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Hydrogel-integrated multimodal physiological and modulation systems

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Hydrogels are emerging as a transformative class of materials for bridging the interface between electronics and biological systems. Their softness, high water content, and tunable ionic/electronic conductivity enable conformal, low-impedance, and biocompatible contact with tissues. This review surveys recent advances in hydrogel-integrated multimodal bioelectronic systems, with an emphasis on the stable signal acquisition, coupled sensing–actuation functions, and stimulus-responsive behaviors that support adaptive interfaces. We compare hydrogels with conventional biointerface materials and highlight key advantages such as stretchability, breathability, ionic conduction, and tissue compatibility. We then discuss representative system-level demonstrations in three domains: closed-loop brain monitoring with ultrasound neuromodulation, gastrointestinal (GI) retention and leakage detection, and cardiac monitoring, pacing, and repair. Finally, we summarize the remaining challenges including long-term stability, scalable manufacturing, and integration with microelectronics and outline opportunities for clinically deployable, autonomous, and personalized hydrogel-based bioelectronic systems.

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Wider impact

This review delineates the critical advances that have established hydrogels as indispensable interfaces for multimodal physiological monitoring and modulation. The field has attracted broad attention because hydrogels uniquely reconcile the mechanical, chemical, and electrical disparities between rigid electronics and soft biological tissues, enabling stable signal acquisition and therapeutic delivery within a single platform. Looking forward, hydrogel systems are anticipated to evolve toward highly integrated, adaptive architectures that unify electrical, chemical, and mechanical sensing with diverse actuation strategies, further augmented by wireless communication and AI-driven feedback. By linking material design principles to system-level demonstrations across neurological, gastrointestinal, and cardiovascular applications, the insights presented herein are expected to guide the development of next-generation bioelectronic systems and to advance materials science toward multifunctional, clinically translatable technologies.

1. Introduction: from soft interfaces to intelligent systems

The field of physiological monitoring has progressed from rigid, bulky instruments to flexible and wearable systems over the past decades.[1,2] Early devices, such as Floyer's pulse watch (18th century) and Riva-Rocci's sphygmomanometer (1896), established foundational principles for tracking physiological signals. By the mid-20th century, electronic monitors became routine in intensive care units for continuous measurement of ECG, blood pressure, and oxygen saturation.[3] In parallel, therapeutic devices matured rapidly: external pacemakers appeared in the 1950s, followed by the first fully implantable pacemaker in 1958.[4] Clinical neurostimulation also expanded in the 1980s and 1990s, including deep brain, spinal cord, and vagus nerve stimulation, which helped establish bioelectronic medicine as a clinical discipline.[5] With advances in microelectronics and soft materials, bioelectronics systems are becoming increasingly integrated with biological tissues.[6] Holter monitoring and portable ECG devices became widely available in the late 20th century, and wearable defibrillators entered clinical use by the 2000s.[6] Today, consumer wearables record ECG, SpO_2, and activity at a population scale, enabling long-term tracking outside clinical settings.[7] The next step is closed-loop bioelectronic systems that combine multimodal sensing with timely interventions (electrical, acoustic, or pharmacological).[8] Realizing such systems requires seamless integration of electronics and biology into soft, flexible platforms. Achieving this goal requires soft, adaptive interfaces that can couple electronics to living tissues while remaining stable under motion and over time. This evolution represents a conceptual shift as earlier devices typically performed a single task either sensing

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or stimulation. In contrast, next-generation platforms aim to integrate sensing, actuation, and adaptive control within one wearable or minimally invasive system. Such closed-loop operation requires interfaces that are not only soft and biocompatible, but also mechanically stable, electrically reliable, and compatible with multiple modalities.

Rigid materials such as metals and silicon often exhibit significant mechanical and interfacial mismatch with soft, hydrate biological tissues.[9,10] Conventional electrodes can irritate the skin and may delaminate under sweat or motion.[11,12] Hydrogels, polymeric networks swollen with water, offer a practical alternative.[13,14] Their high water content and low modulus enable soft, tissue-like compliance, which improves conformal contact at skin and organ surfaces.[9,15] Many hydrogels are also biocompatible and can incorporate biomolecules or drugs without compromising activity.[16] Hydrogels can provide ionic and/or electronic conduction. Ionic salts or conductive fillers (*e.g.*, PEDOT:PSS, carbon nanotubes, graphene) can be introduced to achieve adequate conductivity under physiological conditions.[17] Compared with dry electrodes, ionic hydrogels often yield lower interfacial impedance and more stable contact on soft tissue.[18] Adhesive functional groups (*e.g.*, catechols or amines) further improve attachment through reversible hydrogen bonding, ionic interactions, or covalent anchoring after oxidation.[19,20] Together, these properties make hydrogels attractive as multifunctional coupling layers that support reliable signal acquisition and multimodal integration. Beyond serving as soft and conductive materials, hydrogels increasingly function as system-integrated biointerfaces, mediating mechanical, electrical, chemical, and biological interactions simultaneously. This multifunctional role positions hydrogels not merely as passive electrode coatings, but as active architectural elements that enable multimodal signal transduction and system-level integration.

Biological systems process multiple signals simultaneously, including mechanical, thermal, chemical, and electrical cues.[1] Human skin is a clear example: it senses pressure, temperature, and texture in parallel. Many wearable devices, however, still focus on a single modality, such as heart rate or motion.[21] This gap limits applications in clinical monitoring and in robotics, where multimodal information is often essential.[22] In clinical scenarios, clinicians may need concurrent measurements of ECG, respiration, blood pressure, temperature, and biochemical markers.[23] Similarly, advanced prosthetics and soft robotics demand artificial skins capable of detecting stretch, humidity, touch, and chemical signals.[24,25] These needs motivate the creation of integrated platforms that can both sense and intervene. A conformal patch, for example, can monitor ECG and sweat biomarkers and then trigger electrical stimulation, focused ultrasound, or local drug release when abnormal patterns are detected. Multimodal integration remains difficult because each modality imposes different interface requirements.[8,26] Electrical, optical, and chemical sensing can demand distinct material properties that are not easily combined in one layer.[27,28] Progress will therefore depend on coordinated advances in material design, device integration (flexible circuits, wireless power), and data fusion algorithms.[29,30] In this review, we focus on the materials-to-systems role of hydrogels in enabling such integrated platforms.

Unlike prior reviews that primarily classify hydrogels by single functions (*e.g.*, conductivity, adhesion, or drug delivery), we organize this article around hydrogel-integrated multimodal systems. We treat hydrogels as enabling interfaces that support co-localized sensing, actuation, and feedback control in unified bioelectronic platforms. This review begins by establishing the historical context and evolution of bioelectronic interfaces (Section 1), setting the stage for hydrogel-enabled technologies. Section 2 focuses on hydrogels as functional interfaces for multimodal integration, highlighting their ability to form conformal, adhesive contact for reliable signal acquisition, their dual roles as sensors and modulators, and their responsive behaviors to environmental stimuli such as hydration, pH, and temperature. Building on this material foundation, Section 3 turns to system-level integration of monitoring and modulation, with examples of brain, gastrointestinal, and cardiac systems. Case studies demonstrate how hydrogels enable high-fidelity EEG–FUS coupling for closed-loop brain therapies, long-term gastric residence and leakage detection in the GI tract, and multifunctional pacing and monitoring in the heart. Emerging hybrid systems further illustrate how hydrogels can serve as central hubs for intelligent feedback control, integrating sensing, actuation, and drug delivery into unified platforms. Throughout, we identify critical challenges including long-term stability, seamless electronic integration, and scalability, while also underscoring promising innovations such as nanocomposite formulations, advanced manufacturing techniques and artificial intelligence. By connecting fundamental hydrogel properties with system-level demonstrations, this review aims to chart a path toward next-generation multimodal hydrogel bioelectronics capable of autonomous, closed-loop, and personalized medical interventions. By shifting the perspective from material-centric optimization to system-level integration, this review aims to define a new conceptual framework for hydrogel-enabled bioelectronics.

2. Hydrogel as a functional interface for multimodal integration

2.1. Conformal contact and skin adhesion for reliable signal acquisition

Stable skin contact is paramount for any wearable sensor or stimulator.[31,32] Conventional rigid electrodes or adhesive patches often fail under conditions of sweat or body motion, leading to poor signal fidelity.[12,33] Hydrogels provide a compelling solution due to their intrinsic softness, deformability, and tissue-like modulus (in the kPa–MPa range).[34,35] A hydrogel layer can seamlessly conform to the fine microtextures of skin, minimizing gaps, reducing motion artifacts, and lowering interfacial impedance.[36,37] For example, self-adhesive hydrogel electrodes can maintain consistent ECG readings even during vigorous movement, outperforming conventional wet-gel electrodes.[38,39] A key advantage is the adhesion mechanisms.

