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REVIEW

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Direct Ink Writing 3D Printing of Hydrogel Bioelectronics

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Abstract Direct-ink-writing (DIW) 3D printing has emerged as an indispensable advanced manufacturing technology in biomedical engineering owing to its material compatibility, structural precision, and multimaterial integration capabilities. By digitally programming hydrogel ink deposition, DIW 3D printing enables the controllable fabrication of high-performance hydrogel bioelectronic devices featuring complex 3D architectures, high-fidelity electrophysiological recording/stimulation, and mechanical compliance with soft tissues, thereby establishing a technological foundation for next-generation personalized medical electronics. This review systematically summarizes the recent progress in DIW-printed hydrogel bioelectronics, first elaborating design strategies for hydrogel inks that reconcile printability with functionality through synergistic engineering of rheological behavior, electrical conductivity, tissue adhesion, and biocompatibility. We comprehensively analyzed state-of-the-art wearable and implantable devices fabricated *via* DIW 3D printing, highlighting their advantages in electrophysiological monitoring, precision stimulation, and biosensing. Finally, we conclude by critically evaluating the current challenges and future directions, thereby establishing a framework for DIW 3D printing to become a foundational platform for customized biointegrated interfaces.

Keywords 3D printing; Direct-ink writing; Hydrogel; Bioelectronics; Biointerface

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INTRODUCTION

Bioelectronic technology aims to engineer reliable, high-fidelity interfaces between living tissues (*e.g.*, neural, muscular, and organ) and electronic systems, unlocking new possibilities in neuroscience, clinical diagnostics, and human augmentation.[1–3] Since the invention of cardiac pacemakers, wearable and implantable bioelectronic devices have become indispensable tools for monitoring and treating conditions such as Parkinson's disease, stroke, and cardiovascular disorders.[1,4,5] Nevertheless, the inherent mechanical mismatch between rigid conventional devices (*e.g.*, silicon and metals) and soft, dynamic tissues poses a significant challenge in achieving stable, long-term biointerfacing. This mismatch creates stress at the interface, leading to tissue damage, inflammation, and scar tissue formation, all of which degrade the device performance over time.[1,3,6,7] Compounding this issue, biological systems rely on ions and molecules to transmit signals, while electronics use electrons, a fundamental disconnect which weakens the signal quality and limits the precision of interventions such as neuromodulation.[3,7,8] To overcome these challenges, next-generation bioelectronic materials must be soft, stable in wet environments, and capable of conducting ions.

Hydrogels have emerged as a promising solution because of their unique properties, such as high water content, flexibility, and ionic conductivity, which closely resemble those of natural tissues.[6,7,9] Their softness and stretchability allow them to conform to biological structures, thus minimizing the mechanical mismatch that plagues traditional rigid devices.[7,10,11] Additionally, their porous structure supports efficient ion transport and nutrient exchange, which are both critical for biocompatibility.[10] By embedding conductive materials, such as carbon nanomaterials or polymers (*e.g.*, poly(3,4-ethylenedioxythiophene):poly(styrene sulfonate), PEDOT:PSS), hydrogels can bridge the gap between ionic and electronic signaling.[12,13] Unlike metal electrodes, conductive hydrogels reduce tissue trauma during implantation and resist the body's natural rejection mechanisms.[14] Their flexibility ensures that they move with the body and maintain stable performance over time,[15] whereas their porous design enhances signal clarity for both recording and stimulation.[16] Together, these features establish conductive hydrogels as ideal platforms for engineering high-fidelity, low-damage, and chronically stable bioelectronic interfaces.

The rise of advanced manufacturing, particularly 3D printing, has opened new doors for bioelectronics, enabling devices to seamlessly integrate with the body's complex shapes and movements.[17,18] Traditional methods such as screen printing or photolithography, although reliable, struggle to create the intricate 3D structures needed for high-performance applications.[18–22] By contrast, 3D printing offers un-

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paralleled design freedom, allowing customized devices tailored to individual anatomies.[23] One standout technique, direct-ink writing (DIW), uses precisely controlled extrusion to deposit functional inks with tailored properties (*e.g.*, shear-thinning behavior) through fine nozzles (Fig. 1a).[24,25] Versatility of DIW, such as its compatibility with ceramics, metals, polymers and even living cells, makes it a powerful tool for bioelectronics.[24,26,27] Through the creation of anatomically conformal, personalized 3D structures (Fig. 1b) and the holistic optimization of mechanical, electrical, and biological functions *via* multi-material integration, this technology introduces an advanced bioelectronic device (Figs. 1c and 1d) that establishes a novel paradigm for robust chronic recording and stimulation.

Despite the considerable promise of DIW 3D printing for hydrogel-based bioelectronics, its translation to widespread practical applications is complicated by stringent and often conflicting requirements. Hydrogel inks must strike a delicate balance: easy to print, yet durable, functional, and biocompatible. Meeting these demands requires careful tuning of ink properties, printing conditions, and device performance. Another challenge lies in creating devices that remain stable in the body's ever-changing environment, while integrating multiple materials at different scales. This review addresses these issues by first examining the design of hydrogel inks that meet both printing and functional needs, with a focus on rheology, conductivity, and biocompatibility. Next, we highlight cutting-edge wearable and implantable devices for sensing and therapy. Finally, the key challenges and opportunities that shape the future of this exciting field are outlined.

DESIGN OF 3D-PRINTABLE HYDROGEL INKS

The efficacy of DIW 3D printing as a powerful platform for customized hydrogel-based bioelectronics is critically dependent on rational ink design, which ultimately determines both the printing fidelity and overall device performance.[28,29] Four key factors must be addressed in order to create high-performance hydrogel inks. First, the ink must exhibit highly desirable flow properties, specifically, shear-thinning behavior and quick solidification, to ensure smooth extrusion and sharp, precise shapes after printing. Second, for electrophysiological applications, the ink needs excellent conductivity to support both electronic and ionic signal transmissions. Just as important is the strong tissue adhesion, which keeps the device securely in place on moving tissues, maintaining reliable signal transfer. Finally, biocompatibility is non-negotiable, as the ink must be nontoxic, minimally inflammatory, and stable over time to meet the strict safety demands of *in vivo* use. Balancing these competing requirements requires a carefully integrated design approach (Fig. 1e), which paves the way for bioelectronic devices that are not only high-performance, but also safe and durable in real-world applications.

Rheological Performance

As an extrusion-based additive manufacturing method, DIW 3D printing relies on inks with a shear-thinning rheology. This be-

