

Multiscale piezoionic transduction: From materials engineering to bioelectronic sensing and therapeutic applications

Yueguang Xue^{1,2,4,§}, Weixian Zhou^{2,3,§}, Xin Huang^{1,2,4}, Chubing Lin^{1,2,4}, Minxuan Jia^{1,2,4}, Guanghui Zhang^{1,2,4}, Mengke Zhu², Yi Liu², Ru Bai², Yuan Zhang¹, Shanshan Xu⁵(✉), Ying Liu²(✉)

¹ School of Biomedical Sciences and Engineering, South China University of Technology, Guangzhou 511442, China

² CAS Key Laboratory for Biomedical Effects of Nanomaterials and Nanosafety & CAS Center for Excellence in Nanoscience, National Center for Nanoscience and Technology of China, Beijing 100190, China

³ University of Chinese Academy of Sciences, Beijing 100049, China

⁴ The GBA National Institute for Nanotechnology Innovation, Guangzhou 510700, China

⁵ Institute for Advanced Study, Shenzhen University, Shenzhen 518060, China

§ Yueguang Xue and Weixian Zhou contributed equally to this work.

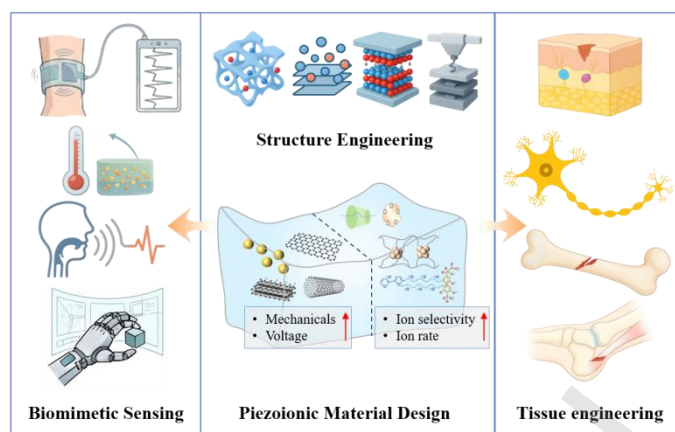
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Piezoionic materials convert mechanical deformation into electrical signals through asymmetric ion transport. Molecular, structural, and interfacial engineering regulates this process for physiological monitoring, neuromorphic interfaces, neuromodulation powered by mechanical energy, drug delivery, and tissue regeneration.

Multiscale piezoionic transduction: From materials engineering to bioelectronic sensing and therapeutic applications

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¹ School of Biomedical Sciences and Engineering, South China University of Technology, Guangzhou 511442, China

² CAS Key Laboratory for Biomedical Effects of Nanomaterials and Nanosafety & CAS Center for Excellence in Nanoscience, National Center for Nanoscience and Technology of China, Beijing 100190, China

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⁴ The GBA National Institute for Nanotechnology Innovation, Guangzhou 510700, China

⁵ Institute for Advanced Study, Shenzhen University, Shenzhen 518060, China

[§] Yueguang Xue and Weixian Zhou contributed equally to this work.

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 Address correspondence to Ying Liu, liuy@nanocr.cn; Shanshan Xu, xuss@szu.edu.cn

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ABSTRACT: Mechanical deformation in living tissues generates electrical cues through ion transport, yet conventional bioelectronic interfaces remain poorly matched to soft, hydrated environments. Piezoionic materials offer a compliant alternative by converting deformation into electrical signals through mechanically perturbed electrochemical potentials and coupled ion-solvent transport rather than lattice polarization. This review examines the physicochemical basis of piezoionic transduction and multiscale strategies spanning ion-polymer interactions, nanoconfined channels, structural gradients, and electrode interfaces. These designs regulate ion selectivity, transport kinetics, electrical output, and energy conversion, enabling physiological sensing, multimodal perception, energy harvesting, and therapeutic intervention. Reported outputs span millivolts to hundreds of millivolts and nanoamperes to milliamperes, and have activated peripheral and autonomic nerves, driven electrochemical drug release, and supported cartilage, bone, and wound repair in vivo. Unstable output and the unquantified dose reaching tissue remain the principal obstacles to clinical devices that integrate diagnosis and therapy.