Hydrogels attach to skin through combined physical and chemical interactions, which is difficult for rigid materials to achieve.[19,40] Particularly noteworthy are mussel-inspired systems, in which catechol or dopamine moieties endow hydrogels with strong adhesion surpassing typical medical tapes.[41,42] These groups engage in hydrogen bonding, π–π stacking, and cation–π interactions.[42] Upon oxidation (*e.g.*, by sodium periodate), catechol is converted to reactive quinone structures, which can further react with amine or thiol groups on skin proteins *via* Schiff base formation or Michael-type addition to yield covalent anchoring[42,43] (Fig. 1a). Over the past decades, extensive research has exploited catechol chemistry to design

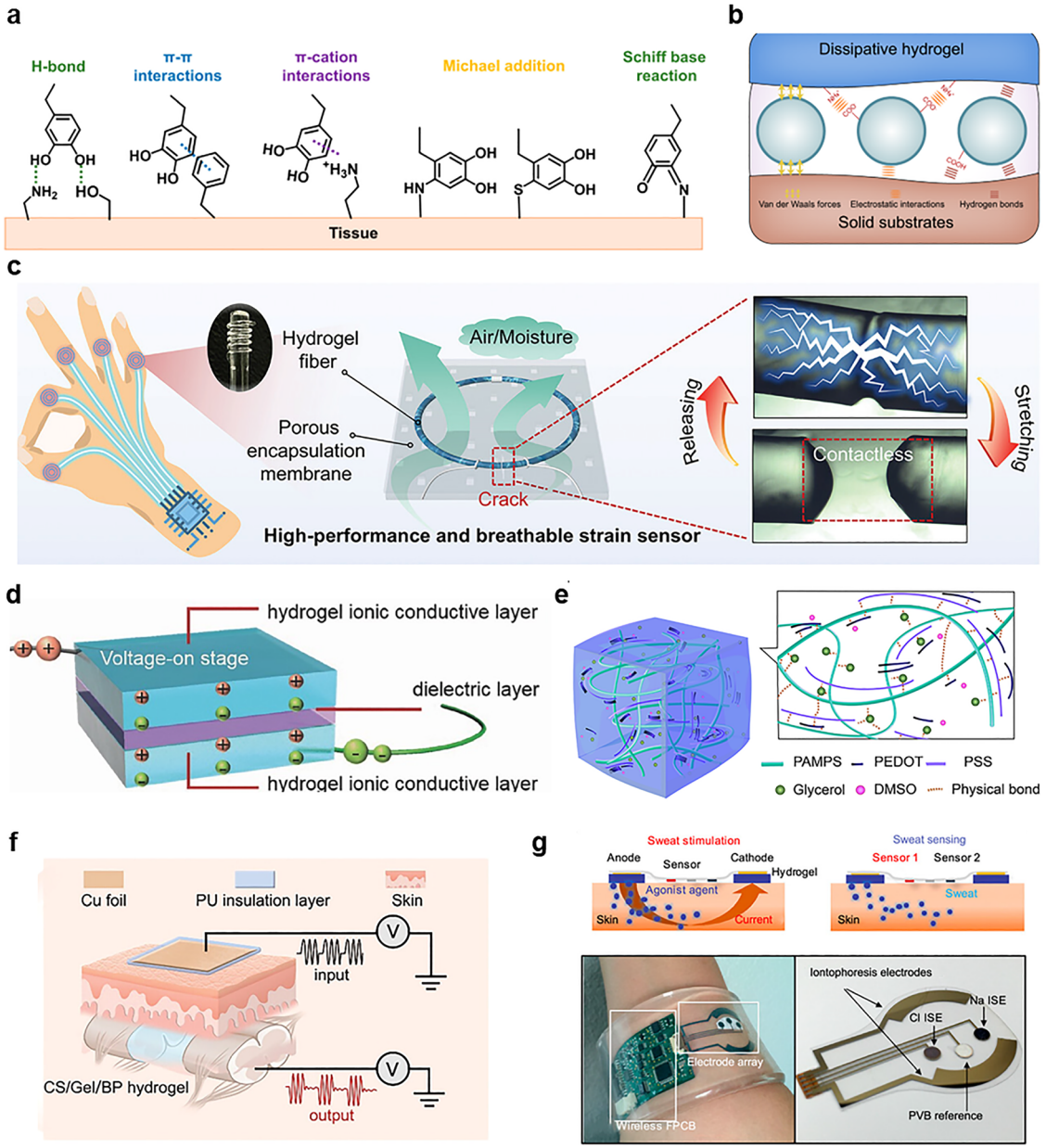

Fig. 1 Hydrogel as a functional interface for multimodal integration. (a) Interactions of the catechol group with biological tissue surfaces.[54] Reproduced from ref. 54 under a CC-BY 4.0 license. (b) Dissipative hydrogel adhesion, in which van der Waals forces, electrostatic interactions, and hydrogen bonds combine to achieve strong attachment on solid substrates.[55] Reproduced from ref. 55 under a CC-BY 4.0 license. (c) Schematic illustration of a high-performance breathable hydrogel strain sensor.[51] Reproduced from ref. 51 with permission from John Wiley and Sons, copyright 2024. (d) Hydrogel ionic conductive layers incorporated into capacitive structures, enabling strain- or motion-induced electrical readouts.[56] Reproduced from ref. 56 with permission from John Wiley and Sons, copyright 2017. (e) Hydrogel networks of an injectable, spontaneously crosslinking hydrogel electrode for EEG applications.[57,58] Reproduced with permission from our previous study reported in ref. 57 copyright 2024. (f) Schematics of wireless electrical stimulation based on conductive and biodegradable hydrogels for spinal cord repair.[59] Reproduced from ref. 59 with permission from John Wiley and Sons, copyright 2024. (g) A schematic illustration and optical image showing the strategy for stimulating sweat release by iontophoresis and for electrochemical analysis of its chemical composition.[60] Reproduced from ref. 60 under a CC-BY-NC 4.0 license.

bioadhesive hydrogel networks.[44,45] For instance, Stalin *et al.* reported a polydopamine-functionalized polyacrylic acid hydrogel that combined exceptional stretchability (2000%) with robust tissue adhesion (85 kPa) while retaining high electrical conductivity.[39] Beyond catechol chemistry, charged polymer networks also contribute to adhesion by forming hydrogen bonds and electrostatic interactions with the skin interface. Building on this principle, Zhao and co-workers designed a nano-adhesive hydrogel that accumulates adhesion energy from nanoscale physical interactions. The resulting adhesion was comparable to covalent bonding and to glass-like cyanoacrylate layers[46] (Fig. 1b). Breathability represents another crucial consideration for comfort and long-term wearability.[47,48] Hydrogels with a porous or micro-structure allow perspiration and water vapor to diffuse outward, mitigating the risk of skin maceration. Some strategies employ natural scaffolds such as gelatin or cellulose to reproduce fabric-like breathability.[49,50] More recently, high-performance breathable hydrogel strain sensors have been demonstrated by integrating crack-engineered hydrogel fibers encapsulated within porous elastomer membranes.[51] This design offered remarkable sensitivity (gauge factor up to 3930), broad detection range (0.02–80%), excellent cycling stability, and structural robustness (Fig. 1c). Other approaches rely on patterned thin films or pore arrays to finely balance moisture retention with gas permeability, ensuring a healthy skin interface during extended usage.[52] Ultimately, conformal hydrogel–skin integration results in superior signal quality. For instance, an injectable hydrogel-based ''electronic tattoo'' electrode maintained interfacial impedance below 40 kΩ cm^2 for more than 20 hours, enabling high-SNR EEG recordings even on hairy regions.[53] More broadly, applications ranging from ECG and EMG monitoring to continuous biochemical sensing benefit from hydrogel electrodes that adhere gently, remain breathable, and adapt dynamically to body movements.

2.2. Dual roles: hydrogel as both a sensor and modulator

Hydrogels can serve dually as sensing platforms and as media for actuation or modulation in biomedical systems.[61] Their intrinsic softness, high water content, and ionic/electronic conductivity allow them to function as tissue-like electrodes.[62,63] In the sensing mode, hydrogels readily transduce mechanical or physiological inputs into electrical outputs.[64,65] For example, ionic hydrogels alter resistance under stretching or compression, thereby enabling piezoresistive readouts.[66,67] This principle has been widely applied in the design of ''artificial skin'' sensors capable of detecting subtle strain or pressure changes through resistance or capacitance modulation, mimicking the tactile acuity of human skin.[56] Such conformal hydrogel-based strain sensors adhere securely to the body and provide stable, real-time electrical tracking of motion, making them attractive for wearable monitoring[68] (Fig. 1d). Beyond strain detection, hydrogels are increasingly tailored for bioelectrical recording.[69] Our group recently reported an injectable, spontaneously crosslinking hydrogel electrode designed for EEG applications. These electrodes maintained a low interfacial impedance of 17.53 kΩ on hairy skin regions, enabling stable recordings for over eight hours. The hydrogel electrodes also exhibited an improved SNR of 23.97 dB compared with commercial wet electrodes. In multichannel studies, the electrodes enabled sleep-stage classification that closely matched clinical scoring, underscoring their potential in continuous electrophysiological monitoring[57,58] (Fig. 1e). Conductive hydrogel electrodes combine biocompatibility and ionic conductivity, allowing them not only to sense but also to deliver electrical cues[59,70] (Fig. 1f). For instance, PEDOT:PSS-based hydrogels have been utilized to both record neural signals and deliver targeted stimulation, surpassing conventional rigid electrodes in conformal contact and charge injection capacity.[71,72] In our earlier work, we developed a PEDOT:PSS-based hydrogel electrode that maintained low impedance for 29 days, outperforming traditional electrodes.[73] Incorporated into a wireless single-channel EEG device, this hydrogel reliably captured α-rhythm modulation between eyes-open and eyes-closed states. More importantly, we demonstrated its feasibility in an online brain computer interface system for functional electrical stimulation, illustrating its promise for post-stroke rehabilitation.[73] Integration of sensing and actuation within a single hydrogel platform further broadens therapeutic opportunities. For instance, multifunctional hydrogel patches have been explored that simultaneously house biosensors (*e.g.*, sweat analyte detectors) and actuators (*e.g.*, heating modules or stimulation electrodes)[60,74] (Fig. 1g). Such architectures pave the way for closed-loop therapies such as hydrogel patch that detects aberrant neural signatures associated with pain and immediately delivers localized stimulation to counteract it.