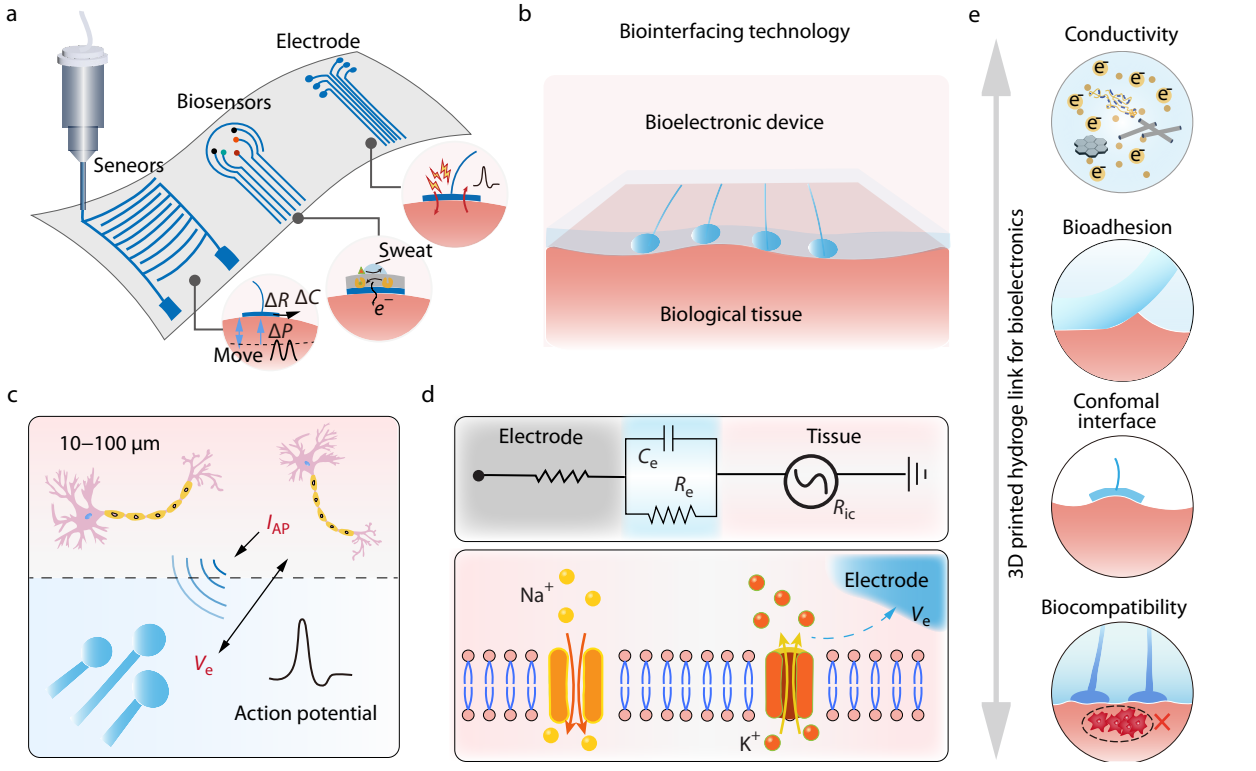

Fig. 1 3D printing of multifunctional hydrogels for advanced bioelectronic interfaces. Direct-ink-writing (DIW) 3D printing enables customized fabrication of hydrogel-based bioelectronic devices (a) capable of conformal integration with complex biological surfaces (b), facilitating neural interfacing through direct tissue contact (c). These devices detect biopotential signals generated by transmembrane ion transport in excitable cells (d), supporting applications in electrophysiological recording, stimulation, and biosensing. Successful implementation requires hydrogel inks meeting specific rheological and functional performance criteria (e).

havior enabled the material to liquefy under high shear rates within the nozzle for smooth extrusion, followed by rapid post-deposition solidification (Fig. 2a). This behavior is commonly described by the power-law model (1):[30,31]

$$\tau = K\dot{\gamma}^{n} \quad (1)$$

or, equivalently, by the viscosity form (2):[30,31]

$$\eta = \frac{\tau}{\dot{\gamma}} = K\dot{\gamma}^{n-1} \quad (2)$$

where τ is the shear stress, $\dot{\gamma}$ is the shear rate, K is the consistency index, and $n < 1$ is the flow behavior index. A smaller n indicates stronger shear thinning, meaning that the apparent viscosity decreases markedly as $\dot{\gamma}$ increases inside the nozzle, which facilitates continuous extrusion through micron-scale nozzles. In contrast, Newtonian fluids (n=1) or shear-thickening fluids (n>1) generally fail to provide the required balance between flowability and controllability for DIW 3D printing (Fig. 2b).[31] The ink's apparent viscosity must also be carefully tuned within a narrow processing window (typically 10^2–10^4 mPa·s at about 10–100 s^{-1});[31] insufficient viscosity causes filament spreading and collapse, while excessive viscosity leads to high extrusion forces and nozzle clogging (Fig. 2c). Post-deposition, the requirement abruptly shifts from flowability to shape stability, which is a transition governed by two key parameters. Primarily, a high yield stress (τ_y) is required to resist flow and maintain the filament shape against gravitational and capillary stresses. To prevent slumping or collapse, τ_y should satisfy

$$\tau_y \gtrsim \gamma/L + \rho g H \quad (3)$$

where γ is the surface trnsion of the suspension, ρ is the density, g is the gravitational acceleration, H is the characteristic height, and L is the characteristic length scale.[31] Second, rapid modulus recovery is paramount. The ink must exhibit a liquid-like behavior ($G'' > G'$) under high shear, but rapidly recovers its elastic modulus (G') to surpass its viscous modulus (G'') upon deposition, enabling a swift transition back to a solid-like state (Fig. 2d). This recovery rate presents a critical trade-off: slow recovery leads to excessive filament coalescence and degraded resolution, whereas an overly rapid transition can impair interlayer bonding and compromise structural integrity.[32] Consequently, achieving high-fidelity DIW 3D printing depends on the coordinated optimization of shear-thinning parameters (K, n), yield stress (τ_y), and the kinetics of modulus recovery (the time-dependent evolution of G' and G''), ensuring an optimal extrudate morphology under varying shear conditions that correlate rheological tuning with filament fidelity, such as diameter consistency, surface smoothness, and minimal buckling (Fig. 2e).

To achieve these rheological properties, hydrogel inks often rely on dynamic reversible crosslinks that switch between flowable and solid-like states under shear.[28] For example, nanocellulose-based inks can be adjusted to enhance shear thinning, yield stress, and recovery, and improve printability and structural stability.[33] Other strategies, such as hydrophobic association or host-guest interactions, create physical networks that break under shear ($G'' > G'$, for easy extrusion) and quickly reform afterward ($G' > G''$, for shape retention).[34] Systems such as thermo-responsive gelatin or PVA/borax networks exemplify this by combining rapid shear-thinning with

