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Research Highlight

Ultrasoft, mass-permeable, and low-impedance hydrogels for tissue-like skin-device interfaces

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Flexible devices constructed on ultrathin polymer substrates have emerged as outstanding candidates for wearable bioelectronics that have superiority in applications in next-generation personalized health monitoring and medical treatment, such as transcutaneous bioanalysis and therapy, and can provide the functionality of detecting biosignals and/or biomarkers [1–3] and delivering drugs [4,5] as feedback via the human skin. For some disease detection and treatment, wearable bioelectronics devices are required to realize point-of-care therapy in practical applications. For example, for diabetes, patients need to check their blood sugar level several times a day and to take regular insulin shots to maintain their blood glucose level, which requires smaller, cheaper, and more convenient delivery devices and tighter skin-device contact to ensure effective drug delivery. However, the current wearable bioelectronic systems still have the problem of nonideal contacts at the electrical/biological interface, where microscale air pockets exist due to imperfect follow of the polymer substrate, even with greatly reduced thickness, on the skin with microscopic wrinkles. This nonideal interface between the electronic device and human skin will affect the fidelity of the obtained biosignals, which would be a serious issue, especially when long-term operation or monitoring is needed. Furthermore, when considering the desired function of therapy, current systems cannot effectively carry a certain amount of therapeutic drugs, generally in the liquid state, for efficient treatment, which greatly limits the capability of bioelectronic systems for customized therapy with instant feedback. Therefore, a new skin-device interface that can solve these problems is critical to bring wearable bioelectronics to the next stage with fully released application potential.

Recently, Kim and colleagues [6] reported an ultrathin, properly functionalized hydrogel that is similar to human tissues. It can be used to construct a soft, moisturized and permeable interface between wearable bioelectronic systems and human skin. This hydrogel is based on poly(acrylamide) (PAAm) with a highly porous structure and ultrathin thickness, which can serve as rapid diffusion and transport channels for target bioanalytes or drug molecules. Furthermore, a low impedance interface between electrodes and human skin can be provided by this hydrogel after poly (3,4-ethylenedioxythiophene):poly(styrene sulfonate) (PEDOT:PSS) functionalization, which is beneficial for capturing bioelectrical signals from the skin or applying electric stimulation to the tissue.

For example, an integrated wearable system with an ultrathin functionalized PAAm hydrogel for transcutaneous bioanalysis and therapy was developed as illustrated in Fig. 1a. It consists of four types of representative bioelectronic devices, including a transcutaneous oxygen pressure ($tcPO_2$) sensor, an impedance sensor, an iontophoretic drug delivery device, and a transcutaneous electrical nerve stimulator (TENS). It is worth mentioning that the ultrathin hydrogels were functionalized differently and integrated on the surface of different devices to provide mass-permeable interfaces for $tcPO_2$ sensors and iontophoretic devices and low-impedance interfaces for impedance sensors and TENS (Fig. 1b). The ultrathin and porous (Fig. 1c) nature of the hydrogel can not only accelerate mass and heat transfer, but also optimize the conformal contact between the bioelectronics devices and human skin. Compared with hydrogels of different thicknesses, the thinner hydrogel showed a better penetrating behavior for both oxygen (Fig. 1d) and rhodamine B (Fig. 1e), where the former substance is the detecting object of the $tcPO_2$ sensor while the latter is selected as a model molecule involved in the drug delivery process. The heat dissipation and thermal conductivity test of the hydrogel also showed the same trend (Fig. 1f), indicating that ultrathin hydrogel can facilitate heat transfer and has advantages when thermal stimulation is needed, such as assisting extraction of oxygen molecules from the blood vessels for $tcPO_2$ sensing. According to the scanning electron microscopy (SEM) image of the hydrogel attached to artificial skin (Fig. 1g), there is almost no gap at the ultrasoft skin-device interface, which increases the effective contact area and helps to realize a low contact impedance with PEDOT:PSS functionalized PAAm hydrogel, especially in the low-frequency range (Fig. 1h). The function of the integrated system was first tested by attaching it to the foot for measuring $tcPO_2$ *in vivo*, where the change in reduction current as a result of changed oxygen concentration extracted from the blood vessels can reflect different leg positions (Fig. 1i). Transdermal drug delivery was further verified by the successful delivery of diltiazem hydrochloride to 8-week-old male Sprague-Dawley rats *in vivo* (Fig. 1j).