2.3. Responsive behaviors enabling adaptive interfaces

One of the most distinctive attributes of hydrogels is their capacity to undergo property changes in response to environmental cues, thereby creating adaptive biointerfaces.[75] Depending on molecular design, hydrogel networks can react to stimuli such as humidity,[76,77] pH,[78,79] temperature,[80–82] light,[83–85] or specific biochemical signals.[86,87] For wearable electronics, this means the interface can sense external variations and adapt accordingly, maintaining stability while providing real-time feedback.[88] Although hydrogels inherently store large amounts of water, uncontrolled swelling or dehydration often compromises functionality.[89] To mitigate this, humectants such as polyols or salts have been incorporated to slow evaporation and stabilize hydration levels.[90,91] A representative strategy was introduced by Wang *et al.*, who designed a lipid-integrated bilayer coating (ALIBC). In this system, lipid assemblies and amphiphilic molecules anchored to the hydrogel surface replicate the protective architecture of cellular membranes, while excess lipids trapped in the hydrogel interior migrate to the surface under stress, forming a dynamic barrier against water loss[92] (Fig. 2a). Unlike hydration, temperature-triggered changes allow on-demand adaptability. Polymers such as poly(*N*-isopropylacrylamide) display lower critical solution temperature (LCST) transitions, where the hydrogel shifts from swollen to collapsed states upon heating[93] (Fig. 2b). This feature has been

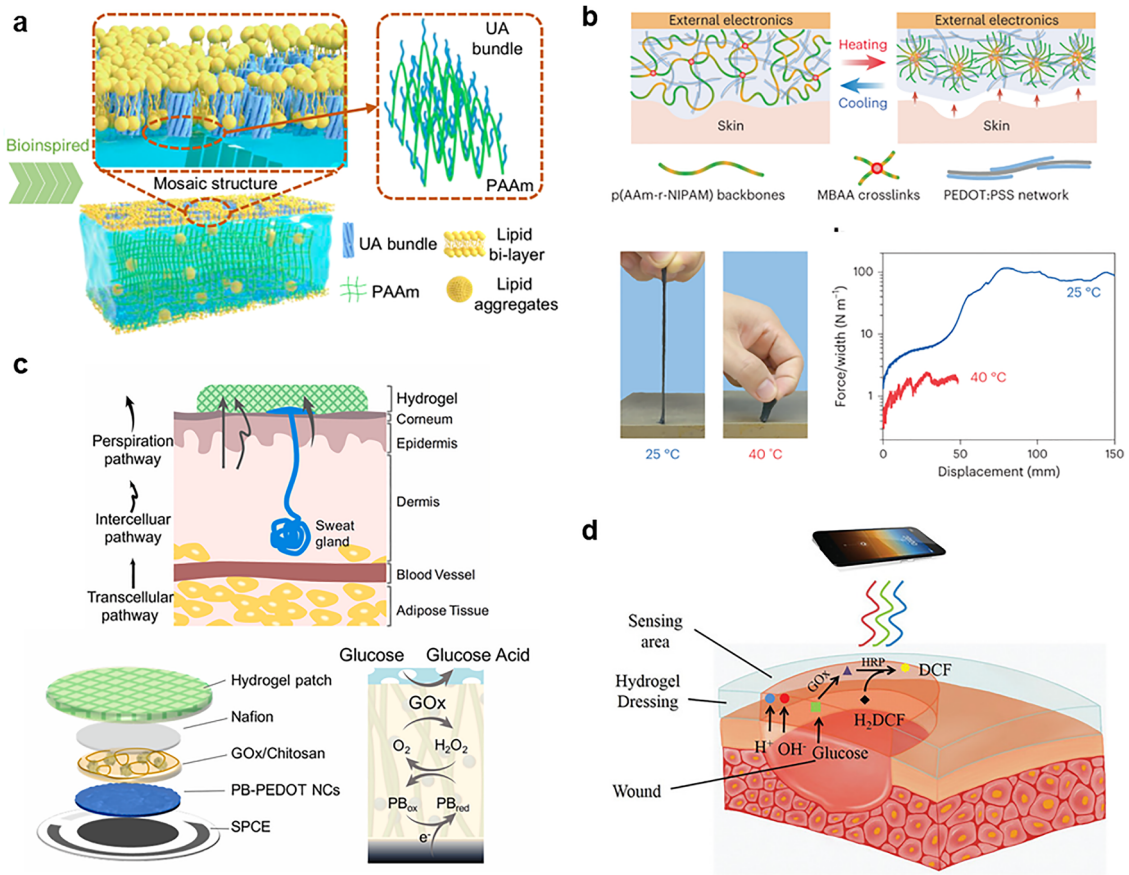

Fig. 2 Responsive behaviors of hydrogels for adaptive interfaces. (a) Schematic illustration of the adaptive lipid-integrated bilayer coating (ALIBC) for hydrogel and internal lipid aggregates.[92] Reproduced from ref. 92 under a CC-BY 4.0 license. (b) Schematic diagram illustrating structural changes of the hydrogel during LCST phase transition, and its photographs and 180° peeling test.[93] Reproduced from ref. 93 with permission from Springer Nature, copyright 2022. (c) Schematic of the design, mechanism and usage of the natural sweat sampling glucose sensor.[95] Reproduced from ref. 95 with permission from Elsevier, copyright 2022. (d) Schematic of the PCB hydrogel dressing for the detection of the pH value and glucose concentration in wound exudate.[96] Reproduced from ref. 96 with permission from John Wiley and Sons, copyright 2019.

used to develop stimuli-controlled adhesives such as a conductive gelatin hydrogel that softens and liquefies under mild warming conditions, enabling painless detachment from the skin.[94] Such "thermal release" designs are particularly attractive for long-term patches, minimizing irritation. Conversely, cooling-sensitive systems help retain elasticity in hot environments, while others function as thermosensitive dressings that constrict when wound temperature rises, signaling infection. Hydrogels containing ionizable moieties can alter swelling, permeability, or conductivity in response to ionic or pH fluctuations, thereby reporting local chemical states. For instance, Lin and collaborators designed a noninvasive sweat-glucose patch where metabolites diffuse into the hydrogel and are enzymatically converted by glucose oxidase (GOx), producing hydrogen peroxide that is electrochemically detected (Fig. 2c). This enabled continuous glucose tracking across multiple skin sites. In another study, Zhang *et al.* engineered a zwitterionic poly(carboxybetaine)-based hydrogel dressing encapsulating pH indicator dye (phenol red) and dual enzyme reporters (GOx and horseradish peroxidase). By capturing smartphone-acquired images and converting them into RGB values, this system successfully monitored wound pH (4–8) and glucose concentrations (0.1–10 mM), providing real-time assessment of diabetic wound healing (Fig. 2d). Such biochemical feedback transforms hydrogels into intelligent diagnostic patches. Hydrogels can also be programmed to mimic tissue-like strain-stiffening: soft and compliant under low loads but progressively stiffer under high deformation, preventing catastrophic rupture. Moreover, incorporating dynamic reversible bonds allows autonomous healing after damage, extending durability during repeated use. Zhang and colleagues reported a rigid self-healing hydrogel with modulus ~50 MPa and tensile strength up to 4.2 MPa, achieved by polymerizing monomers within an oriented lithium montmorillonite nanosheet scaffold. Despite high stiffness, the gel retained impressive self-repair, recovering ~33% of ultimate tensile strength in end-to-end tests and nearly 100% in side-by-side configurations. This juxtaposition of stiffness and reparability illustrates how nanoscale confinement and dynamic bonding can coexist in one system. Some hydrogels even display piezoelectric or mechanoluminescent behavior, converting deformation into electrical or optical signals. Such features could support self-reporting and self-calibrating interfaces. A hydrogel "smart bandage" for instance, may tighten under perspiration to

improve adhesion yet relax when dry to facilitate removal. Similarly, hydrogel strain sensors may auto-correct baseline drift during prolonged use. Overall, responsive hydrogels transform static material–tissue junctions into dynamic, living-like interfaces. Through hydration control, thermal switching, biochemical sensing, and mechanical adaptability, these materials enable self-adjusting platforms that bring bioelectronics closer to the adaptive behavior of natural skin.

2.4. Advantages over traditional materials: stretchability, breathability, ionic conduction, and biointerface compatibility

To facilitate a clearer comparison between hydrogels and conventional biointerface materials, the key mechanical and interfacial properties are summarized in Table 1. Compared to conventional metals, elastomers, and rigid polymers, hydrogels offer an array of advantages for biointerfaces. First, stretchability and mechanical compliance: most hydrogels can tolerate several hundred percent strain without failure.[66,97] Some ultra-tough hydrogels (double-network or nanocomposite gels) even reach 1000–2000% stretch before fracturing.[98] This far exceeds human skin, so hydrogel sensors can conform to joints and muscles in motion without peeling off or breaking.[99,100] In contrast, metals or brittle semiconductors crack easily under bending. Second, breathability and permeability: hydrogels are intrinsically porous and water-rich, allowing oxygen and small molecules (*e.g.* sweat and gases) to diffuse through.[101] This makes them comfortable for long-term wear, as the skin can still "breathe".[102] Pores can be tuned to mimic cotton-like breathability. By contrast, films of rubber or plastic can occlude the skin, causing irritation and sweat accumulation.[103,104] Third, unlike electronic conductors, hydrogels can conduct ions, which is the natural signaling medium in biology.[70] This ionic conduction yields low electrode–tissue impedance and high-quality signal transduction.[105] A conductive hydrogel electrode seamlessly records bioelectric potentials with reduced interfacial noise.[106] Furthermore, hydrogels can incorporate mobile ions for energy generation (*e.g.* tribo/piezoelectric generators that use ion transport) or storage (hydrogel batteries and supercapacitors).[107] Fourth, the water content and softness of hydrogels greatly reduce the foreign-body response. They are generally non-toxic and can be sterilized, making them safe for skin contact or even internal use.[108] Unlike metals, which may corrode or cause inflammation, hydrogels cause minimal immune reactions (often comparable to silicone). They can also promote natural processes – for example, cell-laden hydrogels encourage tissue regeneration in wound healing dressings.[109] In neural or cardiac implants, hydrogel coatings can buffer electrical mismatches and promote electrode–tissue coupling.[110] Finally, hydrogels are highly tunable and multifunctional. Through the choice of polymer chemistry and additives, one can tailor conductivity (electronic or ionic), optical clarity, magnetic response, or even add biochemical sensitivity.[111,112] Nanofillers (graphene, nanocellulose, and silver nanowires) can be dispersed for improved mechanical or electrical performance.[113–115] Hybrid hydrogel–elastomer composites combine the best of both worlds. Emerging manufacturing processes (3D printing and laser cutting) allow complex hydrogel architectures (microchannels and gradient stiffness) to be realized.[116–118] In summary, hydrogels transcend traditional materials in applications that demand softness, conformality, and interface with biology.