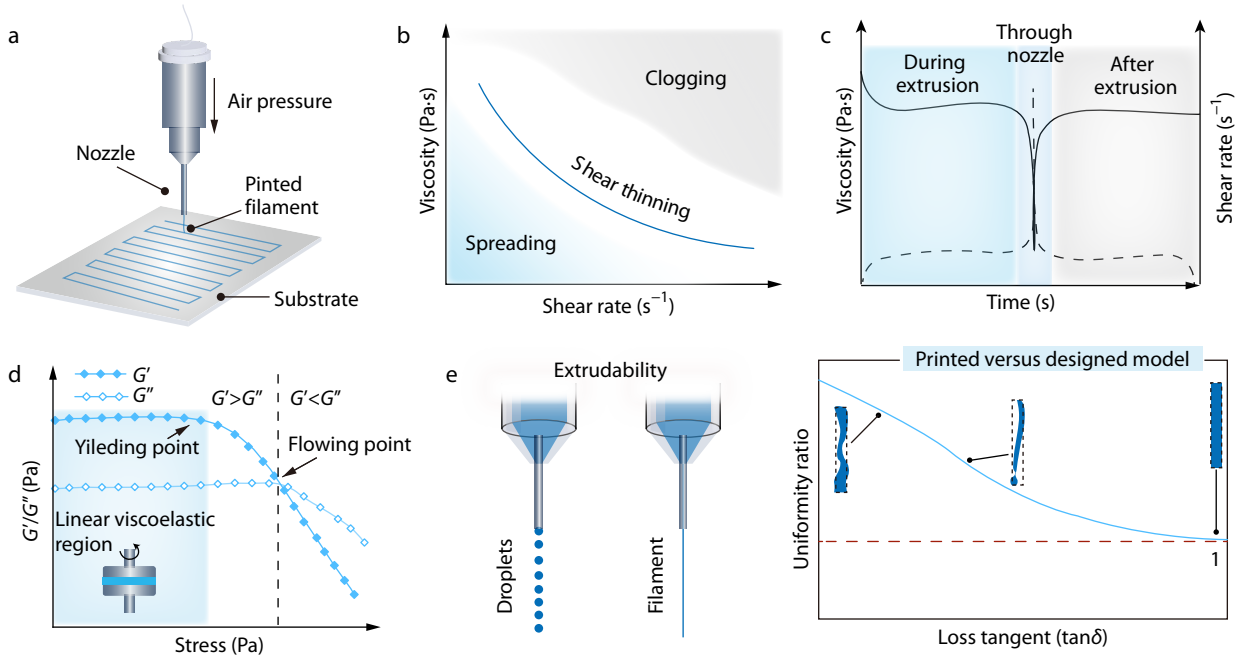

Fig. 2 Design strategies for 3D-printable hydrogel inks with tunable rheological properties. (a) Pneumatic extrusion-based DIW 3D printing setup enabling room-temperature deposition of complex architectures; (b) Viscosity-shear rate curve defining the operational window (*e.g.*, shear-thinning regime) for stable extrusion and shape retention; (c) Three-step shear test demonstrating structural recovery post-extrusion, where viscosity restoration after high-shear confirms thixotropic behavior essential for layer fusion; (d) Storage modulus (G') and loss modulus (G'') versus shear stress, identifying the linear viscoelastic regime (LVR), yield point (critical stress for flow initiation), and flow point (transition to liquid-like behavior); (e) Extrudate morphology under varying shear conditions, correlating rheological tuning with filament fidelity (*e.g.*, diameter consistency and surface smoothness) and minimal buckling.

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self-healing for stretchable, repairable hydrogels.[35] Another approach uses diffusion-controlled crosslinking, such as alginate ink gelling in a calcium bath, which ensures smooth flow during printing and instant solidification afterward.[36] Together, these methods demonstrate how smart ink design can precisely control rheology, laying the groundwork for advanced 3D-printed hydrogels.

Conductive Performance

Although printability is essential, achieving high electrical conductivity in hydrogel inks is critical for advanced bioelectronic devices. This is typically accomplished by incorporating conductive fillers, such as carbon nanomaterials, metallic nanowires, or MXenes (Fig. 3a).[28,37] However, loading these fillers near the percolation threshold often creates a trade-off that disrupts the rheological properties of the ink (Fig. 3b). High filler concentrations can increase the viscosity due to particle entanglement, raising extrusion pressure, while rigid particles may impair shear-thinning and recovery or even clog the nozzles (Fig. 3c).[38] Consequently, the paradigm is shifting from simple physical blending to synergistic network engineering, where coordinated filler-matrix interactions are harnessed to co-optimize both conductivity and rheological performance.

Unlike particulate fillers, intrinsically conducting polymers such as polythiophene (PTh), polyaniline (PANi), and PEDOT:PSS offer functionalizable backbones and excellent processability, making them ideal for conductive hydrogel inks (Fig. 3d).[39,40] Among these, PEDOT:PSS is notable for its water solubility, tunable conductivity, and film-forming ability, making it widely used in flexible bioelectronics.[41] However, its tendency to aggregate in hydrogels complicates rheological control for 3D printing. Zhao *et al.*[42] developed a freeze-dried, re-dispersible PEDOT:PSS nanofibril ink that achieved shear-thinning and yield stress for high-resolution printing (about 30 μm features over 20 layers) while maintaining 28 S·cm^{-1} conductivity. However, pristine PEDOT:PSS is mechanically brittle, which limits its stability to dynamic tissues. Blending with other polymers can improve stretchability but often sacrifices conductivity. To resolve this, Zhao *et al.*[43] further developed a bi-continuous PEDOT:PSS-polyurethane hydrogel combining high conductivity (11 S·cm^{-1}), extreme stretchability (>400%), and tissue-like softness (<1 MPa modulus). This approach establishes a new de-

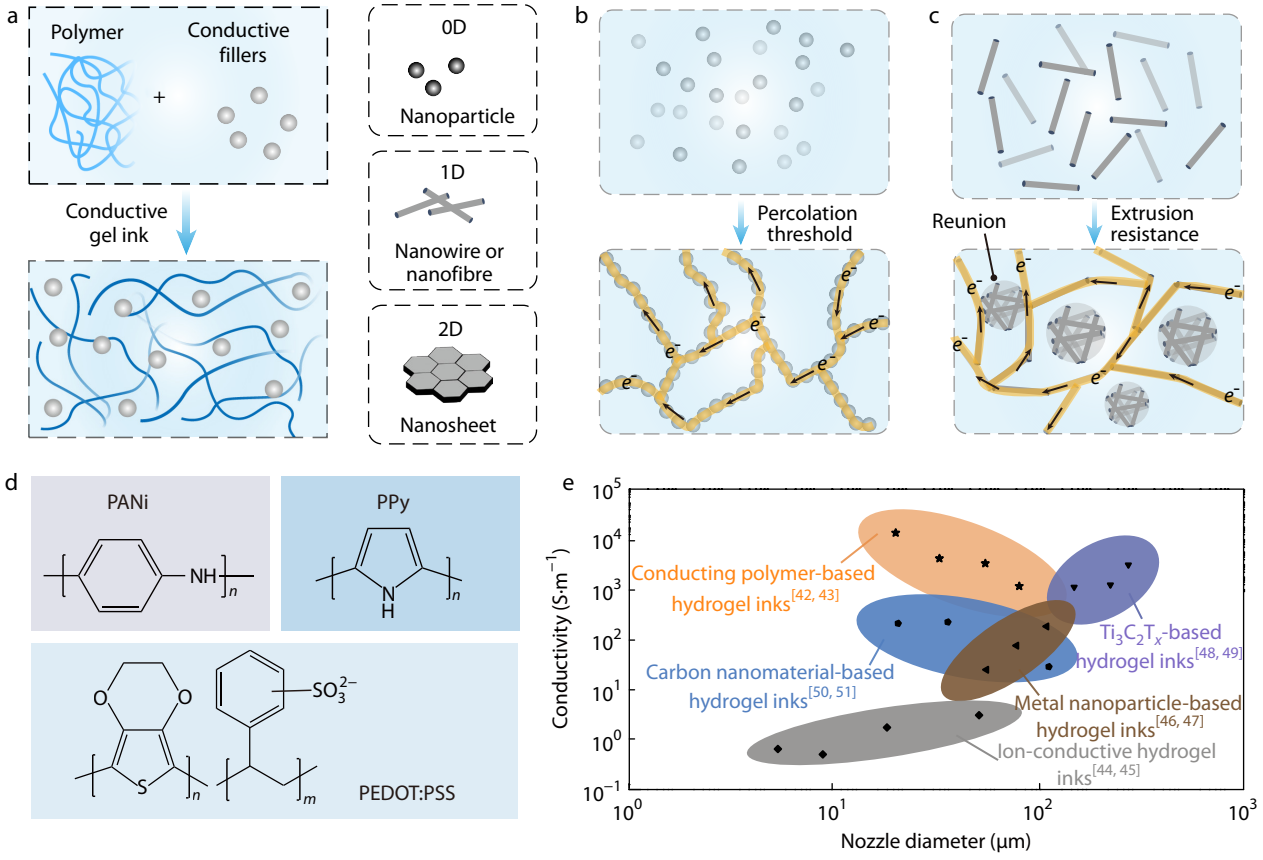

Fig. 3 Design strategies for developing 3D-printable hydrogel inks with excellent electrical conductivity. (a) Conductive hydrogel inks formulated by dispersing nanofillers (0D nanoparticles, 1D nanowires/nanofibers, or 2D nanosheets) into polymer gel precursors to establish percolating conductive networks; (b) Evolution of filler organization with increasing volume fraction, transitioning from isolated particles to a percolated network beyond the percolation threshold; (c) Printing fidelity is compromised by the aggregation of hydrophobic nanofillers resulting from surface energy mismatches and scale disparities with hydrophilic polymer chains; (d) Conductive polymers are incorporated into ink formulations to reconcile the conflicting requirements of printability and conductivity; (e) Comparative analysis of printing resolution versus conductivity for hydrogel inks incorporating ionic conductors, metal nanoparticles, MXene, carbon nanomaterials, and conductive polymers, synthesized from previously-reported literatures.[42–51]