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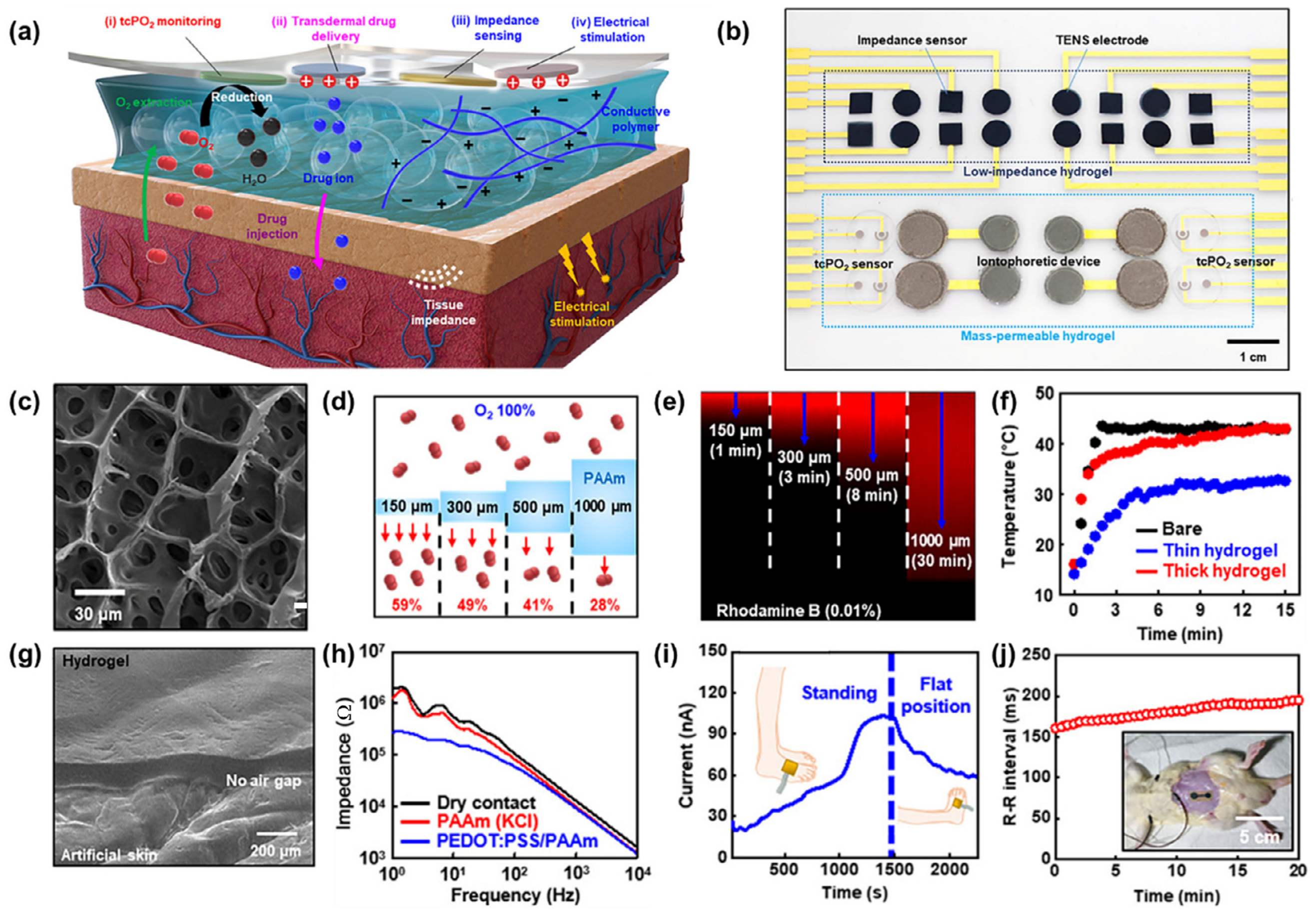

Fig. 1. (Color online) Schematic (a) and optical image (b) of integrated wearable bioelectronics with a hydrogel interface. (c) SEM image showing the porous structure of the hydrogel. Penetration test of (d) oxygen and (e) rhodamine B through hydrogels with different thicknesses. (f) Temperature versus time plots of the heat transfer test. (g) SEM image of the tissue-like, ultrasoft hydrogel mounted on artificial skin. (h) Electrochemical impedance spectroscopy analysis of the contact impedance using different electrodes. (i) Reduction current measured by a $tcPO_2$ sensor *in vivo* on a foot. (j) Drug delivery experiment on a Sprague-Dawley rat. Reprinted with permission from Ref. [6], Copyright © 2021 The American Association for the Advancement of Science.

In summary, a wearable bioelectronic system with a porous, ultrathin hydrogel interface has been reported that can provide low contact impedance for capturing bioelectric signals with high fidelity, enhanced mass permeability for efficient drug delivery, excellent thermal conductivity for effective heat stimulus, and conformal contact with the skin for stable, long-term monitoring. These outstanding characteristics enabled by this newly developed hydrogel provide a great alternative solution to the problems existing in current wearable bioelectronics. The cross-linked polymeric networks make it possible for drugs to be stored for later on-demand delivery. Furthermore, hydrogels are generally biocompatible and widely used in biomedical applications, so they may be able to be adopted quickly for clinical trials. All of these findings will shed light on strategies to push this technology toward the next stage for advanced health care and therapy.

Conflict of interest

The authors declare that they have no conflict of interest.

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