KEYWORDS: piezoionic, mechanoelectrical transduction, intelligent soft materials, neuromorphic ionic interfaces, tissue regeneration

1 Introduction

Mechanotransduction serves as a ubiquitous signaling modality in biological systems where soft tissues and specialized membrane channels convert physical forces into ionic currents to regulate physiological functions ranging from tactile sensation to cardiovascular homeostasis[1–3]. Replicating this ion-based mechanism in synthetic materials is a central goal of bioelectronics. Conventional rigid piezoelectric materials are mechanically and functionally mismatched with soft biological tissues, limiting their long-term stability and biocompatibility in wearable and implantable devices[4–7]. Piezoionic materials offer a distinct solution in which the operating principle arises from the asymmetric migration of mobile ions induced by mechanical stress within a hydrated polymer matrix, rather than from classical piezoelectric polarization[8, 9]. Piezoionic transduction is therefore a specific form of mechanoelectrical transduction, the broader conversion of mechanical input into electrical output. Its physical basis lies in mechano-ionic coupling among deformation, solvent flow, electrochemical potential, and ion transport. Although early

studies in fixed-charge polyelectrolyte networks noted this effect[10], Dobashi et al. demonstrated that pressure gradients in electrolyte-infused hydrogels without fixed polymer charges can generate ionic currents[11]. These findings confirm that piezoionic transduction does not require a charged polymer backbone and broaden the design space for soft interfaces based on ion-mediated mechanoelectrical transduction (**Fig. 1**).

Although the fundamental principles of piezoionic transduction are established, the intrinsic ion mobility difference in simple aqueous electrolytes typically yields low voltage and current outputs, necessitating advanced engineering to amplify differences in ion mobility and establish directional ion transport. At the molecular level, precise manipulation of ion-polymer interactions has proven effective in differentiating transport rates. For instance, grafting crown ether moieties onto the polymer backbone creates specific host-guest traps that strip the hydration shells of target cations, thereby selectively accelerating their migration relative to anions and amplifying the voltage response[12]. Complementing this kinetic regulation, macroscopic structural engineering focuses on establishing

built-in electrochemical gradients to rectify ion flux. The construction of gradient polycation and polyanion heterojunctions introduces intrinsic transmembrane

potentials that supplement the stress-induced signal, significantly boosting the open-circuit voltage and power

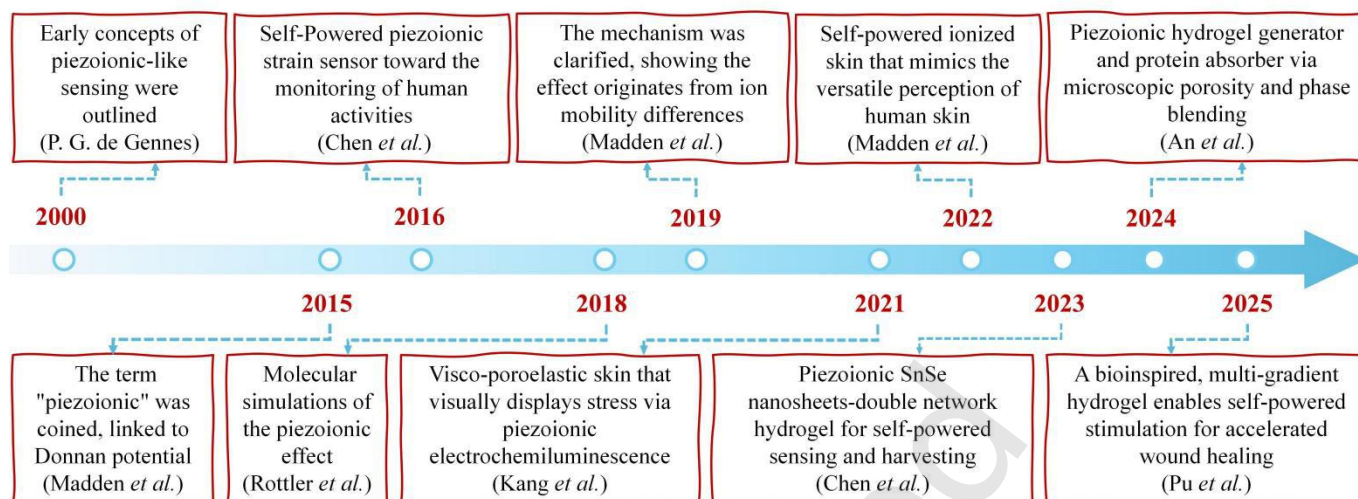


Figure 1 Timeline of key developments in piezoionic materials.