sign paradigm for high-performance implantable bioelectronics by effectively resolving the traditional trade-off between the electrical and mechanical performance. Among the various classes of conductive hydrogel inks, PEDOT:PSS-based ink systems have emerged as a leading platform, demonstrating superior electrical performance and printing resolution (Fig. 3e).[42–51] This progress has solidified their role as critical material foundations for next-generation implantable bioelectronic devices.

Adhesive Properties

Strong adhesion is essential for high-performance bioelectronic interfaces to ensure reliable signal recording and precise neuromodulation.[52] Traditional methods, such as suturing or physical attachment, often fail to form a stable bond with soft tissues, leading to poor signal quality (Figs. 4a and 4b). Although 3D-printed ultrathin hydrogel electrodes excel at forming conformal contact on relatively static surfaces such as skin, they struggle to maintain a durable bond on continuously deforming organs such as the heart and gastrointestinal tract.[53] For bioelectronic devices to function effectively in these environments, adhesive performance must be a core design consideration, enabling stable integration and long-term signal fidelity (Fig. 4c).

Adhesion between hydrogels and biological tissues is primarily mediated through four fundamental pathways: hydrogen bonding, mechanical interlocking, electrostatic interactions, and covalent bonding (Fig. 4d). The strength of these adhesive interactions is quantitatively assessed using standardized methods, where lap-shear tests measure the shear strength, which represents the maximum stress parallel to the interface required to induce shear failure. The shear strength can be calculated [52]

$$\text{Shear strength} = \frac{F_{max}}{WL} \tag{4}$$

where F_{max} is the maximum force in the lap shear test, L is the length, and W is the width. Another quantitative metric for char-

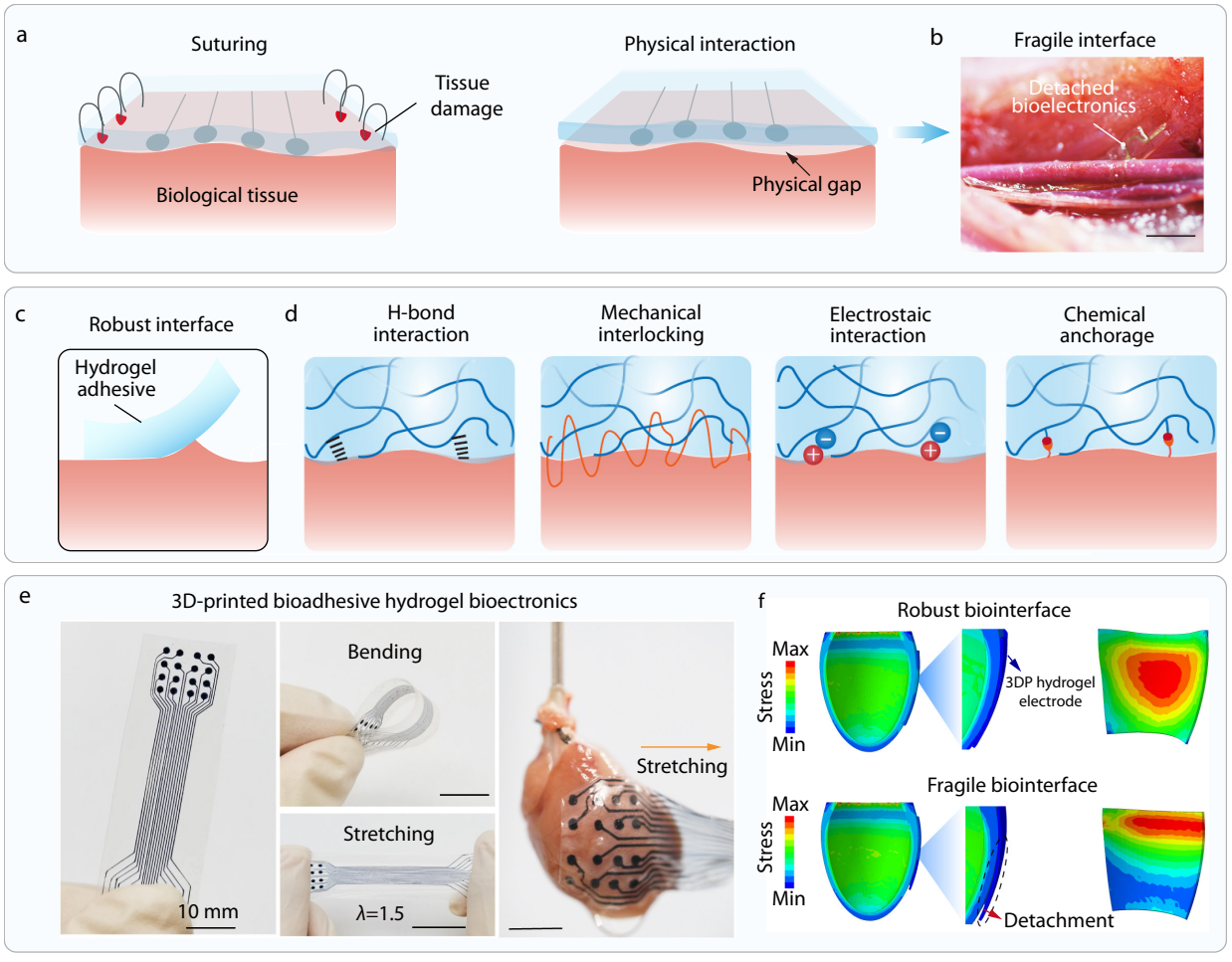

Fig. 4 Design strategies for constructing seamless interfaces between hydrogel electronics and biological systems. (a) Suturing-based attachment of bioelectronic devices onto target tissues; (b) Physical adhesion demonstrating device delamination and displacement under weak interfacial bonding (Reproduced with permission from Ref. [54]; Copyright (2021), John Wiley and Sons.); (c) Hydrogel adhesive layer enabling robust biointerfaces through conformal integration; (d) Adhesion mechanisms: hydrogen bonding, mechanical interlocking, electrostatic interactions, and chemical anchoring; (e) 3D-printed all-hydrogel electronics maintaining stable adhesion on *ex vivo* perfused hearts during deformation; (f) Finite element analysis of a hydrogel-heart interface under 30% strain reveals that robust adhesion minimizes stress concentration and prevents delamination, in stark contrast to the interfacial failure observed in non-adhesive scenarios; (e, f: reproduced with permission from Ref. [56]; Copyright (2024), John Wiley and Sons.)

acterizing interfacial adhesive capability is the interfacial toughness (Γ), which represents the energy required to propagate a crack along the bonded interface. and peeling tests were used to evaluate the energy dissipation during debonding. The interfacial toughness can be calculated:[54]

$$\Gamma = \frac{2F_{plateau}}{W} \quad (5)$$

where $F_{plateau}$ is the plateau force in peel test, W is the width.

