengthens the operational lifetime of flexible electronic arrays for cardiac electrophysiology.

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Recording cellular electrical activity *in vivo* is challenging. Today's electronics are still hard to integrate into biological tissues, especially for sustained operation[1]. In fact, the inherent mechanical and chemical mismatches between biological tissues and traditional bioelectronic devices have led to device failure, mostly because of the foreign-body response[2] and of material degradation by biological fluids. During the past decade, bioelectronic interfaces have been designed with flexible architectures (typically by using ultrathin or porous designs[3,4]) and with mechanical properties similar to those of tissues[3]. However, surface passivation of bioelectronic devices remains a significant challenge, in particular because flexible architectures typically exhibit high surface-area-to-volume ratios and contain polymeric components (which cannot sustain the high temperatures needed for depositing a dense passivation layer).

The integration of bioelectronic implants into tissue *in vivo* for stable operation therefore calls for the development of an efficient encapsulation technique that can protect the electronics from degradation by biofluids. Ideally, any bioelectronic device that is intended for prolonged use must be encapsulated by a material that is biocompatible, ultrathin, of low flexural rigidity and defect-free over centimetre areas, and that has a lifespan of multiple decades in physiological conditions. Reporting in *Nature Biomedical Engineering*, John Rogers, Igor Efimov and colleagues now show that one such material is a thermally grown silicon dioxide (SiO_2) layer that serves as a dielectric protective seal for flexible electronic arrays[5]. They also demonstrate that the passivated arrays can be used for continuous electrophysiological mapping of the heart.

The deposition of a passivation layer on metal or on other device components typically takes place at the end of the fabrication protocol. However, Rogers and co-authors began the fabrication process with the passivation layer, which was made via thermal oxidation of a silicon wafer. This allowed for the harsh conditions needed to achieve defect-free passivation. The authors then used standard semiconductor-processing techniques to fabricate high-quality electronics on top of the oxide layer. After device fabrication was complete, the bottom wafer was removed by a combination of dry-etching steps that yielded an almost-perfect SiO_2 barrier over the functional components. Hence, the fabrication approach is compatible with existing lithography and microelectronics technology and easily scalable to the size of any commercially available wafer, and could thus allow for large-enough electronic arrays for covering virtually any organ in the human body (Fig. 1a). To demonstrate scalability, the authors passivated a flexible silicon transistor array in which the passivation layer was also used as a dielectric layer for capacitive coupling of the tissue to the adjacent mapping element (that is, for the electric-field-mediated transfer of energy between the two). In this way, the authors achieved direct tissue–SiO_2–gate coupling to the adjacent semiconductor channel of the signal-amplifier transistor (Fig. 1b), thus eliminating signal crosstalk.

To test the devices, Rogers and co-authors performed a series of bending and soak tests. Repetitive bending to a 5 mm radius for 10,000 cycles did not alter the electrical performance of the electronic arrays. And after soaking a device for 120 days in phosphate-buffered saline, the leakage current remained four

