news & views

BIOELECTRONIC DEVICES

Epidermal electrophysiology at scale

Large-area electrode arrays for epidermal electrophysiology offer new possibilities for the control of prosthetic devices and the monitoring of brain function.

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Cutaneous electrophysiology is used clinically to non-invasively (or minimally invasively) probe the function of the heart (via electrocardiography; ECG), muscles (by electromyography; EMG), nerves (via nerve-conduction studies; NCS) and brain (through electroencephalography; EEG). These techniques use discrete electrodes or small needles that are bulky, cause discomfort to the patient, provide limited density of recording sites, and are not suitable for long-term use. Moreover, the devices are largely incompatible with magnetic resonance imaging (MRI), prohibiting combined investigations that would provide complementary structural and metabolic information. Advances in flexible electronics have enabled soft and ultrathin electronic devices that conform to the body like a tattoo, providing excellent mechanical and electrical contact with the skin[1–4]. Such epidermal-electronics technology, however, has so far been limited to interfacing with a few square centimetres of tissue. John Rogers and colleagues now report in *Nature Biomedical Engineering* the fabrication and applicability of MRI-compatible epidermal-electrophysiology devices with dramatically larger areas, and demonstrate their use in controlling prosthetic devices and in monitoring brain function[5].

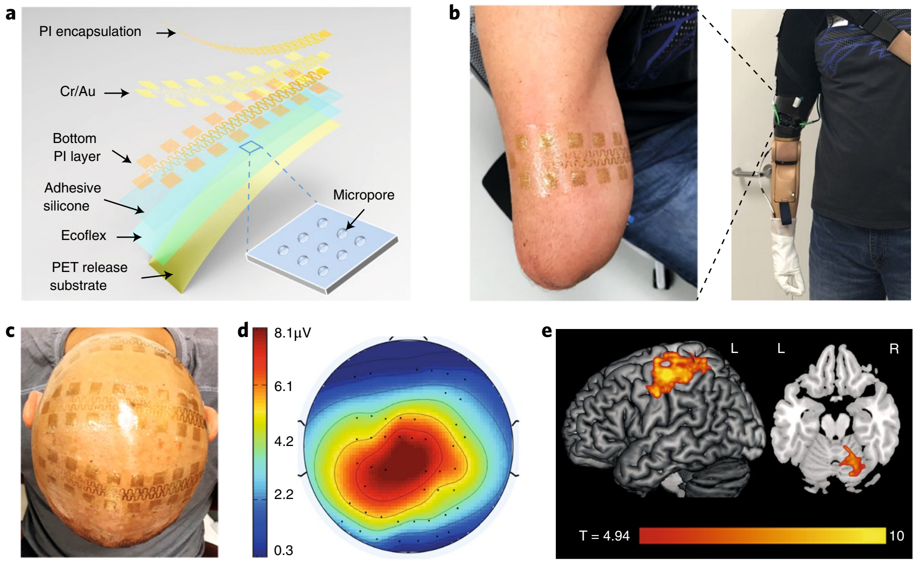

Fig. 1 | Large-area epidermal electrode arrays, and examples of their applications. a, The different layers in the electrodes. PI, polyimide; Cr/Au, chromium/gold; PET, poly(ethylene terephthalate). Ecoflex is a commercial soft silicone rubber. **b**, Electrode arrays laminated on an amputated upper limb. **c**, Electrode arrays covering the scalp. **d**, An example of an event-related-potential map (the result of a specific brain response). **e**, An example of EMG-informed functional MRI signals overlaid on structural MRI templates. The signals show the association between EMG activity in the right forearm and blood-oxygen-level-dependent (BOLD) signal in the left motor cortex, right cerebellum and cuneus (a region of the brain's occipital lobe). L, left; R, right. Panels reproduced from ref. [5], Springer Nature Ltd.

Rogers and colleagues used fabrication processes designed to enable facile handling of the electronics and their easy attachment to skin. Two components, an electrode array and an adhesive support, were fabricated independently and then brought together. The electrode array consists of gold electrodes and serpentine wires, with polyimide insulating layers (Fig. 1a). On the side contacting the body, the insulation layer only covers the wires and allows the electrodes to establish direct contact with the skin. Photolithography on an 8-inch silicon wafer enabled the fabrication of large-area arrays with micrometre-scale feature patterns. The arrays are then removed from the wafer by using a water-soluble adhesive tape, and placed on the adhesive support, which consists of a bilayer silicone coating on a poly(ethylene terephthalate) foil. The assembled structure is gently pressed against the body and the polymer foil is removed to reveal a thin, skin-conformable device, which is sufficiently flexible to allow for repeated application to the skin without causing fracture defects, folds or distortions.