density beyond the limits of homogeneous materials[13]. These strategies, evolving from simple physical confinement to sophisticated molecular recognition and gradient engineering, represent a pivotal advancement in optimizing the energy conversion efficiency of soft ionotronics. The functional scope of piezoionic materials is currently transitioning from passive mechanical sensing to active therapeutic intervention and information processing. While initial applications were primarily directed toward wearable sensors for monitoring physiological activities such as pulse and limb motion[14, 15], recent advances utilize the dynamic ionic response to emulate biological computation. By exploiting nonlinear ionic transport and threshold-based firing behaviors, piezoionic devices can now function as

neuromorphic interfaces that simulate synaptic plasticity and perform logic operations[16–18]. More significantly, these materials are being engineered as self-powered platforms for in situ biomedical therapy. The ionic currents generated by mechanical deformation are sufficient to stimulate peripheral nerves for neuromodulation or to drive the release of therapeutic agents[19, 20]. Additionally, the localized bioelectric fields established by piezoionic scaffolds have been shown to influence cellular behavior, promoting the regeneration of tissues such as cartilage and bone by reprogramming the metabolic microenvironment[21–23]. This evolution marks a shift towards autonomous bioelectronic systems where the material acts as both the energy harvester and the therapeutic effector.

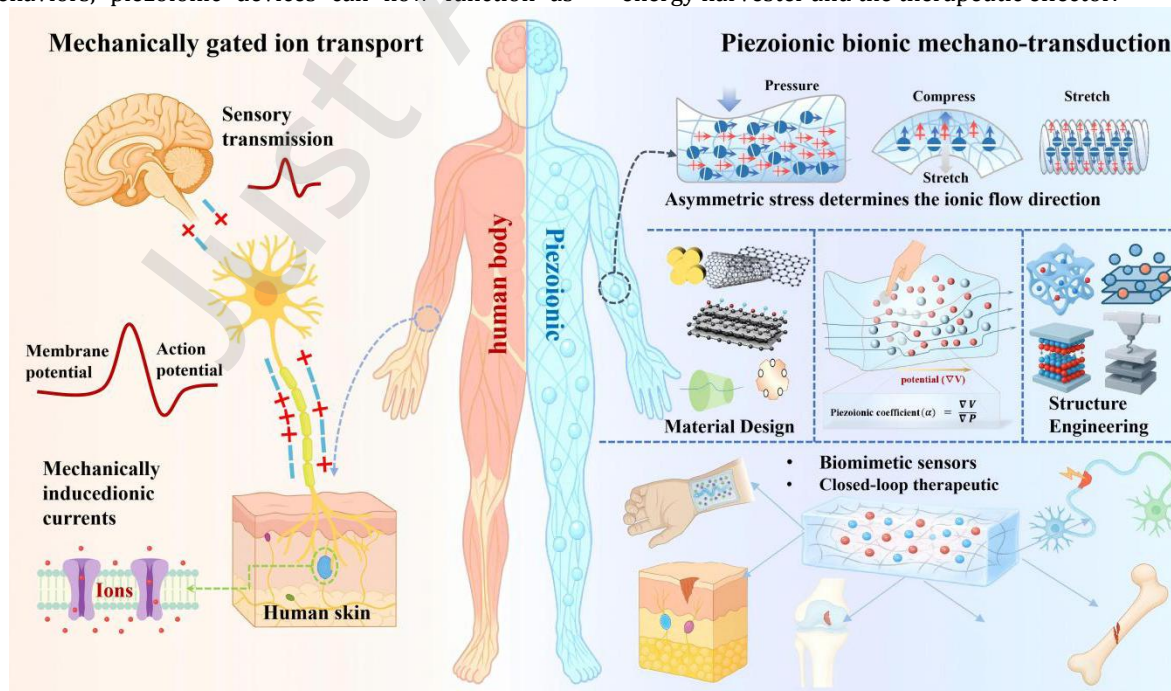


Figure 2 Schematic illustration of the working mechanism, fabrication strategies, and biomedical applications of piezoionic materials.

