

Better electronics from immiscibility

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A bicontinuous conducting polymer hydrogel with high electrical conductivity, stretchability and fracture toughness in physiological environments achieves high-fidelity monitoring and effective stimulation of tissues and organs.

Metallic electrodes have served as the standard mode of interfacing for electrophysiological recording and stimulation of various tissues and organs¹. Despite their widespread use, metallic electrodes lack some of the important properties of tissues and/or organs for improved interfaces, specifically intrinsic mechanical softness, high water content, and mixed ionic and electronic conductivity². Now, writing in *Nature Materials*, Zhou and colleagues³ present a bicontinuous hydrogel made of interpenetrating networks of an elastomer and a conducting polymer for in vivo all-hydrogel bioelectronics. The bicontinuous conducting polymer hydrogel (BC-CPH) enables long-term electrophysiological recording of the heart as well as stimulation of the sciatic nerve and spinal cord in rats.

Hydrogels based on conducting polymers are used in bioelectronics applications because they combine the softness of biological tissues with the electronic properties of metallic devices, have good biocompatibility, are stable in physiological fluids and remain functional over long durations (weeks to months)². Nonetheless, balancing the mechanical properties and electrical conductivity of these hydrogels to mimic the softness of tissues and to improve recording quality and stimulation efficacy is challenging⁴. Several studies have extensively developed mechanically tough hydrogels but most of these have low electrical conductivities and their water content does not match that of biological tissue. Efforts to increase the conductivity of these hydrogels have been made at the expense of their mechanical properties⁵, limiting their long-term applicability. Moreover, many existing hydrogels are not compatible with conventional processing methods, such as rapid additive manufacturing, further limiting their use in bioelectronics devices.

To overcome these challenges, Zhou and colleagues fabricated a conductive hydrogel made from interpenetrating networks of hydrophilic polyurethane with poly(3,4-ethylenedioxythiophene):polystyrene sulfonate (PEDOT:PSS). They first optimized the blending ratio of PEDOT:PSS to polyurethane, leading to the bicontinuous phases that simultaneously achieve favourable electrical and mechanical