3. System-level integration: monitoring and modulation in one platform

3.1. Brain state detection and neuromodulation

A central goal in neurotechnology is to achieve simultaneous brain monitoring and therapeutic modulation in a single, non-invasive platform.[119] Electroencephalography (EEG) provides continuous, real-time access to cortical dynamics, capturing pathological events such as epileptic seizures or abnormal oscillations.[120] In parallel, focused ultrasound (FUS) offers a means to deliver targeted neuromodulation deep into neural tissue without the need for surgical intervention.[121,122] Integrating these two modalities opens the possibility for closed-loop neurotherapies, for example, detecting pathological EEG activity and immediately applying FUS to regulate neural circuits. Hydrogels play a pivotal role in enabling such integration. Their high-water content and mechanical softness improve the interfaces for both EEG and FUS.[46] Conventional EEG electrodes often rely on wet conductive gels to lower skin impedance, but these can dry out, irritate skin, and degrade over time.[123] In contrast, hydrogel electrodes provide a stable, biocompatible alternative: they maintain low interfacial impedance, high conductivity, and gentle yet firm adhesion to skin.[12,124] Their compliance minimizes motion artifacts, preserving EEG fidelity even during concurrent interventions. Table 2 summarizes the system-level functions of hydrogels in neural systems and the corresponding metrics and challenges. Despite these advantages, hair interference remains a major obstacle for

Table 1 Comparison of several key properties between hydrogels and conventional materials (range depends on formulation and protocol)

Material	Elastic modulus	Maximum strain	Interfacial impedance	Air permeability	Long-term stability
Hydrogels	~1–100 kPa	>100–1000%	~0.5–20 kΩ cm^2	High	Moderate, limited by dehydration and swelling
Metals (Au, Ag, Pt)	~10–200 GPa	<1%	~20–200 kΩ cm^2	None	High stability, poor tissue compatibility
Elastomers (PDMS)	~0.1–10 MPa	100–500%	>500 kΩ cm^2	Low	High mechanical stability, limited biointerface quality
Rigid polymers (PI, PET)	~1–5 GPa	<10%	>1 MΩ cm^2	None	High structural stability, poor conformability

Table 2 Neural systems: hydrogel technologies for EEG recording and neuromodulation

Application	Hydrogel strategy	System function	Key metrics	Challenges
Wearable EEG electrodes	Ionic conductive, self-hydrating hydrogels	Low-impedance neural recording	Impedance stability over hours–days	Hair interference, dehydration, and motion artifacts
EEG–FUS coupling	Acoustic-transparent hydrogel	Simultaneous sensing and stimulation	Stable ultrasound transmission	Acoustic–electrical crosstalk
Closed-loop neuromodulation	Adhesive conductive hydrogels	Co-localized sensing and actuation	Real-time signal fidelity	Synchronization and artifact suppression

high-fidelity EEG acquisition, as even sponge-like conductive hydrogel electrodes that partially compress into the irregular topography of hair and scalp often fail to sufficiently reduce contact impedance under realistic conditions.[94,125,126] These challenges point to the necessity of refining electrode materials and architectures. Recently, Wang and colleagues introduced a biocompatible, skin-paintable conductive biogel specifically engineered for EEG recording on a hair-covered scalp. A feature of this material is its thermally reversible phase transition between a viscous fluid and a viscoelastic gel, which imparts excellent spreadability on the skin and *in situ* gelation capability. This unique behavior not only facilitates conformal contact with hairy scalp surfaces but also allows the electrode interface to dynamically adapt to movement, thereby maintaining stable and reliable signal quality over extended periods (Fig. 3a). Our group recently developed a porous, conical 3D soft electrode architecture integrated with an advanced hydrogel formulation composed of glycerol, potassium chloride, and sodium 2-acrylamido-2-methylpropane sulfonate[127] (Fig. 3b). This combined design enables the electrodes to effectively bypass hair layers and establish direct contact with the scalp, while the soft conical geometry ensures low contact pressure for user comfort. At the same time, the hydrogel's ionic conductivity and conformability contribute to maintaining low interfacial impedance, thereby supporting stable, long-duration, and high-quality EEG acquisition.

For FUS applications, acoustic coupling between the transducer and skin is essential.[128] Traditional ultrasound gels are prone to drying, limiting their long-term use. Hydrogels provide an ideal alternative, functioning as stretchable solid coupling layers that maintain hydration and acoustic matching to tissue.[129] Their high-water content minimizes reflection and energy loss, while bioadhesive hydrogel couplants integrate seamlessly with wearable FUS transducer arrays, eliminating air gaps and sustaining skin contact during motion[130,131] (Fig. 3c). For example, Lee and colleagues demonstrated a wearable ultrasonic patch using calcium-modified silk hydrogel as the coupling layer, achieving transmission performance comparable to commercial gels while ensuring reliable adhesion.[132] Similarly, our previous research developed a long-term adhesive hydrogel couplant that maintained $<13\%$ acoustic intensity loss over 35 days, enabling stable neuromodulation[133] (Fig. 3d). Moreover, Son *et al.* introduced a soft morphable cortex-adhesive (SMCA) sensor, which combined a catechol-infused alginate hydrogel layer, a flexible electrode array, and a self-healing polymer substrate[134] (Fig. 3e). This ECoG-like sensor adhered tightly to cortical surfaces and, crucially, maintained stable attachment under ultrasound exposure. Strong hydrogel tissue adhesion suppresses motion artifacts and enables reliable EEG acquisition during transcranial FUS. Using this platform, the authors demonstrated closed-loop epilepsy therapy in rodents: EEG detected early seizure activity in real time, automatically triggering FUS pulses targeted to cortical regions, which promptly aborted seizures. Overall, hydrogel couplants make it feasible to conduct continuous or wearable ultrasound brain stimulation outside controlled laboratory settings. By coupling high-fidelity brain state monitoring with responsive neuromodulation, personalized therapies for epilepsy, Parkinson's disease, depression, and other neurological disorders become achievable. Hydrogel-integrated EEG–FUS remains in its infancy, but rapid advances in soft materials and flexible electronics are accelerating its progress toward clinical reality.[135] Future designs are likely to incorporate multichannel EEG arrays and beamforming ultrasound transducers into flexible caps or even headband-like ''ultrasonic brain–computer interfaces''. Such systems could continuously track neural biomarkers of seizures or affective states and automatically deliver corrective FUS stimulation without clinician intervention.

As reflected in Table 2, hydrogel-enabled EEG–FUS systems consistently rely on three shared design principles: (i) soft, hydrated interfaces for low-impedance electrical coupling, (ii) acoustically transparent and stable coupling layers for ultrasound delivery, and (iii) adhesive or self-hydrating chemistries that preserve interface integrity during motion and prolonged operation. Despite these advances, several technical bottlenecks continue to limit real-time EEG–FUS integration. Motion-induced artifacts, hydration-dependent signal drift, and acoustic–electrical crosstalk remain significant challenges during simultaneous recording and stimulation. Moreover, precise temporal synchronization among neural state detection, signal processing, and ultrasound actuation is difficult to achieve in fully wearable and wireless implementations. Addressing these challenges will be essential for translating hydrogel-enabled EEG–FUS platforms from experimental demonstrations toward robust, closed-loop neurotherapeutic systems.

3.2. Gastrointestinal monitoring and stimulation

The gastrointestinal (GI) tract plays a central role in digestion, nutrient absorption, and systemic health.[136,137] Disorders such as motility dysfunction, anastomotic leakage, and post-operative