Large-area epidermal devices must be permeable to water vapour to allow sweat to escape, and sufficiently stretchable to conform to curved body shapes. Rogers and co-authors designed the devices to be breathable by imprinting the adhesive layer with polymer spheres. This leads to a regular array of pores, with dimensions that can be tuned to control the degree of water-vapour permeation. The serpentine structure of the wires ensures that the device can be stretched to accommodate local deformations without breaking the electrical connections. The authors then tested the use of the devices for controlling EMG prosthetics and for assessing brain function via full-scalp EEG. Current EMG-driven prostheses that partially restore function after limb loss make use of robotic limbs that use a liner with embedded electrodes. The recorded signals are fed to a computer, where a classifier algorithm that is trained to interpret the user's intended movements controls the prosthesis. In this context, large-area electrode arrays are of primordial importance in order to record from as many muscle groups as possible and to enable several degrees of freedom[6]. In comparison to traditional electrodes in prostheses, epidermal electrodes reduce mechanical load to the skin and allow sweat to escape.

The authors show that the large-area devices fulfil these requirements (Fig. 1b) and that they can be worn for several days without causing skin irritation. Furthermore, they enable high classification accuracy and a reduction in errors from motion artefacts and the repeated use of the prosthesis (that is, taking it off and putting it on). Also, when applied to cover the full scalp (Fig. 1c), the electrode arrays recorded high-quality EEG signals across it (Fig. 1d). Compared to the currently used individual or helmet-mounted electrodes, the authors' epidermal electrode arrays offer a range of advantages, such as ease of mounting and the capacity for chronic recordings in a format that does not interfere with daily activities or sleep.

In MRI, strong magnetic fields inside the scanner interact with the metal electrodes. This can cause artefacts in the images and deteriorate the quality of electrophysiology recordings. Moreover, during a scan the electrodes can heat up, and lead to adverse events for the patient. An important feature of the devices developed by Rogers and co-authors is their compatibility with MRI. The fractal architecture of the electrode mesh minimizes the interaction with magnetic fields, allowing for higher-quality MRI images and electrophysiology recordings while preventing the electrodes from heating up. Although the electrode's fractal architecture increases the contact impedance compared to that of solid films, this is remedied by coating the electrodes with a conducting polymer gel. Furthermore, the MRI compatibility of the electrodes enables combined investigations with functional imaging and EMG, allowing, for example, the identification of associations between muscle response and brain activity (Fig. 1e).

Rogers and co-authors' large-area epidermal electrode arrays may have an impact on ECG, EMG, NCS, EEG and other electrophysiological applications. The arrays could be used to investigate and monitor cardiac, muscular and/or neural functions in patients during everyday activities. Such dynamic and long-term assessments should increase the chances of detection of abnormal activity, and thus facilitate timely and informed interventions. The combination of different modalities (such as EEG and EMG), via such unobtrusive epidermal devices that interrogate large areas of tissue, could prove to be powerful for the study of sleep and epilepsy, and for rehabilitation. Also, when studying the complex functional activity of the brain, the possibility to combine large-area electrophysiology with structural and metabolic data from MRI should increase diagnostic accuracy; after all, epilepsy, movement disorders and surgical workup for functional neurosurgical resection require extensive electrophysiological information. Beyond medical applications, large-area epidermal bioelectronics might also play a role in sport and fitness, allowing accurate measurements of motor activity during exercise. However, an important limitation of epidermal electronics is the presence of hair, which grows at an average rate of 0.3 mm per day[7]. Good adhesion of epidermal devices requires thorough and constant removal of hair, which limits longer-term applications, particularly for EEG. Similarly, the volume of subcutaneous adipose tissue needs to be relatively small, to reduce the distance between the electrodes and the underlying target (such as muscle).

A key feature of Rogers and colleagues' work is the use of photolithography as a patterning method. Lithography is a proven manufacturing technique, which allows reliable access to high-resolution features but limits the ultimate size of the device to that of the wafer used. Additive-manufacturing techniques[8], such as inkjet printing and aerosol jetting, offer poorer resolution but would facilitate devices with even larger areas (that could cover the entire scalp, for example), and yield monolithic fabrication strategies and facile customization for individual patients. It will be interesting to see how far these techniques can be pushed towards the reliable fabrication of complex biomedical devices. Future large-area devices will undoubtedly include additional capabilities, such as optical and biochemical sensors and actuators, which are already being developed in wearable formats[3,4]. And the eventual integration of power, processing and communication components will yield autonomous systems that can replace the large, bulky and cable-connected devices that crowd operating theatres and emergency rooms.

On the one hand, epidermal devices are non-invasive, well tolerated by users, and can be placed on patients outside the hospital setting. On the other hand, their applications are limited by the devices' reduced selectivity to neural structures or muscle fibres (in both stimulation and recording), and by the low signal-to-noise ratio of the recordings[9]. Yet, as Rogers and co-authors note, controlling a prosthetic limb typically requires an invasive surgical intervention (such as targeted muscle reinnervation[10]), with only the prospect of controlling major muscle groups rather than fine movements. Looking ahead, the ability to conform to arbitrary body shapes, to cause minimal trauma when implanted, and to interrogate a large-area of tissue while allowing for the transport of fluid (such as cerebrospinal fluid), may make large-area epidermal-electrophysiology devices suitable for surgical implantation on muscles, the brain cortex or the heart. This would pave the way for these devices to be used in a broader range of systems and applications, such as advanced brain–machine interfaces, the monitoring of epilepsy and the selective control of muscles. ❒

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