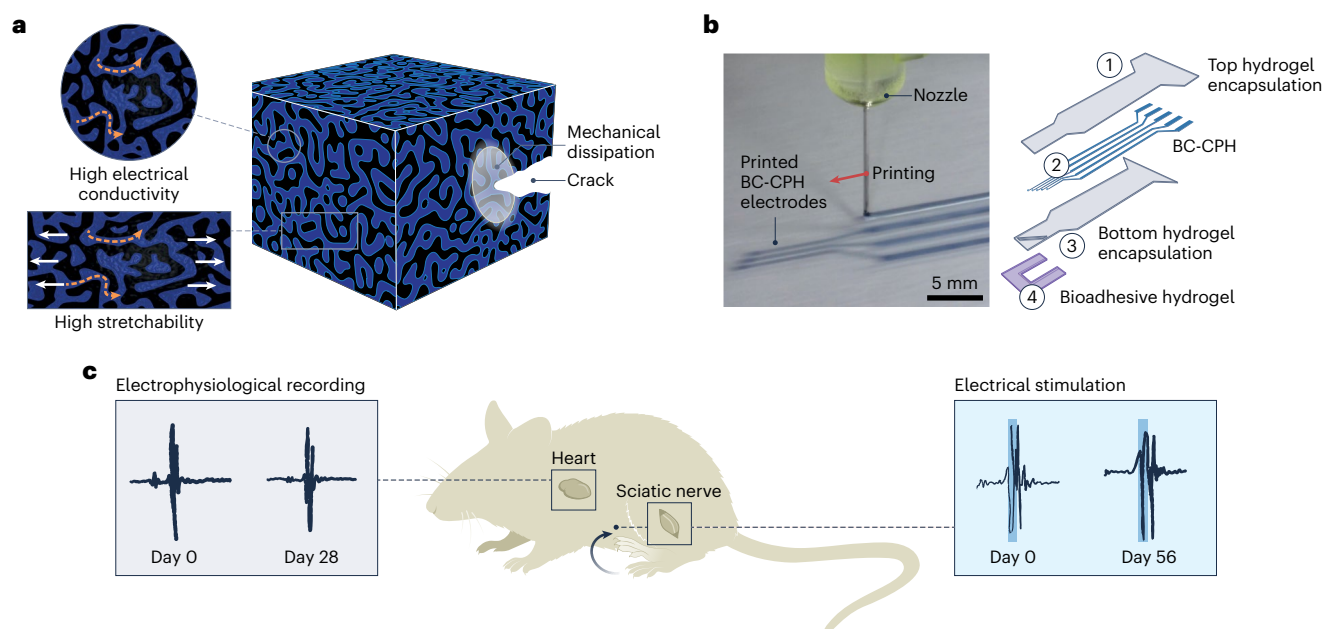


Fig. 1 | All-hydrogel devices based on bicontinuous interpenetrating polymers. **a**, The BC-CPH achieves high conductivity (orange arrows), high stretchability (white arrows) and high fracture toughness due to the synergy of the interpenetrating electrical PEDOT:PSS-rich phase (blue) and the hydrophilic polyurethane-rich mechanical phase (black). **b**, All-hydrogel device made by monolithically 3D printing the BC-CPH biointerface, which is then encapsulated

by two insulating hydrogel layers, one of which contains a bioadhesive hydrogel for tissue integration. **c**, In vivo demonstration of all-hydrogel devices for stable, minimally invasive, long-term and high-efficacy electrophysiological recording and electrical stimulation (with the blue rectangles indicating the stimulation pulses) in a rat model. Figure adapted with permission from ref. 3, Springer Nature Ltd.

properties (Fig. 1a). Specifically, the BC-CPH exhibits desirable electronic properties for biointerface recording and stimulation, including high conductivity (more than 11 S cm^{-1}), low electrode-tissue impedance, high charge storage capacity, charge injection capacity and cyclic stability. Additionally, the BC-CPH demonstrates improved physical properties (such as softness and high water content) that match those of soft tissues, while being mechanically robust with high stretchability (more than 400%) and high fracture toughness (more than $3,300 \text{ J m}^{-2}$). Moreover, the BC-CPH ink allows for facile preparation of tunable formulations for various materials processing methods, including spin-coating, electrospinning, micro-moulding and 3D printing. By leveraging the advantages of 3D printing (Fig. 1b), the authors fabricated all-hydrogel devices composed of BC-CPH, a bioadhesive hydrogel and an insulating polyurethane hydrogel in a short duration (<10 min), enabling soft, intimate and stable contact with soft tissues and on-demand minimally invasive detachment.

In rats, the all-hydrogel devices enable high-fidelity recording of electrophysiological signals from the heart as well as high-efficacy stimulation of the sciatic nerve and spinal cord (Fig. 1c). Notably, the long-term operation of the all-hydrogel devices demonstrates higher electrocardiogram signal quality and improved stimulation efficacy for hindlimb movement compared with that on the day of implantation. In biocompatibility studies, the all-hydrogel devices show low cytotoxicity and lower tissue damage and foreign body response (over 2 months) compared with the elastomer-based control devices.

Several challenges and opportunities need to be addressed to fully exploit the potential of the biointerfacing hydrogel devices. Instead of using adhesive hydrogels, it would be prudent to confer bioadhesive properties to conductive hydrogels that need to directly adhere to tissues, thereby retaining stable electrode placement and high-fidelity signal transduction, which could enable chronic recording of the same neurons over many months. Also, elucidating the fundamental aspects in the development of stretchy, conductive hydrogels could shed light on further increasing conductivity in tandem with achieving high stretchability and tissue-level softness. Advances in materials' designs demand a deeper and more extensive understanding of the structure–property relationships of conductive hydrogels and their hybrids at multiple length scales, leading to general design

principles that could replace often intensive qualitative evaluations and trial-and-error methods.

Moving forward, miniaturized high-density electrode arrays can be realized by refining ink formulations and printing conditions. But monolithic photopatterning of hydrogel materials and devices can provide an exciting lever for improved recording capabilities for large neuronal populations⁶. However, a major barrier to the chronic use of implants is the foreign body reaction, inducing tissue damage and device performance deterioration. Zhou and colleagues' hydrogel device requires further assessments of biocompatibility and careful validation in large-animal models, while demonstrating that the immune response of the tissue-interfacing materials is minimized. The viscoelastic properties of the hydrogels can also further be explored to mimic the extracellular matrix, such that various cellular behaviours are minimally affected or carefully regulated⁷. Nevertheless, the work by Zhou and colleagues highlights the potential of hydrogel bioelectronics in fuelling advances in merging electronics with biological systems like those envisioned in science-fiction tales.

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Published online: 28 June 2023

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Competing interests

The authors declare no competing interests.