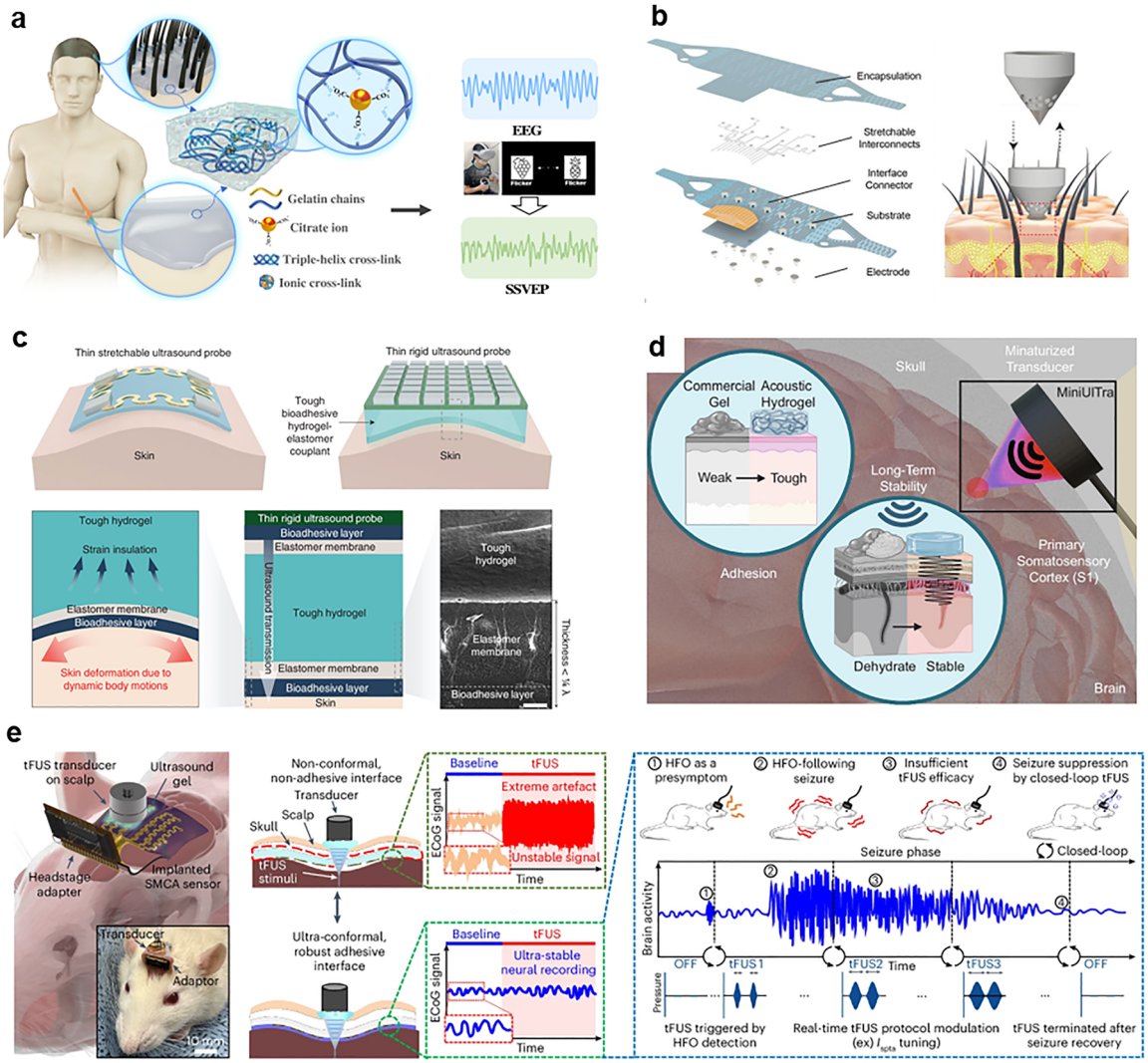

Fig. 3 Integration of hydrogel interfaces enabling simultaneous brain monitoring and modulation. (a) Schematic illustration showing the concept of an on-skin paintable biogel for hairy scalps for EEG recording.[94] Reproduced from ref. 94 under a CC-BY-NC 4.0 license. (b) Detailed view of the MindStretcH system with porous conical 3D electrodes integrated with a GKAmp hydrogel for hair penetration and stable scalp contact.[127] Reproduced with permission from our previous work ref. 127 copyright 2025. (c) Design and imaging performances of the bioadhesive ultrasound (BAUS) device.[131] Reproduced from ref. 131 with permission from The American Association for the Advancement of Science, copyright 2022. (d) Illustration of MiniUlTra that, with the aid of a hydrogel, continuously adheres to the scalp targeting the primary somatosensory cortex, providing strong adhesion, low acoustic attenuation, and a miniaturized transducer.[133] Reproduced with permission from our previous work ref. 133 copyright 2025. (e) SMCA sensor for ultrastable brain interfacing enables closed-loop tFUS neurotherapy.[134] Reproduced from ref. 134 with permission from Springer Nature, copyright 2024.

complications remain difficult to detect and manage in real time.[138] This motivates the development of next-generation technologies for long-term, minimally invasive monitoring and localized therapeutic stimulation. Hydrogels, with their soft mechanics, high water content, and bioadhesive properties, are emerging as enabling materials in this domain.[138,139] A key challenge for ingestible devices is retaining functionality in the dynamic stomach environment.[140] Traditional capsules transit rapidly and cannot support chronic monitoring.[141] To overcome this, Zhao and colleagues demonstrated a swallowable hydrogel capsule that expanded to gastric dimensions within an hour and remained intact for nearly a month[142] (Fig. 4a). Beyond temperature sensing and drug release, such platforms could be adapted to host miniature sensors for pH, pressure, motility, gas, or electrolytes.[142] Beyond gastric-retentive designs that primarily address residence time, recent work has demonstrated the feasibility of long-term, active gastrointestinal systems enabled by electroadhesive hydrogel interfaces. For example, Ying *et al.* reported a hydrogel-based electroadhesive platform capable of stable attachment to gastrointestinal tissue while supporting wireless operation over extended periods.[143] This system illustrates how hydrogel interfaces can simultaneously provide mechanical anchoring, electrical functionality, and compatibility with wireless power transfer and communication modules. By enabling stable tissue coupling without rigid fixation, such designs address key challenges for chronic gastrointestinal

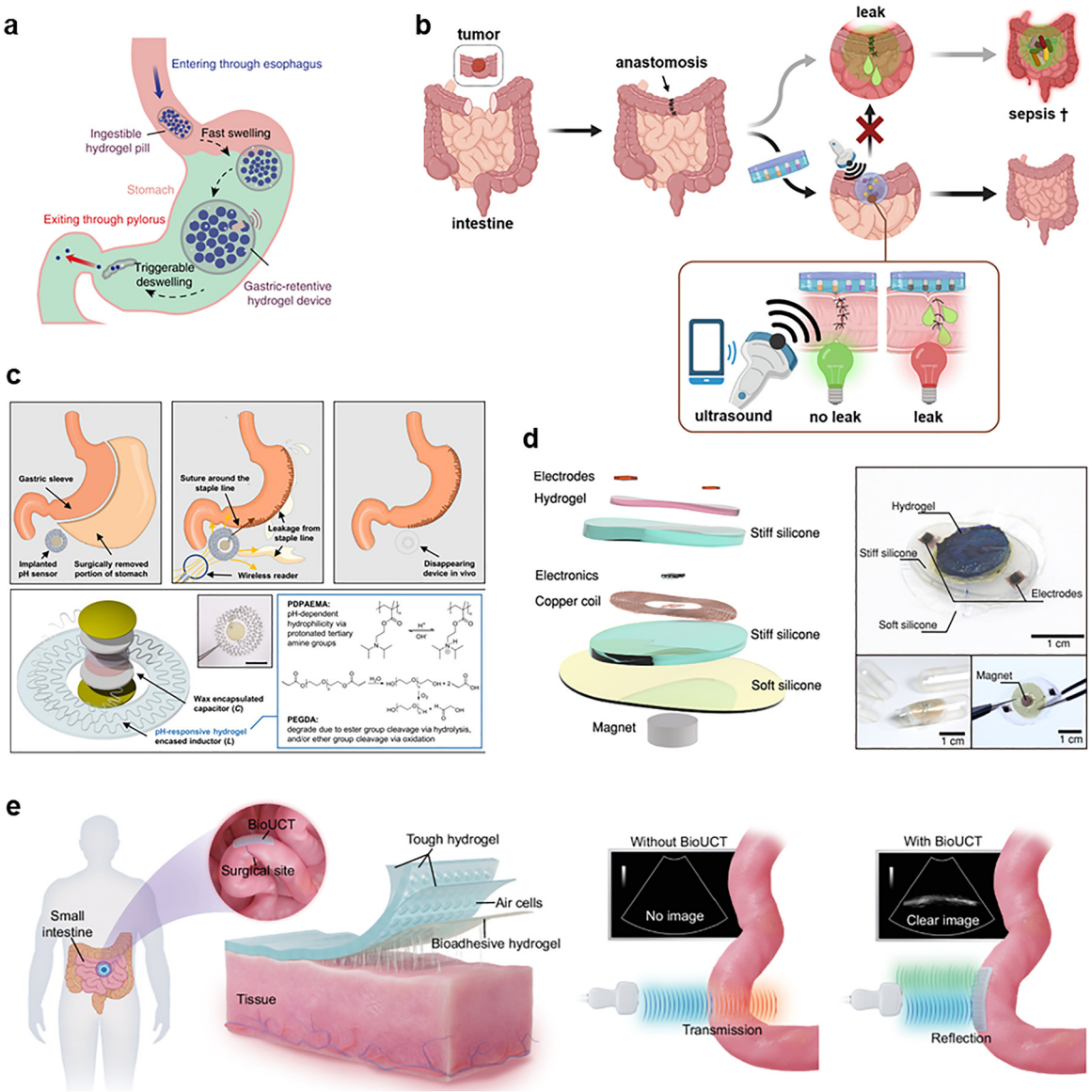

Fig. 4 Hydrogel-enabled gastrointestinal monitoring and stimulation. (a) An ingestible hydrogel capsule that rapidly swells in the stomach for gastric retention and long-term monitoring.[142] Reproduced from ref. 142 under a CC-BY 4.0 license. (b) A hydrogel sealing and sensing patch for surgical anastomosis: the layered structure combines adhesion, leak sealing, and ultrasound-detectable responses to digestive fluids.[145] Reproduced from ref. 145 under a CC-BY 4.0 license. (c) A bioresorbable wireless sensor with a pH-responsive hydrogel transduction layer for real-time leakage detection *via* inductive-capacitive coupling.[146] Reproduced from ref. 146 under a CC-BY 4.0 license. (d) Ingestible robotic interface (IngRI) incorporating hydrogel–elastomer hybrid adhesion and wireless magnetic guidance for localized gastric stimulation.[149] Reproduced from ref. 149 under a CC-BY 4.0 license. (e) Biodegradable ultrasonic contrast tape (BioUCT) consisting of a tough hydrogel with embedded microbubbles and a bioadhesive backing, enabling high-contrast ultrasound imaging of intestinal motility, which naturally degrades over time.[150] Reproduced from ref. 150 under a CC-BY 4.0 license.