The pursuit of stable and long-lasting bioelectronic interfaces has led to the development of fabrication strategies that fall into two distinct categories: layered integration and monolithic integrated design. Zhao *et al.*[55] used multimaterial 3D printing to create a fully hydrogel-based bioelectronic system by combining an adhesive layer with conductive circuitry. The adhesive layer bonded strongly to the beating heart through hydrogen bonds and covalent amide linkages. The rational design of the hydrogel network enables the simultaneous achievement of conductivity and tissue adhesion capabilities. A representative example by Liu *et al.*[56] formulated a multifunctional hydrogel ink by unifying a bioadhesive polymer (PAA-NHS), biocompatible polymers (CTS and PVA), and a conductive component (PEDOT:PSS) within a hydrogel system. It forms a tough 3D network *via* amide reactions and hydrogen bonding, whereas a dry-state crosslinking strategy ensures robust tissue adhesion (about 200 J·m^{-2} interfacial toughness). The resulting hydrogel electrodes maintained stable adhesion to wet heart surfaces, even under mechanical stress (Fig. 4e). Mechanical simulations revealed that strong adhesion redistributes interfacial stress, preventing delamination (Fig. 4f). This synergy between adhesion and mechanical compliance is key for durable bioelectronic interfaces in dynamic tissues.

Biocompatibility

The development of biocompatible inks is crucial for the long-term success of *in vivo* 3D-printed hydrogel bioelectronics. An ideal ink must meet three key requirements: (i) chemical inertness, ensuring that no toxic by-products are released; (ii) mechanical properties that match host tissues to minimize implantation trauma; and (iii) biological compatibility, fostering a supportive environment for cellular function while reducing immune responses.[57] A common strategy is to formulate hydrogel matrices from inherently biocompatible polymers (*e.g.*, gelatin, CTS, and PVA). These materials possess excellent biocompatibility and enable tissue-matching moduli (about 10–500 kPa), thereby mitigating interfacial stress, tissue damage, and chronic inflammation.[6] Additionally, a porous, hydrated structure is essential for facilitating oxygen and nutrient exchange, as well as waste removal, creating a microenvironment that promotes cellular activities, such as adhesion and proliferation.[58] Hydrogels that support both ionic and electronic transport are particularly valuable because they enhance signal transduction and improve recording and stimulation efficiency by lowering the interfacial resistance.

Programmable biodegradability is essential for implantable bioelectronics to ensure biosafety without compromising the functionality.[59] By tailoring the degradation kinetics to align with tissue regeneration or therapeutic timelines, these materials eliminate the need for surgical removal.[60] Designing degradable hydrogel inks requires careful control of the degradation rate, mechanisms, and electrical performance. Common approaches incorporate natural polymers, such as gelatin, chitosan, or hyaluronic acid, which break down *via* hydrolysis, enzymatic action, or cellular activity.[61] Degradation rates can be fine-tuned by adjusting the molecular weight, crosslink density, or chemical modifications, allowing lifetimes ranging from days to months. While some conductive fillers resist degradation, their byproducts can be safely cleared by macrophages and renal excretion, thereby preventing toxicity.[62] For example, Huang *et al.*[63] created a PEDOT-gelatin hydrogel electrode that degraded over 28 days without neurotoxic effects while supporting neuronal adhesion and signal transmission. This balance between performance and biocompatibility highlights the potential of such materials for long-term bioelectronic applications.

APPLICATIONS OF 3D-PRINTED HYDROGEL BIOELECTRONICS

By merging the tissue-like properties of hydrogels with the versatility of 3D printing, hydrogel bioelectronics have revolutionized biomedical devices, enabling highly customized designs and integrated functionalities.[64] Unlike traditional planar methods, this layer-by-layer approach allows the fabrication of devices spanning macro- to micro-scale dimensions. It also supports the spatial organization of diverse components such as conductive pathways, sensors, and adhesives, thus overcoming long-standing challenges in structural complexity and functional integration. These devices have already proven to be effective in electrophysiological recording, precise stimulation, and multimodal biosensing (Fig. 5a). A significant advantage of this digitally driven manufacturing paradigm is the on-demand co-design of materials, structures, and functions, which allows for the optimization of overall device performance. By leveraging their soft, tissue-mimetic mechanics and customizable 3D architectures, these devices establish electrically robust interfaces with biological tissues, characterized by stable contact and low interfacial impedance. This capability is crucial for enabling atraumatic, high-quality signal acquisition and accurate and efficient electrical stimulation (Figs. 5b and 5c). This section details the application of 3D-printed hydrogel bioelectronics in bioelectrical activities, such as electrophysiological recording and electrical stimulation, along with their utility in non-bioelectrical domains involving multimodal biosensing of physicochemical variables, such as mechanical strain, tissue temperature, and the detection of specific chemical molecules.

Electrophysiological Recording

Electrophysiological recording is indispensable for understanding neural, cardiac, and muscular activities, but signal integrity remains a persistent challenge.[1,2,56] Techniques such as electroencephalography (EEG), electrocorticography (ECoG), electrocardiography (ECG), and electromyography (EMG) rely on accurate signal transduction, which is complicated by the mismatch between the ionic dynamics in tissues and electronic signals in devices.[5,65] This disparity leads to interfacial polarization, charge accumulation, and waveform distortion. Non-faradaic processes and sluggish electrochemical kinetics further degrade high-frequency performance, resulting in signal attenua-