Here, we review the recent advances in piezoionic materials, deconstructing the physicochemical principles that govern

mechano-ionic coupling and analyzing how multiscale material engineering strategies translate these principles

into improved material and device performance. The expanding landscape of applications is then surveyed, from biomimetic sensing and neuromorphic interfaces to mechanically activated neuromodulation, drug delivery, and tissue-repair systems, followed by a discussion of the critical challenges and future directions for the field (Fig. 2).

2 Mechanisms of piezoionic transduction: stress induced asymmetric ion migration

The piezoionic effect arises when mechanical deformation generates a pressure or strain gradient that drives asymmetric migration or redistribution of mobile ions within an ion-conducting matrix. Differences in ionic

transport under convective or diffusive flow then produce a net voltage or current. This transport basis distinguishes piezoionic transduction from responses dominated by lattice polarization, contact electrification, thermodiffusion, or deformation-dependent capacitance. Elucidating this transduction mechanism demands a multiscale framework linking macroscopic poroelasticity to microscopic ion dynamics. Mathematical models integrating Poisson-Nernst-Planck equations and molecular simulations quantify these transport phenomena across diverse deformation modes[9]. We discuss the physicochemical foundations of the piezoionic effect to support prediction and optimization of the magnitude and temporal characteristics of piezoionic outputs.