monitoring and stimulation. Surgical reconnection of the GI tract is lifesaving, yet leaks occur in ~10% of cases, often with severe outcomes.[144] To address this, Alexandre *et al.* designed a layered hydrogel patch that combines sealing with real-time sensing of leakage[145] (Fig. 4b). The construct integrates non-adhesive backings, bioadhesive support layers, and enzyme- or pH-responsive sensing modules. When exposed to digestive fluids, the hydrogel undergoes structural and acoustic changes detectable by ultrasound, while simultaneously reinforcing the surgical site. This dual-function patch illustrates how hydrogels can both secure anastomoses and provide early-warning signals of leakage. Complementing patch-based designs, Rogers and colleagues developed a bioresorbable wireless sensor that monitors local pH changes to detect gastric leakage[146] (Fig. 4c). Here, a pH-responsive hydrogel serves as the transduction element, coupled to an optimized inductive-capacitive circuit for wireless readout. In preclinical models, the system achieved rapid (<1 h) and reliable detection of simulated gastric leaks, with stable performance for up to seven days. The bioresorbable nature of the platform eliminates the need for device retrieval,

making it attractive for post-surgical monitoring. While monitoring is critical, therapeutic modulation is equally important. For example, Traverso and colleagues introduced an ingestible, battery-free robotic interface (IngRI) designed for chronic gastric stimulation (Fig. 4d). IngRI consists of lithographically defined thin-film circuits embedded in an elastomer substrate that conformally adhere to the gastric mucosa after release from a capsule. A hydrogel–elastomer hybrid layer ensures tissue retention for at least 48 hours, while wireless magnetic guidance allows precise positioning. The device can deliver programmable electrical pulses wirelessly through near-field inductive coupling. Hydrogels have also been explored for intestinal imaging and motility assessment. Post-surgical complications such as dysmotility or obstruction require repeated imaging.[147] Standard modalities (MRI, CT) provide resolution but are costly and impractical for continuous monitoring, while ultrasound is limited by poor soft-tissue contrast.[148] To overcome this, Zang developed a biodegradable ultrasonic contrast tape (BioUCT), which comprises an ultrathin acoustic hydrogel layer with embedded microbubbles, adhered to the intestinal surface by a bioadhesive hydrogel backing[149] (Fig. 4e). The unique design provides strong ultrasound reflectivity ($>90\%$), enabling high-contrast intestinal imaging for two weeks and it degraded naturally within 12 weeks in pigs. This approach allows non-invasive, longitudinal monitoring of bowel motility after resection. Overall, these advances underscore the versatility of hydrogels as active, multifunctional interfaces that combine chronic residence, physiological monitoring, leakage detection, and therapeutic modulation. Moving forward, their integration with flexible electronics and wireless communication is expected to yield closed-loop systems capable of detecting pathological events and delivering timely interventions, ultimately transforming the management of gastrointestinal disorders.[143]

In summary, the diverse gastrointestinal systems discussed above illustrate that hydrogel-enabled platforms operate under fundamentally different mechanical and chemical constraints depending on their intended mode of deployment. Representative gastrointestinal system types, design constraints, hydrogel roles, key performance metrics, and translational considerations are summarized in Table 3. Swallowable, gastric-retentive hydrogels are primarily designed to undergo controlled shape transformation or expansion to ensure prolonged residence, imposing stringent requirements on mechanical robustness, elasticity, and resistance to gastric motility and highly acidic environments. In contrast, adhesive or sealing hydrogel patches prioritize strong yet reversible wet adhesion, rapid deployment, and compatibility with dynamic mucosal surfaces, often favoring localized interfacial stability over extended residence time. Bioresorbable hydrogel sensors and biodegradable ultrasonic contrast tapes are governed by an entirely different design logic, in which predictable degradation kinetics, transient functionality, and minimal long-term tissue interaction are paramount. Recognizing these distinct design regimes is essential for contextualizing material selection and performance metrics across GI applications. Importantly, it underscores why no single hydrogel formulation can satisfy all operational requirements within the gastrointestinal tract, highlighting the need for application-specific, system-level co-design strategies.

3.3. Cardiac health management

Cardiovascular disease remains the leading cause of mortality worldwide, and technologies that combine continuous monitoring with therapeutic intervention are urgently needed.[151,152] Traditional rigid electrodes and pacemakers provide valuable functions but often suffer from poor tissue integration, mechanical mismatch, and risks associated with long-term implantation.[135] Hydrogels, due to their softness, conductivity, and bioadhesive capabilities, are increasingly recognized as key enablers for next-generation cardiac bioelectronics.[153,154] On the monitoring side, Deng and colleagues reported an electro-bioadhesive (e-bioadhesive) interface that rapidly integrates bioelectronic devices with wet and dynamic tissues[155] (Fig. 5a). By introducing graphene oxide into a poly(vinyl alcohol) hydrogel and interpenetrating it with NHS-functionalized poly(acrylic acid), they created a thin graphene nanocomposite hydrogel that swells anisotropically upon hydration, removing surface water and forming robust adhesion within seconds. This interface enabled stable epicardial ECG recordings in beating rat hearts for more than two weeks without arrhythmic side effects, demonstrating strong bioelectronic compatibility.[155] In contrast, Li *et al.* developed a complementary approach with a conformal adhesive hydrogel patch (CAHP) composed of functionalized polyaniline and PVA[156] (Fig. 5b). This patch adhered directionally to curved epicardial tissue, resisted nonspecific attachment, and supported both electrophysiological monitoring and synchronized electrotherapy in infarcted rat hearts. Such dual-function devices illustrate how hydrogel–polymer hybrids can unify diagnosis and treatment within one

Table 3 Gastrointestinal systems: hydrogel platforms under diverse constraints

System type	Design constraints	Hydrogel role	Key metrics	Translational considerations
Swallowable gastric-retentive devices	Acidic environment, peristalsis	Mechanical anchoring and sensing	Residence time, mechanical robustness	Size control, safety
Adhesive/electroadhesive patches	Wet, dynamic mucosa	Stable tissue attachment	Adhesion durability	Reversibility, mucosal safety
Bioresorbable sensors and tapes	Transient operation	Temporary sensing/contrast	Degradation kinetics	Predictable clearance
Wireless GI systems	Power and communication integration	Interface and system coupling	Wireless stability	Encapsulation and longevity

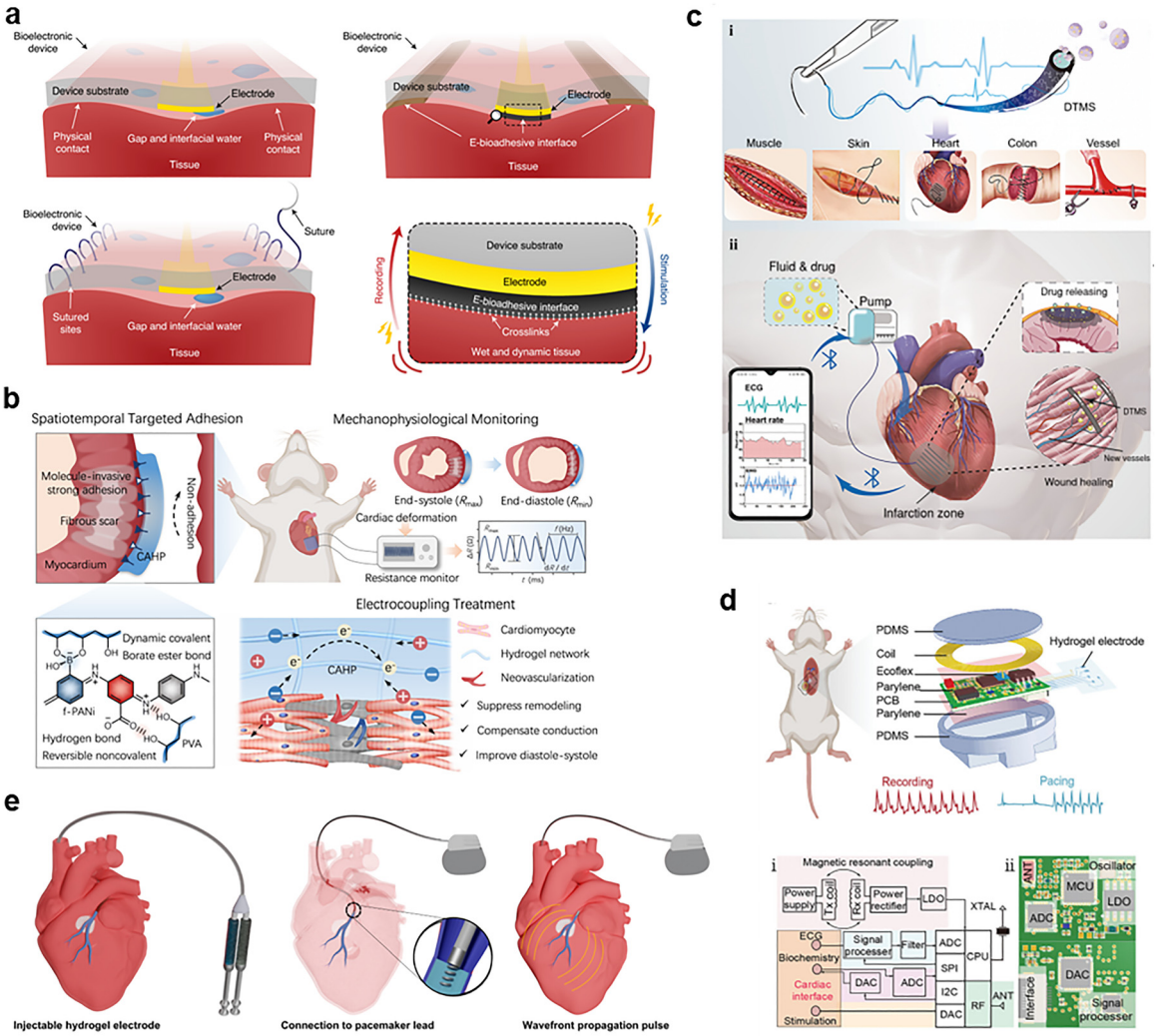

Fig. 5 Hydrogel-enabled cardiac health management. (a) Electro-bioadhesive (e-bioadhesive) interface integrating a graphene oxide PVA–PAA hydrogel with bioelectronic devices for rapid adhesion to wet beating tissue and stable epicardial ECG recording.[155] Reproduced from ref. 155 with permission from Springer Nature, copyright 2020. (b) Conformal adhesive hydrogel patch (CAHP) composed of polyaniline and PVA, achieving directional adhesion to epicardial tissue, enabling electrophysiological monitoring and synchronized electrotherapy.[156] Reproduced from ref. 156 under a CC-BY 4.0 license. (c) Diagnostic–therapeutic–monitoring suture (DTMS) constructed from a multifunctional hydrogel with conductive and drug-delivery microchannels, supporting wound closure, sensing, and localized therapy.[157] Reproduced from ref. 157 under a CC-BY 4.0 license. (d) A wireless stretchable pacing device (WSPD) incorporating conductive hydrogel electrodes with wireless power, pacing, and real-time sensing modules for closed-loop cardiac monitoring and stimulation.[159] Reproduced from ref. 159 under a CC-BY 4.0 license. (e) Injectable hydrogel electrodes filling venous pathways to form flexible, conductive conduction channels for multipoint myocardial activation, enabling uniform pacing and low-energy termination of arrhythmias.[160] Reproduced from ref. 160 under a CC-BY 4.0 license.