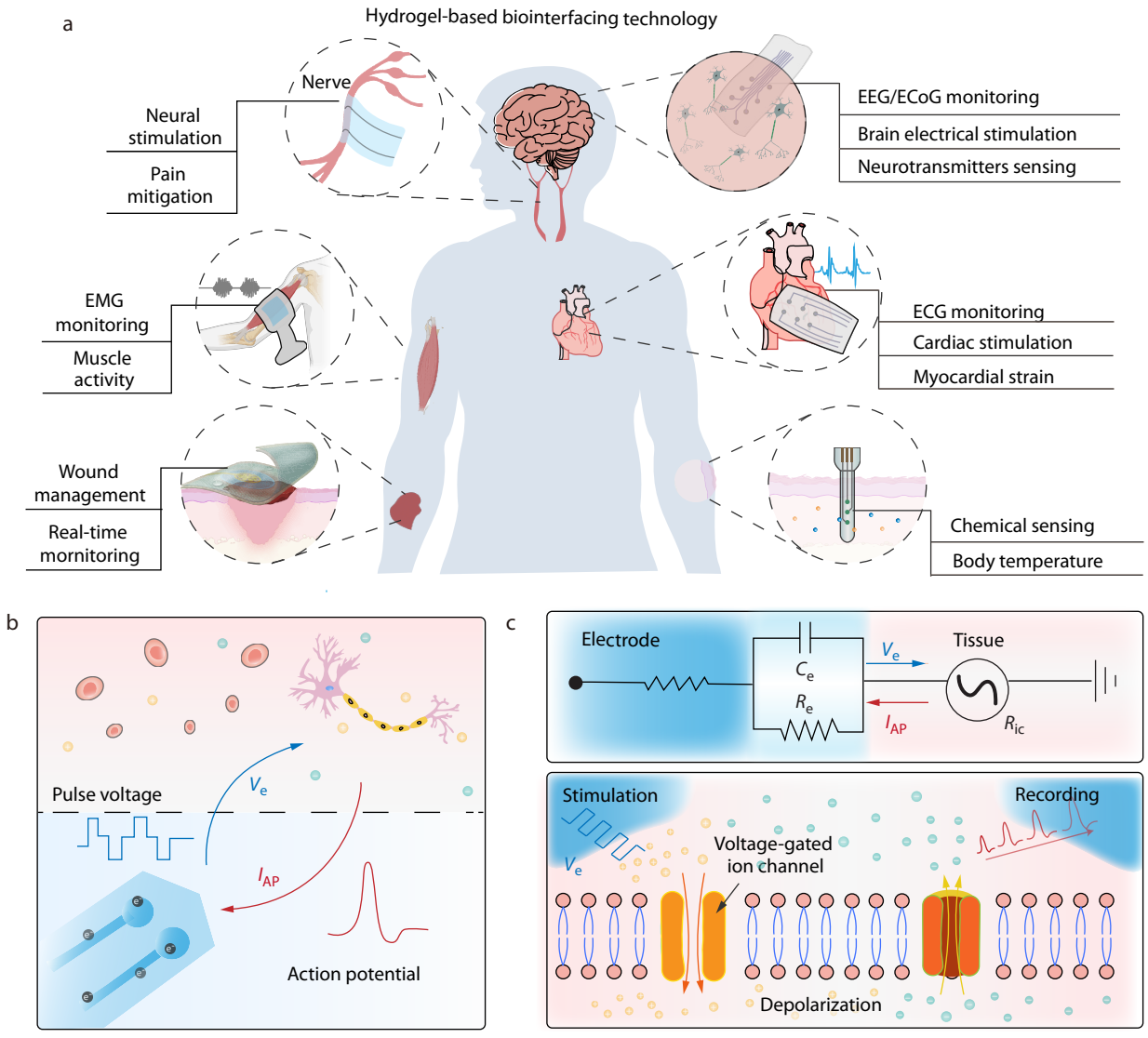

Fig. 5 3D-printed hydrogel bioelectronics for bioelectronic interfacing. (a) Multifunctional platform enabling continuous high-fidelity monitoring of electrophysiological signals (*e.g.*, ECG, EMG) and physiological parameters (*e.g.*, sweat biomarkers, temperature), while delivering therapeutic electrical stimulation to promote tissue repair (*e.g.*, skin, nerve regeneration) and modulate organ functions (*e.g.*, cardiac rhythm, neurotransmission); (b) Schematic of bidirectional electrical communication between hydrogel electronics and biological tissues; (c) The underlying mechanism enables a bidirectional signal conversion, transducing ionic currents from cellular activity into electronic signals for monitoring and reversing the process for stimulation.

tion and fidelity loss.[66,67] For wearable systems, motion artifacts, which may be caused by everyday activities, such as limb movement or breathing, are a major source of noise, undermining signal reliability.[68] Zhou *et al.*[69] addressed this using an all-hydrogel device featuring a conductive silver-based ink, which achieved stable skin contact and minimized artifacts during ECG recording. However, anatomical variability and dynamic deformation still complicate interface stability, leading to uneven current distribution and reduced therapeutic efficacy.

To improve wearable interfaces, Naguib *et al.*[70] developed a handheld 3D printing method for fabricating personalized hydrogel electrodes that precisely conform to the skin topography (Figs. 6a and 6b). These electrodes outperformed their commercial Ag/AgCl counterparts, boosting the EMG signal-to-noise ratio (SNR) by 88% and reducing the stimulation current by 36%. Such advancements are critical for applications such as prosthetic control, where decoupled EMG can discern individual muscle activations, enabling intuitive, multi-degree-of-freedom movements (Fig. 6c).[71] Long-term stability of implants is vital. Devices must withstand dynamic loads from cardiac beating, respiration, and muscle contraction, without provoking inflammation.[72] Liu *et al.* [56] used a bioadhesive hydrogel platform to achieve a stable interface (SNR is about 40) for high-fidelity ECG mapping (Figs. 6d–6f). However, single-neuron recording remains challenging owing to the size mismatch between the hydrogel electrodes (about 100 μm) and neuronal somata (about 20 μm). To bridge this gap, Zhao *et al.*[42] engineered a PEDOT:PSS-based neural probe with about 30 μm resolution, enabling single-cell recordings in freely moving mice (Figs. 6g–6i). The probe maintained sta-

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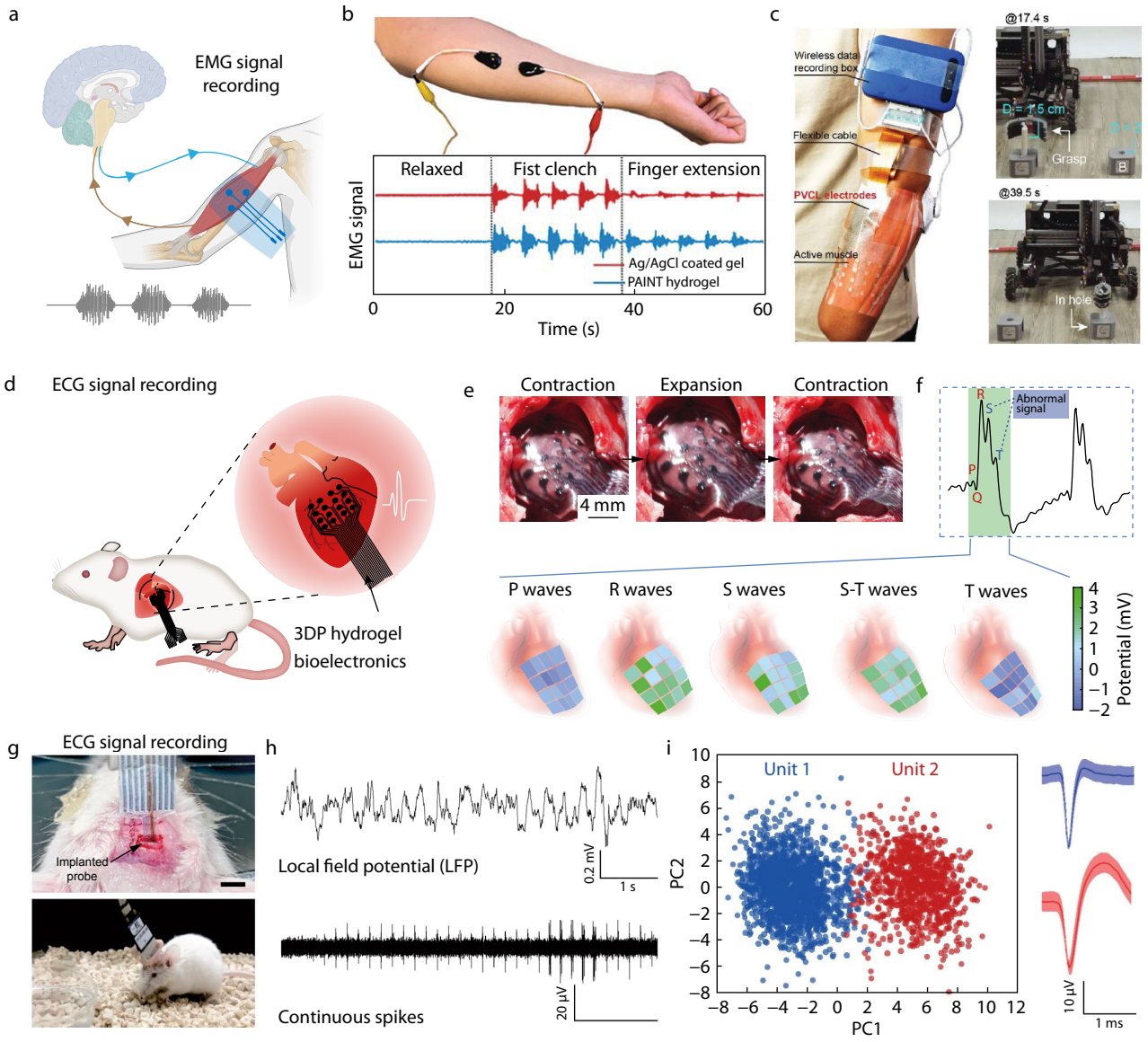