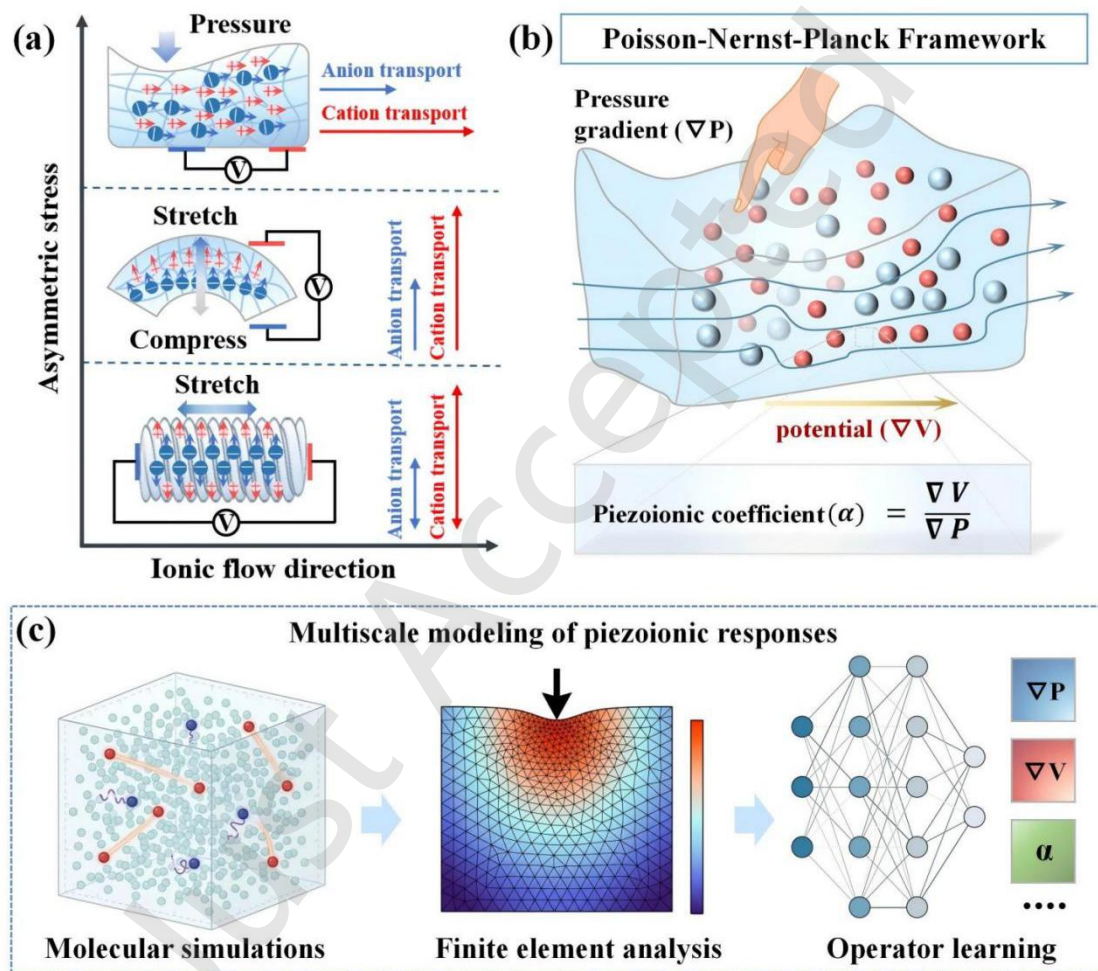


Figure 3 Principles and multiscale modeling of the piezoionic effect. (a) Asymmetric ion migration induced by compression, bending, and tensile stretching. (b) Theoretical framework based on the Poisson-Nernst-Planck equations, defining the piezoionic coefficient as the ratio of the generated potential gradient to the applied pressure gradient. (c) Multiscale modeling framework integrating molecular simulation, continuum finite-element analysis, and data-driven operator learning for evaluating and predicting piezoionic responses.

2.1 Mechanical pressure gradients drive convective ion flow and redistribution

Non-uniform mechanical stress serves as the primary thermodynamic driver, establishing internal pressure or chemical potential gradients that force a convective flow of solvated ions relative to the polymer backbone[11, 24, 25]. While the fundamental outcome of charge separation is universal, the specific physical gradient driving this ionic imbalance is strictly dictated by the mode of mechanical

deformation (Fig. 3(a)). In polyelectrolyte systems such as polyacrylic acid hydrogels, the polymer chains act as a negatively charged and immobile backbone due to network interlocking, while the dissociated counter ions remain free to migrate. Upon uniaxial compression, the local density of the polymer network increases and creates a localized region of high ionic concentration. Driven by the thermodynamic requirement to equilibrate chemical potential, protons or other counter ions diffuse directionally

from the compressed region to the uncompressed domain[26]. The magnitude of the resulting electrical signal correlates directly with the concentration gradient established by the deformation magnitude. A more intricate transport phenomenon emerges under bending deformation where a strain gradient exists across the material thickness. The non uniform deformation generates a pore pressure gradient that drives the convective flow of the solvent[27]. As the solvent moves from the compressed inner layer to the stretched outer layer, it entrains mobile cations and anions. Due to differences in hydrated radii and interactions with the polymer matrix, the transport rates of cations and anions diverge within this convective stream, leading to a net macroscopic charge separation and flexoelectric polarization. The flexoelectric coefficient in these systems serves as a metric for the efficiency of converting the strain gradient into electric polarization and highlights the critical role of fluid dynamics coupled with ionic transport in the transduction mechanism.

In contrast to bulk hydrogels, fibrous piezoionic systems utilize a dynamic interfacial mechanism governed by the modulation of the electrical double layer. When a gel electrolyte coated carbon nanotube yarn undergoes asymmetric stretching, the deformation propagates along the fiber and induces a dynamic squeezing of the electrolyte infiltrated within the twisted structure[28]. The reduction in inter bundle spacing forces a redistribution of ions at the electrode and electrolyte interface. Unlike the continuous solvent flow observed in hydrogels, the signal generation in these high surface area electrodes arises from the disruption of the electrochemical equilibrium. Tensile stress causes the densification of the yarn core, which physically expels ions from the electrical double layer into the bulk gel. The polarity of the generated voltage is determined by the specific adsorption affinity of the ions; anions with lower hydration energy typically desorb more readily than strongly hydrated cations[29]. The resulting potential gradient along the yarn allows for self-powered sensing without external bias. The mechanism effectively converts the mechanical work done against electrostatic attraction and steric repulsion within the double layer into electrical energy.