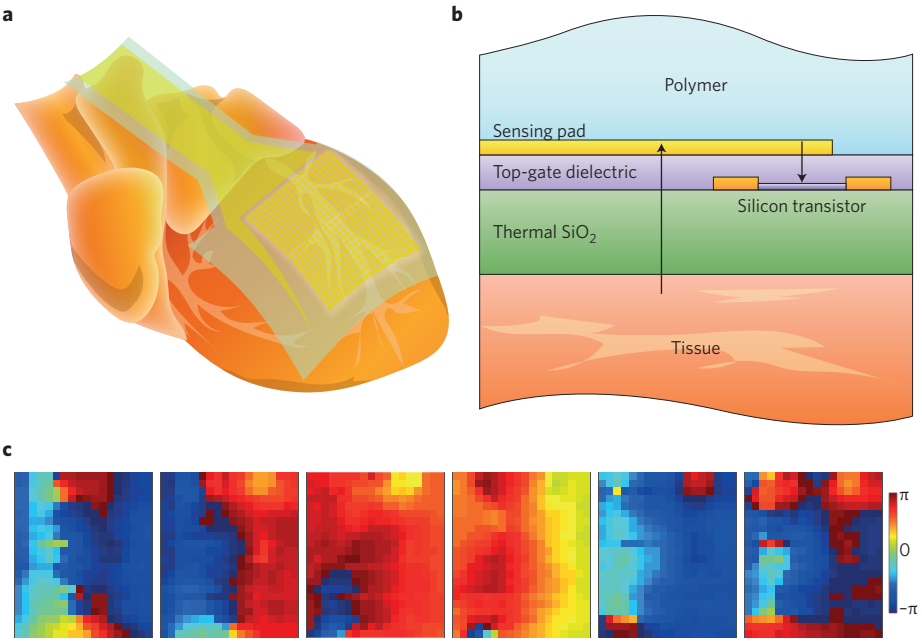

Figure 1 | High-density electrophysiological mapping of the heart by means of stable and capacitively coupled transistor arrays. **a**, Transistor arrays placed over the epicardium. **b**, Schematic of the sensing mechanism. The SiO_2 layer serves three roles: as a fabrication substrate, as an encapsulation layer and as a signal-transduction component. Bioelectric signals from the tissue are capacitively coupled to the metal sensing pad and then amplified by the silicon transistor. Arrows denote signal flow. **c**, Phase maps measured at different time points (over a period of 50 ms) during ventricular fibrillation. Panel **c** reproduced from ref. [5], Macmillan Publishers Ltd.

orders of magnitude lower than those of other cardiac electrophysiology devices. On the basis of a computational model and previous accelerated-degradation experiments at extreme conditions of temperature and pH (ref. [6]), the authors concluded that the dissolution rate for thermal SiO_2 (~15 nm per year) would allow a 1-μm-thick passivation layer to survive in physiological conditions for many decades.

Rogers and co-authors demonstrated the biomedical potential of the passivated devices by using them to electrically map isolated rabbit hearts. Also, because the devices are highly transparent, they were able to simultaneously carry out electrical and optical mapping of the heart. The interpolated activation maps from both the electrical and optical signals strongly correlated during both sinus rhythm and cardiac pacing. By analysing the electrophysiological phase maps (Fig. 1c), the authors detected singularity points that were associated with ventricular fibrillation (a serious disturbance in cardiac rhythm resulting from disorganized electrical activity).

Although the feasibility of the approach should be validated with other bioelectronic implants, Rogers and colleagues' encapsulation strategy promises to make bioelectronic arrays sufficiently stable for long-lasting measurements. Also, because the technique can enable the complete encapsulation of all the electrically sensitive components, less biocompatible materials and devices (such as those made from certain group-III and group-V semiconductors) may now be considered for integration into implantable bioelectronics. Moreover, adapting the encapsulation approach to devices for capacitive electrical stimulation would open up applications in, for example, peripheral nerve stimulation to treat chronic pain and in deep brain stimulation for Parkinson's disease. And the high transparency of the SiO_2 layer allows it to be integrated into optoelectronic devices for *in vivo* optical stimulation. This would enable, for example, optogenetics for the simultaneous modulation of the activity of neurons or of cardiomyocytes with a light-emitting-diode-based optical stimulus that is decoupled from the electrical recordings.

Passivated devices may also enable heart pacemakers, defibrillators and other implantable electrical stimulators that do not trigger a significant foreign-body response. Indeed, on the one hand, the smaller and thinner the implanted sensing or stimulating device, the milder the foreign-body reaction[7]; on the other hand, devices with a large area-to-volume ratio degrade faster. Therefore, an ultrathin encapsulation layer that degrades slowly may enable the development of small and thin yet stable bioelectronic implants.

Furthermore, Rogers and colleagues' simple and elegant passivation approach could in principle be adapted to existing 3D fabrication techniques and to other device architectures, such as those used in microelectromechanical systems, microfluidic channels and pumps controlled electronically[8], as well as to structures made by 3D printing. ❐

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