Fig. 6 Schematic of 3D-printed hydrogel bioelectronics for electrophysiological recording. (a) Schematic of hydrogel bioelectronics for EMG monitoring, enabling (b) direct skin-conformal printing of electrodes for high-fidelity signal acquisition (Reproduced with permission from Ref. [70]; Copyright (2024), John Wiley and Sons). (c) Decoupled EMG signals facilitate precise robots (Reproduced with permission from Ref. [71]; Copyright (2023), John Wiley and Sons). (d) Multi-channel hydrogel electrodes designed for *in vivo* ECG recording, with (e) images demonstrating conformal adhesion to a dynamically contracting rat heart; (f) High-fidelity ECG signals and 16-channel biopotential mapping from infarcted hearts (Reproduced with permission from Ref. [56]; Copyright (2024), John Wiley and Sons). (g) Implanted soft neural probes in freely moving mice capture (h) local field potentials (0.5–250 Hz) from the dorsal hippocampus, with (i) principal component analysis isolating distinct single units (Reproduced with permission from Ref. [42]; Copyright (2019), Springer Nature).

ble operation for two weeks, capturing clear action potentials for neural-circuit analysis.[28] These innovations highlight the potential of hydrogel bioelectronics to overcome long-standing barriers in both wearable and implantable applications, paving the way for more precise and reliable biomedical devices.

Electrical Stimulation

Bioelectrical stimulation is a cornerstone of bioelectronics, enabling precise physiological interventions by modulating cellular membrane potentials through controlled current applications.[73] By adjusting parameters such as amplitude, frequency, and pulse waveform, this technique can depolarize excitable cells, such as neurons or cardiomyocytes, to trigger action potentials and downstream physiological responses.[74,75] In addition to neuromodulation, electrical stimulation has shown promise in wound repair, where it mimics natural bioelectrical cues to accelerate healing. For example, it promotes fibroblast activity and angiogenesis, which are critical for tissue regeneration (Figs. 7a and 7b). In diabetic wounds, where healing is often impaired, electrical stimulation offers a non-pharmacological therapy that not only enhances closure but may also reduce infection risk (Figs. 7c and 7d).[76]

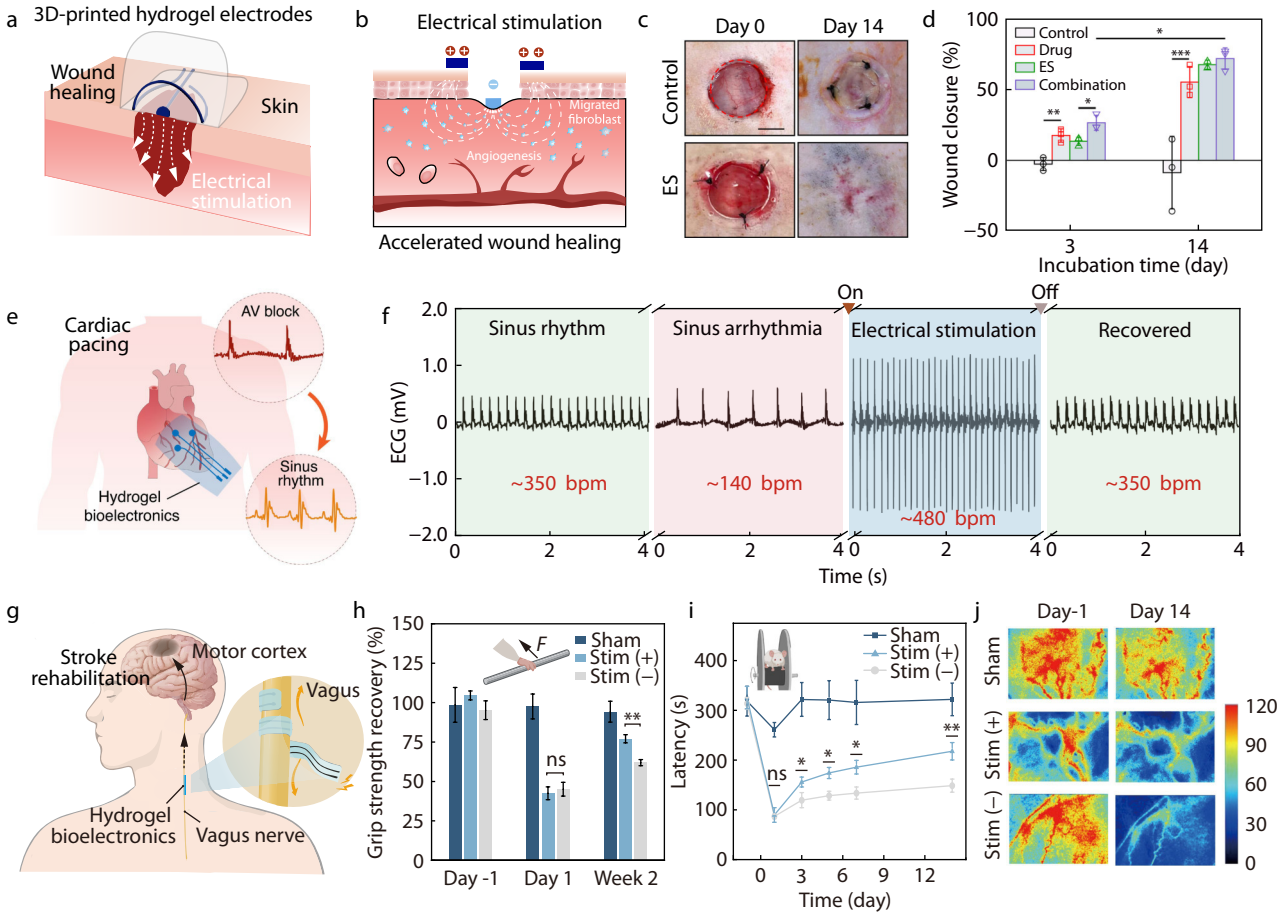

Fig. 7 3D-printed conductive hydrogel electrodes for electrophysiological modulation. (a) Schematic of hydrogel bioelectronics for wound management, leveraging (b) electrical stimulation to accelerate healing, with (c) images showing enhanced recovery in rats versus controls. (d) Quantitative wound closure analysis for untreated, drug-only, electrical stimulation-only, and combined therapy groups (Reproduced with permission from Ref. [76]; Copyright (2023), The American Association for the Advancement of Science). (e) Hydrogel-based cardiac pacing system restoring (f) synchronized rhythm in AV block by increasing heart rate (Reproduced with permission from Ref. [14]; Copyright (2023), John Wiley and Sons). (g) Stroke rehabilitation platform tracking (h, i) behavioral metrics (forelimb grip strength, latency, normalized drop speed) over 2 weeks, and (j) laser speckle contrast imaging of cortical blood flow during vagus nerve stimulation (Reproduced with permission from Ref. [78]; Copyright (2025), John Wiley and Sons).

