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Seamless biointerfaces in devices

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Seamless wet-tissue adhesive bioelectronics, realized by the assembly of strain-insensitive elastomeric electronics and a hydrogel adhesive, allow closed-loop therapeutic modulation.

Implantable bioelectronics offer the opportunity to investigate a range of physiological functions and are promising for therapeutic modulation at device–tissue interfaces. However, achieving sustained performance in living organisms is challenging, owing to the dynamic nature of physiological environments and subsequent foreign body responses.

Effective implantable bioelectronics require more than physical implantation – the devices demand seamless, biocompatible and robust integration with the target tissue while maintaining functionality. While compliant interfaces composed of soft materials[1] or thin-film geometries[2] have previously been explored to alleviate mechanical mismatches, bioadhesive-mediated seamless interfaces are a promising strategy for implantable devices[3,4]. Bioadhesive interfaces can provide stable yet atraumatic integration between the device and the target tissue to mitigate distortion of biological signals by maintaining consistent device–tissue contact. However, implementing bioadhesive interfaces in multi-functional bioelectronics requires innovative approaches to achieve a seamless yet functional integration of device components such as electrodes, sensors, device substrates and the bioadhesive layer.

Writing in *Nature Materials*, Li et al. report a stretchable elastomer–hydrogel biphasic assembly that achieves a multi-modal bioelectronic platform[5]. The device consists of liquid metal-based, strain-insensitive electrodes and stretchable sensors seamlessly assembled with molecularly integrated elastomer and tissue-adhesive hydrogel layers via direct ink writing. The resultant multifunctional device offers atraumatic tissue integration through a tissue-adhesive hydrogel interface and enables multimodal sensing and modulation of physiological systems, such as the closed-loop sensing and control of blood glucose level in diabetic rats in vivo.

Historically, microfabricated thin films have been used to form bioelectronic interfaces with target organs, which subsequently evolved into flexible elastomeric substrates[1,6]. Yet, although these devices have