platform.[156] Moving beyond patches, Zeng and co-workers drew inspiration from vascular networks to design multifunctional hydrogel sutures with embedded microchannels and conductive polypyrrole[157] (Fig. 5c). These diagnostic–therapeutic–monitoring sutures (DTMS) not only closed wounds but also provided real-time electrophysiological sensing, programmed drug delivery, and wireless readouts. In preclinical models, DTMS reduced infarct size and preserved cardiac function, underscoring the potential of hydrogel-based sutures to transform cardiac repair strategies. While adhesive hydrogels and sutures focus on surface interfaces, pacing requires robust integration of electrodes within cardiac tissue.[158] Fang and colleagues addressed this by developing a wireless stretchable pacing device (WSPD) that incorporated conductive hydrogel electrodes with high conductivity ($\sim$160 S m^{-1}), elasticity, and long-term adhesion. The device combined four functional modules including wireless power transfer, pacing circuitry, real-time ECG/biochemical sensing, and wireless communication allowing simultaneous pacing and monitoring[159] (Fig. 5d). In animal models, WSPD maintained stable electrochemical performance for more than 31 days, adapting to continuous myocardial contraction. Importantly, its wireless design and hydrogel–tissue integration reduce surgical risks associated with batteries and rigid metals, paving the way for closed-loop pacing systems. Even more transformative, injectable hydrogel electrodes have been developed to reach deep myocardial regions

inaccessible to conventional leads[160] (Fig. 5e). In porcine models, such hydrogels filled coronary venous pathways and converted into flexible conductive electrodes capable of capturing Purkinje fibers and bundle branches. Compared with traditional point pacing, this strategy achieved uniform myocardial activation, minimized conduction delays, and showed potential to terminate reentrant arrhythmias at low energy, approaching a "painless defibrillation" modality. By tailoring hydrogel chemistry (*e.g.*, hydrogels with myocardium-matched stiffness and ionic conductivity), these electrodes established Purkinje-like conduction channels, providing multipoint activation along their length. In summary, these advances illustrate how hydrogels enable a new generation of soft, multifunctional cardiac interfaces that span surface monitoring, therapeutic stimulation, and deep-tissue pacing (Table 4). Across epicardial ECG electrodes, adhesive pacing patches, multifunctional sutures, wireless pacing systems, and injectable conductive hydrogels, hydrogels serve as conformal electrical interfaces that accommodate continuous myocardial motion while maintaining stable signal transduction. Key performance metrics emphasized in cardiac applications include signal stability under dynamic strain, reduced pacing thresholds, and high strain tolerance during repetitive contraction. At the same time, persistent challenges remain, particularly with respect to chronic adhesion durability, long-term mechanical fatigue, and seamless integration with power management and wireless electronics. Addressing these challenges will be essential for translating hydrogel-enabled cardiac bioelectronics toward closed-loop systems capable of simultaneous monitoring, pacing, and therapeutic intervention in real-world clinical settings.

3.4. Hybrid systems enabling closed-loop feedback control

Hybrid systems combining monitoring and modulation are paving the way for next-generation bioelectronic medicine, offering real-time, personalized interventions.[161,162] Hydrogels are central to these systems due to their ability to integrate multiple functional components, such as sensors, electrodes, and drug depots, into a single biocompatible matrix.[163] Recent advances in closed-loop systems across various organ systems demonstrate the power of hydrogel-based electronics for intelligent feedback control.[63,124,164] Shin and colleagues developed an injectable tissue–interface conduit (IT-IC) hydrogel using a phenylboronic acid–mediated multi-crosslinking strategy[165] (Fig. 6a). The design combined irreversible biphenyl bonds for structural stability, reversible coordination between PB groups and conductive gold nanoparticles, and weaker multivalent ionic interactions within the polysaccharide backbone. This hierarchical bonding allowed the hydrogel to dissipate stress during injection and rapidly recover afterward, providing resilience and self-healing superior to conventional covalent gels. In preclinical demonstrations, the IT-IC hydrogel restored muscle continuity, supported regeneration, and mediated bidirectional communication with nearby nerves, thereby integrating into closed-loop robotic rehabilitation systems where EMG signals could trigger neural stimulation and *vice versa*.[165] Moreover, Qu *et al.* developed HydroElex, a hydrogel-based neuroelectronic implant for closed-loop seizure treatment[164] (Fig. 6b). This device continuously monitors brain activity, and upon detecting pathological patterns predictive of a seizure triggers an electrical bias that causes the hydrogel electrodes to release an anti-epileptic drug at the seizure focus. This integration of electrical sensing and pharmacological release enables real-time, precise intervention, reducing systemic side effects compared to continuous drug administration. Closed-loop systems are also making strides in other physiological areas. Jiang *et al.* introduced a wireless smart bandage with hydrogel electrodes to monitor wound conditions and deliver on-demand microcurrent stimulation to promote healing[93] (Fig. 6c). This system significantly accelerated wound closure in mice, demonstrating the effectiveness of hydrogel-based closed-loop systems in non-neural applications. In addition, hybrid systems for diabetes management and respiratory aids are being developed, such as glucose-sensing patches combined with insulin microinfusion systems and neuromuscular stimulation for maintaining airway patency. Building these hybrid systems involves integrating multiple components: sensors (electrical, chemical, optical), actuators (electrical stimulation, drug delivery), control units (often AI-driven), and power/communication modules. Hydrogels simplify this architecture by serving as both sensing and actuating elements, as demonstrated in examples like HydroElex and the smart bandage. Recent studies also show the integration of AI in closed-loop systems. For example, Kim developed a Brain-AI Closed-Loop platform where EEG data was wirelessly transmitted to an AI system, which adapted machine behavior based on detected brain potentials[166] (Fig. 6d). This concept is being explored for medical applications, where onboard microcontrollers with AI models could predict events like seizures or arrhythmias and intervene preemptively, reducing reliance on manual or open-loop systems. For clinical adoption, closed-loop hybrid systems must ensure safety, reliability, and ease of use. They must function autonomously, with minimal user input and long-term stability. The ongoing progress in multi-modal materials, flexible power sources, and AI integration suggests these systems will be able to provide personalized care, transforming patient treatment.

Table 4 Cardiac systems: hydrogel interfaces for monitoring and modulation

Application	Hydrogel design	Functional role	Performance metrics	Challenges
Epicardial electrodes	Soft conductive hydrogels	Conformal electrical interface	Signal stability under motion	Mechanical mismatch
Hydrogel pacing patches	Adhesive, conductive networks	Electrical stimulation	Reduced pacing threshold	Long-term durability
Multifunctional cardiac patches	Stretchable hydrogel composites	Sensing and actuation	High strain tolerance	Integration with electronics