Maintaining stable mechanical and electrical coupling with dynamic tissues is essential for invasive applications, such as cardiac pacing or deep brain stimulation. Mechanical mismatches or interfacial instability can compromise performance and safety, while high impedance increases the risk of tissue damage owing to elevated charge densities.[13] Hydrogel electrodes, owing to their tissue-like softness and dual ionic/electronic conductivity, effectively address these challenges. For instance, conducting polymer hydrogel coatings have enabled low-voltage cardiac pacing (about 0.7 V) and restored normal heart rhythms without adverse effects (Figs. 7e and 7f).[14] However, targeting small neural structures, such as the vagus nerve, remains difficult because of the need for durable conformal interfaces.[77] Liu *et al.*[78] tackled this with a 3D-printed, self-curling hydrogel electrode that wraps around nerves upon hydration, achieving an ultralow impedance (about 150 Ω) and minimal stimulation thresholds (about 10 mV). In stroke models, this design improved motor recovery and cortical reperfusion, highlighting its potential for precise neuromodulation (Figs. 7g–7j).

Biosensing

Physiological states are complex and dynamic, reflected not only in bioelectrical activity but also in key physicochemical parameters such as mechanical strain, temperature, and pH.[1,2] These interdependent variables form a multidimensional information space, which is critical for understanding health and disease. For instance, mechanical strain provides direct insights into tissue mechanics and function, making it invaluable for monitoring activities, such as muscle contraction or respiration.[79] However, many conductive hydrogel strain sensors face significant limitations, including pronounced hysteresis (>5%) and susceptibility to interference from multiaxial deformations.[80] These issues compromise accuracy and durability, hindering real-world applications. Recent advances, such as a PEDOT:PSS-PVA hydrogel with a microphase-separated network, have addressed these challenges.[81] Fabricated *via* DIW and freeze-

thaw crosslinking, these sensors exhibit ultralow hysteresis (<1.5%) and high stretchability (about 300%), enabling precise tracking of physiological activities from subtle swallowing motions to large joint movements. When configured as multichannel arrays, they even support complex applications, such as sign-language recognition.

Body temperature fluctuations are tightly linked to metabolic activity and stress responses, but hydrogel-based sensors often struggle with long-term stability owing to water evaporation. This can lead to dehydration, cracking, and baseline drift in resistance measurements.[82] This limitation can be mitigated by incorporating multiple crosslinking mechanisms or introducing biocompatible, high-boiling-point solvents into the hydrogel design to suppress water loss and maintain the structural/electrical integrity over time.[83]

Beyond temperature, continuous biomarker monitoring is essential for tracking metabolic dynamics and disease progression.[84,85] Electrochemical biosensors that leverage 3D-printed conductive hydrogels offer a promising solution. The precision of DIW printing allows for seamless integration of conductive matrices with biorecognition elements (*e.g.*, enzymes or aptamers), enabling the fabrication of flexible, high-surface-area electrode arrays. These platforms are capable of real-time detection of critical biomarkers, such as glucose, lactate, and neurotransmitters, providing molecular-level insights into physiological states.[86] Recent innovations have highlighted the potential of DIW printing for multianalyte monitoring. For example, Nolan *et al.*[87] developed a nanocomposite ink combining PEDOT:PSS, silicone elastomer, activated carbon, and Pt microparticles to print multielectrode arrays on flexible substrates. Nafion coating further enhanced the stability and selectivity, allowing the simultaneous detection of glucose, lactate, and glutamate. This approach not only validates the utility of DIW for parallel multianalyte tracking but also opens new avenues for studying cellular microenvironments. By integrating material design with advanced manufacturing, these systems pave the way for more comprehensive and reliable physiological-monitoring tools.

CONCLUSIONS AND OUTLOOK

This review highlights recent breakthroughs in 3D-printed hydrogel bioelectronics, from innovative material designs to their transformative applications. We explored how hydrogel inks can be engineered to balance printability with functionality, emphasizing the interplay between rheology, conductivity, adhesion, and biocompatibility. We also examined the performance of implantable and wearable systems fabricated *via* DIW and related techniques, showing their potential in electrophysiological recording, precise stimulation, and multimodal biosensing. Despite these substantial advances, several key directions require further investigation.

(1) Integrated multifunctional printing: current devices often focus on single functions; however, physiological processes are inherently multidimensional. A key goal is to develop multi-material, multi-scale 3D printing techniques that enable the seamless integration of sensing, actuation, and therapeutic modules. Achieving this will require advances in interfacial fusion, such as optimizing the ink rheology and polymerization, to ensure robust bonding between dissimilar materials. Hybrid printing methods could bridge the gap between microscale biomimicry and macroscale mechanical conformity, while spatiotemporal programming could create "smart" systems that adapt to physiological cues in real time.

(2) Intelligent manufacturing. The reliance on artisanal expertise limits the standardization and scalability of 3D-printed bioelectronics. Data-driven intelligent manufacturing frameworks must be developed to address this issue. Such systems would combine comprehensive material and process databases with machine learning to predict and optimize the device performance. *In situ* monitoring and closed-loop feedback could further enhance quality control, enabling real-time adjustments and defect correction during fabrication.

(3) Personalized applications. The future of 3D-printed bioelectronics lies in personalized applications, moving beyond anatomical fitting to functional customization. Advanced manufacturing can produce electrode arrays with intricate 3D geometries tailored to individual neuroanatomical and electrophysiological profiles. By co-integrating heterogeneous elements, 3D printing can enable multimodal sensing platforms for targeted health monitoring, accelerating the clinical translation of personalized diagnostics and therapies.

BIOGRAPHY

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Conflict of Interests

The authors declare no interest conflict.

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Graphical Abstract

Direct Ink Writing 3D Printing of Hydrogel Bioelectronics

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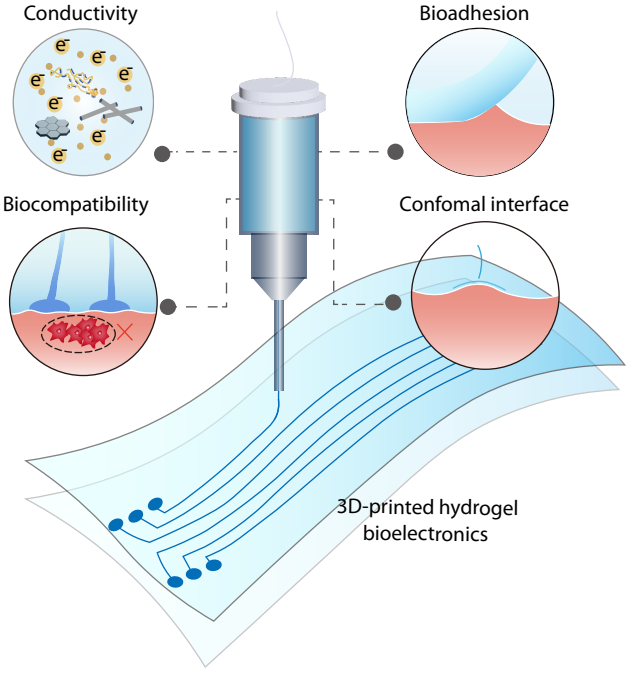
Direct-ink-writing 3D printing provides a versatile platform for fabricating advanced hydrogel bioelectronics. This review outlines recent advances, beginning with hydrogel ink design that balances printability and functionality through rheology, conductivity, adhesion, and biocompatibility. It subsequently emphasizes their application in state-of-the-art bioelectronics, highlighting their advantages in electrophysiological recording, stimulation, andbiosensing.



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