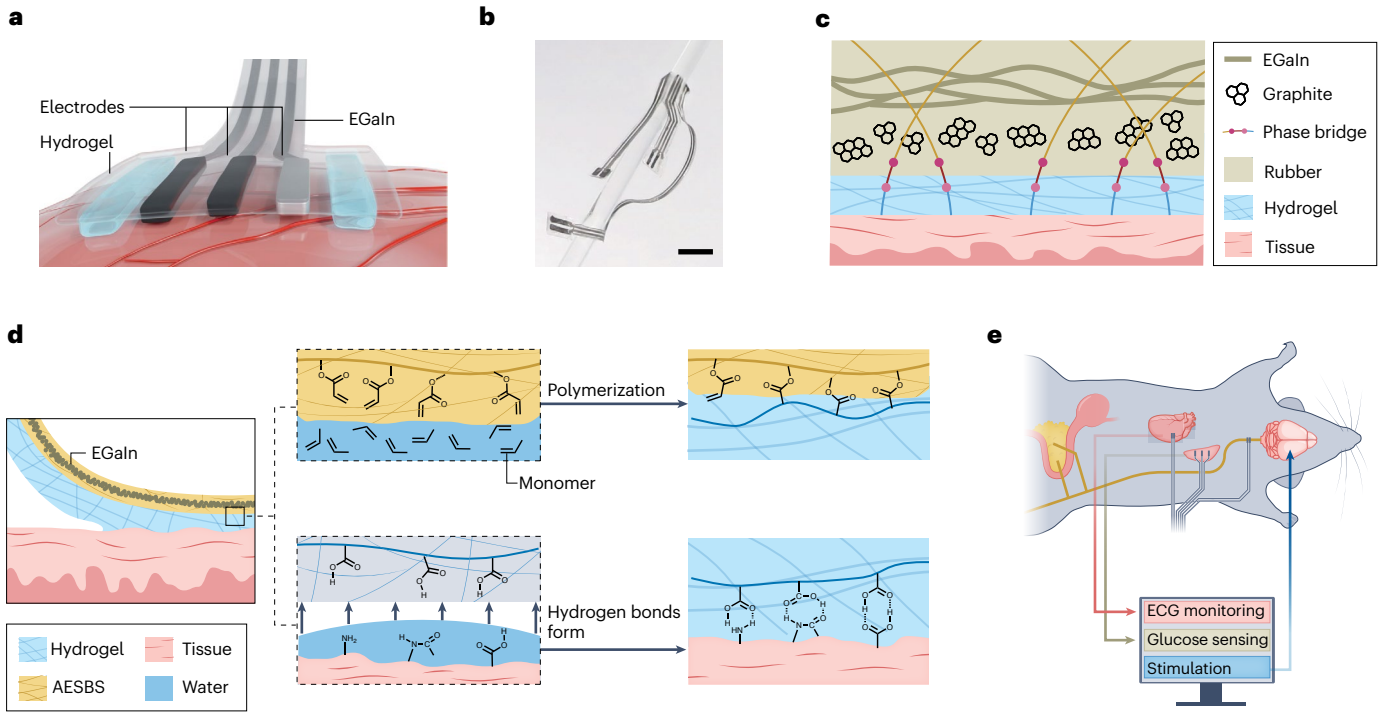

Fig. 1 | Seamless wet-tissue adhesive bioelectronics. a, Schematic illustration of the ElHyX architecture. EGaIn, eutectic gallium indium. **b**, Photograph of an integrated ElHyX device combining electrophysiological sensing, biomolecular monitoring and neural modulation for closed-loop disease management. Scale bar, 1 cm. **c**, Schematic illustration of the ElHyX composition. **d**, Schematic of ElHyX formation via in situ hydrogel polymerization on a chemically modified elastomer. AESBS, acrylyl-opening epoxidized poly(styrene–butadiene–styrene). **e**, Schematic of the multifunctional ElHyX device implanted in a diabetic rat, showing the ECG sensor attached to the heart, the glucose sensor on the outer rib surface and nerve cuff wrapped around the vagus nerve. Figure adapted from ref. 5, Springer Nature Limited.

evolved to mitigate mechanical mismatches, they inherently lack the ability to form a seamless interface with the host tissue over chronic implantation periods[7]. This deficiency often results in device dislocation, leading to undesirable outcomes such as off-target stimulation, loss of signal fidelity and irreversible tissue damage. To ensure firm fixation, these devices have typically relied on surgical procedures such as suturing or extensive wrapping, which can cause incidental trauma to the underlying tissue. Furthermore, from an electronic standpoint, although solid metal wires are initially effective, they are vulnerable to fatigue from repeated bending or stretching, which can cause mechanical failure of wires. Concurrently, rigid metal electrode pads are prone to biofouling – a phenomenon that challenges the operational longevity of bioelectronics and, more critically, impedes the in vivo electrochemical sensing of biomolecules. Ultimately, the sustained use of these devices has been limited by such architectural incompatibilities.

To overcome these bottlenecks, Li et al. report a strain-insensitive, stretchable elastomer–hydrogel biphasic bioelectronic device, ElHyX, that maintains both electrical integrity and a stable adhesive device–tissue interface even under excessive strains (Fig. 1a). In this approach, a hydrogel bioadhesive firmly anchors the elastomeric electronics to the tissue surface, preserving a stable electrode–tissue interface capable of bioelectrical and biomolecular sensing alongside neuromodulation (Fig. 1b). The strain-insensitive electronics comprise conductive elements – where conductive fillers like liquid metal and graphite form a robust percolation network – and an encapsulating layer composed of an elastomeric substrate (Fig. 1c). To merge these components, a cohesive hydrogel–elastomer assembly is prepared by the in situ polymerization of a hydrogel adhesive onto a reactive elastomer (Fig. 1d). The resulting ionically conductive hydrogel adhesive forms a tight seal with the underlying tissue through robust intermolecular bonds, thereby maintaining a stable conductive pathway between the biological substrate and the stretchable electrodes. As a result, this electrical interface remains firmly anchored, reliably recording electrocardiogram (ECG) signals despite the dynamic mechanical interferences of the surrounding environment.

Li et al. establish a stable, multifunctional device capable of closed-loop operations, where individual sensors are fabricated via direct ink writing for customization and implanted into their respective targets. The device is shown to function for simultaneous ECG monitoring, glucose sensing and vagus nerve stimulation for blood glucose regulation in diabetic rats (Fig. 1e). Unlike existing devices that provide individual functions without cross-functional integration, the device offers closed-loop functionality comprising sensing of glucose level and heart rate and stimulation of vagus nerve for real-time regulation of blood glucose in a single seamlessly-integrated device. The combination of strain-insensitive stretchable electrodes and seamless biointerfaces enable a high-performance multi-functional bioelectronic interface that was previously inaccessible by conventional approaches.

Establishing such a stable interface is fundamental to ensuring the accuracy of biosensing and the fidelity of subsequent closed-loop diagnostics – cornerstones for the realization of personalized medicine. When coupled with electrode patterning technologies, the device reported by Li et al. may offer an insight to achieve highly selective stimulation, driven by superior spatial resolution. Ultimately, for these technological breakthroughs to be clinically translated, rigorous, long-term validation in freely moving pre-clinical animal models and in clinical trials remain as future works. Furthermore, to extract clinically meaningful insights, fusing the high-fidelity biological signals captured by such bioadhesive bioelectronic interfaces with deep learning models may provide greater potential, along with advances in artificial intelligence.

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Competing interests

The authors declare no competing interests.