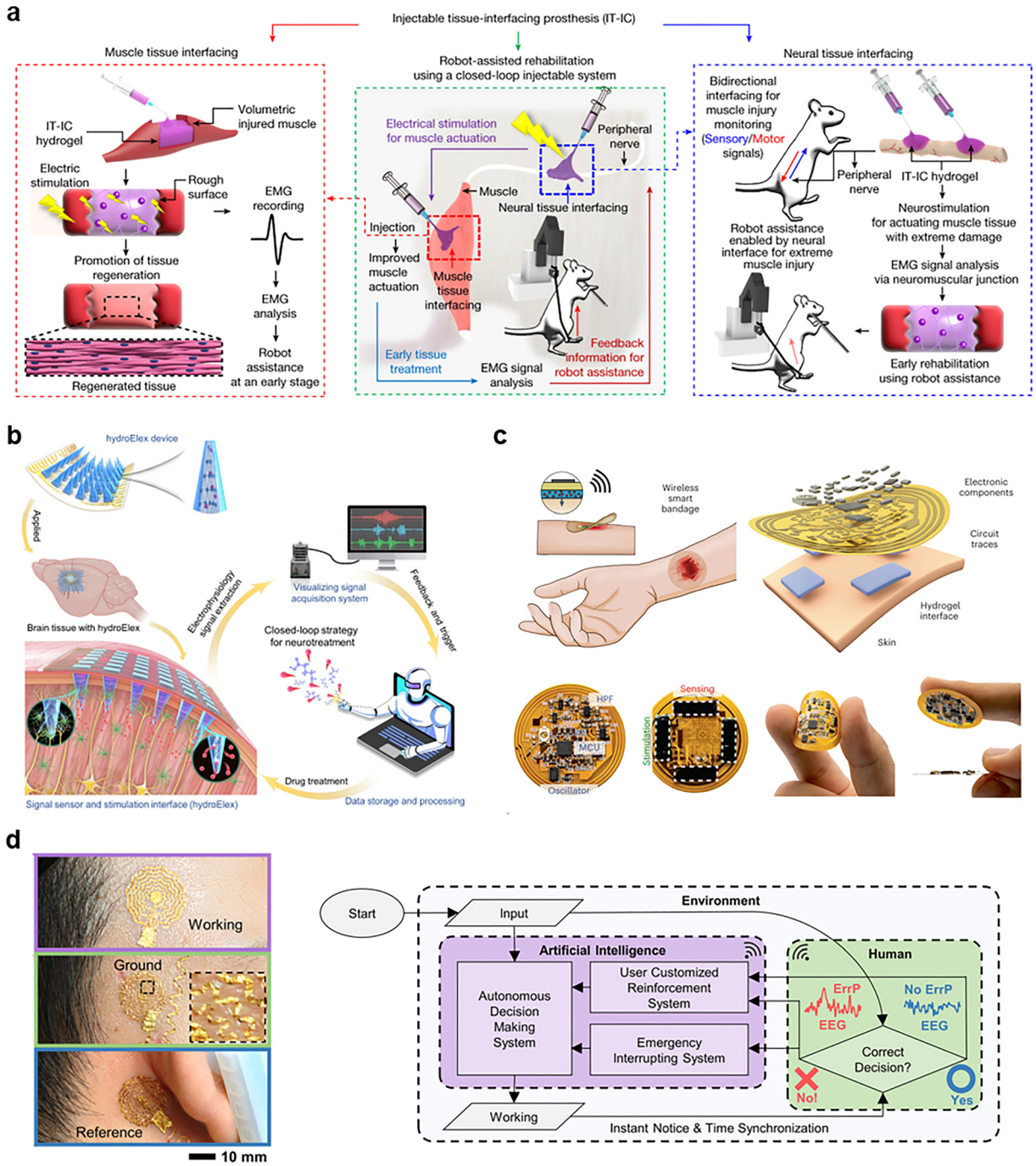

Fig. 6 Hybrid hydrogel-based systems enabling closed-loop feedback control. (a) An injectable tissue–interface conduit (IT-IC) hydrogel supporting muscle regeneration, EMG recording, and bidirectional nerve interfacing for robot-assisted rehabilitation.[165] Reproduced from ref. 165 with permission from Springer Nature, copyright 2023. (b) A HydroElex neuroelectronic implant integrating hydrogel electrodes for closed-loop seizure monitoring and on-demand drug release.[164] Reproduced from ref. 164 under a CC-BY-NC 4.0 license. (c) A wireless hydrogel-based smart bandage enabling real-time wound monitoring and micro-current stimulation to accelerate healing.[93] Reproduced from ref. 93 with permission from Springer Nature, copyright 2022. (d) A brain–AI closed-loop platform combining hydrogel electrodes, wireless EEG acquisition, and AI-driven decision making for autonomous feedback interventions.[166] Reproduced from ref. 166 under a CC-BY 4.0 license.

4. Prospective applications and outlook

Hydrogels exhibit a unique combination of tissue-level compliance, high water content, and tunable electrical and biochemical functionality, enabling their conformal integration with biological systems while supporting multimodal sensing and actuation. These attributes position hydrogels as key enablers of next-generation bioelectronic medicine. Looking ahead, hydrogel-based platforms are expected to move beyond

single-function components and evolve into intelligent, closed-loop systems that integrate physiological monitoring, therapeutic modulation, and adaptive feedback within unified architectures. Such systems could enable continuous, real-time disease management outside traditional clinical settings.

One promising direction lies in personalized neuromodulation. Hydrogel-integrated EEG–FUS platforms may be developed into wearable, headband-like systems capable of high-fidelity neural recording while delivering targeted ultrasound stimulation in response to detected pathological activity. When coupled with machine learning algorithms, these platforms could enable predictive intervention anticipating epileptic discharges or aberrant oscillatory patterns associated with neuropsychiatric disorders thereby shifting treatment paradigms from reactive to proactive neuromodulation.

In the gastrointestinal domain, hydrogels offer a foundation for long-resident ingestible or adherent devices that combine pH, motility, and biochemical sensing with localized therapeutic actuation. Integration of wireless communication and power modules could allow these systems to provide early warning of complications such as anastomotic leakage, dysmotility, or inflammation, while simultaneously delivering corrective stimulation or controlled drug release. Such minimally invasive yet continuous monitoring platforms would address a critical unmet need in chronic digestive disease management and post-surgical care.

Cardiac applications represent another fertile area for hydrogel-enabled innovation. Injectable or suture-integrated conductive hydrogels may establish bioelectronic conduction pathways that bypass infarcted myocardium, enabling biological pacing or arrhythmia suppression with reduced energy requirements compared to conventional defibrillation. In parallel, multifunctional bioadhesive hydrogel patches that integrate sensing, pacing, and drug delivery functions could redefine cardiac repair strategies by merging diagnosis and therapy into seamless, tissue-conformal interfaces.

Across diverse application domains, long-term stability remains a central bottleneck for translating hydrogel-integrated bioelectronic systems from laboratory demonstrations to real-world use. Common failure modes include dehydration and uncontrolled swelling that alter mechanical and electrical properties, biofouling-induced degradation of interfacial performance, mechanical fatigue under repeated deformation, and progressive loss of adhesion at tissue–device interfaces. Emerging strategies to address these challenges span both material- and system-level approaches. At the materials level, self-hydrating formulations, dynamic or reversible crosslinking networks, and zwitterionic or antifouling chemistries have been explored to enhance durability under physiological conditions. At the system level, hybrid architectures incorporating protective encapsulation, compliant interlayers, and modular replacement of hydrogel components are increasingly adopted to mitigate long-term degradation. Importantly, these efforts underscore that long-term reliability is not solely a materials optimization problem, but a system-level challenge that requires coordinated advances in hydrogel chemistry, interface engineering, and device architecture. Consolidating these strategies into integrated design frameworks will be critical for enabling stable, closed-loop, and clinically deployable hydrogel-based bioelectronic systems.

A second intrinsic limitation stems from trade-offs among mechanical compliance, electrical conductivity, and structural durability. Soft, low-modulus hydrogels are essential for minimizing tissue irritation and ensuring conformal contact; however, enhancing ionic or electronic conductivity often requires denser polymer networks or conductive fillers that compromise softness and stretchability. Conversely, mechanically robust formulations designed to withstand repeated deformation may exhibit reduced interfacial conformity or elevated impedance. These competing requirements underscore the absence of a universally optimal hydrogel formulation and highlight the necessity of application-specific optimization rather than single-parameter material enhancement.

From a system-level perspective, integration of soft, hydrated hydrogels with rigid microelectronic, power management, and wireless communication components remains non-trivial. Mechanical mismatch at hydrogel–electronics interfaces can induce stress concentration, delamination, and failure under cyclic loading. Maintaining stable electrical and acoustic coupling while ensuring robust encapsulation against moisture ingress further complicates system design. Although emerging approaches such as island–bridge architectures, compliant interlayers, and hybrid soft–rigid packaging have partially mitigated these issues, seamless integration into fully autonomous, wireless bioelectronic systems continues to limit long-term reliability.

Scalability represents another critical yet often underemphasized barrier to translation. Many reported hydrogel platforms rely on bespoke synthesis or small-batch fabrication methods that are poorly suited for large-scale deployment. Clinically viable systems will require reproducible, cost-effective manufacturing processes compatible with established device production pipelines. Achieving this goal demands precise control over hydrogel composition, crosslinking density, and hydration state to ensure batch-to-batch consistency in mechanical, electrical, and interfacial performance. Importantly, scalability should be addressed as a co-design challenge involving hydrogel chemistry, device architecture, and packaging strategies, rather than as a materials-only consideration.

Finally, regulatory and manufacturing constraints further shape the translational landscape. Many hydrogels are sensitive to conventional sterilization methods, including steam, radiation, or chemical agents, which can alter network structure or functional additives. Packaging must preserve hydration while maintaining sterility and mechanical integrity during storage and deployment. Moreover, hydrogel-integrated systems often span multiple regulatory classifications, encompassing materials, medical devices, and combination products, thereby complicating approval pathways particularly for internal, implantable, or mucosal applications.

Looking forward, the convergence of hydrogel materials with advanced manufacturing and artificial intelligence is expected to accelerate progress. Additive manufacturing, gradient

structuring, and nanocomposite engineering will expand the hydrogel design space, enabling spatially controlled mechanics, conductivity, and responsiveness. Simultaneously, AI-driven fusion of multimodal data streams from hydrogel interfaces can transform continuous physiological signals into actionable clinical insights, supporting autonomous and personalized decision-making. Together, these advances position hydrogel-integrated bioelectronics to move beyond laboratory demonstrations toward clinically translatable, personalized, and preventive healthcare systems, reshaping the future of human–machine interfacing in medicine.

5. Conclusion

In summary, hydrogels have evolved from soft conductive materials into system-level enablers that bridge electronics and biology, supporting integrated sensing, modulation, and adaptive control across physiological systems. By uniting sensing, stimulation, and responsive behaviors within a hydrated and biocompatible matrix, hydrogel-based systems are redefining physiological monitoring and therapeutic modulation across neural, gastrointestinal, and cardiac domains. The recent demonstrations of closed-loop hybrid architectures further illustrate the potential of hydrogels to serve not only as passive interfaces but also as active hubs for intelligent feedback control. Despite challenges in long-term stability, scalable integration, and regulatory translation, ongoing advances in material design, nanocomposite engineering, and adaptive manufacturing continue to expand the capabilities of hydrogel bioelectronics. Looking forward, this system-oriented evolution marks a transition from function-specific hydrogel components toward intelligent, hydrogel-integrated bioelectronic systems, redefining how materials, devices, and physiology converge in next-generation healthcare technologies.

Author contributions

H. W. initiated and supervised the project. M. Y. and J-C. H. coordinated the figure collection, analysis and writing of the manuscript. All authors contributed to the discussions and revised the manuscript at all stages.

Conflicts of interest

The authors declare no conflicts of interest.

Data availability

No new datasets were generated or analysed during the preparation of this review. All data supporting the conclusions of this review are derived from previously published sources, which are appropriately cited.

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