The ultimate determinant of the piezoionic response magnitude and polarity lies in the physicochemical disparity between cationic and anionic transport properties. Whether driven by bulk diffusion, poroelastic convection, or interfacial desorption, the net signal depends on how distinct ionic species interact with the confining environment. Experimental observations reveal that the sign of the voltage can invert based on electrolyte concentration and solvent type, indicating a crossover in effective mobility[30]. At the molecular level, ions with rigid hydration shells experience greater steric hindrance and drag when navigating through a collapsing polymer mesh compared to ions with flexible solvation shells. Furthermore, the presence of fixed background charges on the polymer chains introduces Donnan exclusion effects that selectively suppress the transport of co-ions while enhancing counter-ion mobility. Consequently, the piezoionic effect is fundamentally the macroscopic manifestation of such

microscopic inequalities in ionic transport numbers.

2.2 Multiscale modeling elucidates ion transport dynamics

Elucidating the physicochemical origins of the piezoionic effect demands a sophisticated theoretical hierarchy that spans from continuum thermodynamics to atomistic kinetics. At the macroscopic level, the prevailing model couples poroelasticity theory with the Poisson-Nernst-Planck equations to describe the hydrogel as a biphasic medium (**Fig. 3(b)**). In this framework, an externally applied mechanical stress establishes a hydrostatic pressure gradient (∇P), which serves as the primary driving force for the convective transport of the interstitial electrolyte. The fundamental origin of the piezoionic potential (∇V) is mathematically derived from the disparity in the transport properties of cationic and anionic species relative to the solvent flow. According to the foundational theory established by Dobashi *et al.* [11], the piezoionic coefficient (α) is explicitly defined by the differential diffusion coefficients of the mobile ions (Eq. (1)):

$$\alpha = \frac{\nabla V}{\nabla P} = -\frac{eN\kappa}{\sigma\eta} \left[\frac{D_+}{D_{0+}} - \frac{D_-}{D_{0-}} \right] \quad (1)$$

where e is the elementary charge, N is the ion concentration, κ is the matrix permeability, σ is the ionic conductivity, and η is the fluid viscosity. The terms $D_{\pm}$ and $D_{0\pm}$ represent the diffusion coefficients within the hydrogel and in the bulk solution respectively. This equation elegantly quantifies how the voltage polarity and magnitude are strictly dictated by the specific mobility difference between cations and anions.

To capture the transient dynamics of this process in complex geometries, finite element analysis has proven indispensable. Recent computational studies have formalized the governing physics into a coupled system of partial differential equations[31]. The total flux of an ionic species κ (F_{κ}) is described as the superposition of advection, diffusion, and electromigration. Specifically, the advective flux (F_{adv}^{κ}) is driven by the pressure gradient and modified by a hindrance factor β^{κ} representing ion polymer interactions (Eq. (2)):

$$F_{adv}^{\kappa} = -\beta^{\kappa} \chi^{\kappa} \rho \frac{k}{\mu} \nabla P \quad (2)$$

In this expression, χ^{κ} is the mass fraction of species κ , ρ is the fluid density, k is the permeability of the porous medium, and μ is the fluid viscosity. This advective term is then integrated into the total flux equation, which also accounts for diffusive transport due to mass fraction gradients ($\nabla \chi^{\kappa}$) and electromigration driven by the electric field ($\nabla \chi^{\kappa}$) (Eq. (3)):

$$F^{\kappa} = -\beta^{\kappa} \chi^{\kappa} \rho \frac{k}{\mu} \nabla P - \rho \phi D^{\kappa} \nabla \chi^{\kappa} + \rho \chi^{\kappa} \frac{D^{\kappa} z^{\kappa} e}{k_B T} \nabla \psi \quad (3)$$

Here, ϕ represents the porosity of the hydrogel, D^{κ} the diffusivity of species κ , z^{κ} is the valence number, k_B is the Boltzmann constant, and T is the absolute temperature. Finally, the evolution of the electric potential is governed by the Poisson equation, which couples the net charge density to the dielectric properties (Eq. (4)):

$$\nabla^2 \psi = -\frac{1}{\epsilon} \sum_{\kappa} \frac{1000 \rho \phi \chi^{\kappa} z^{\kappa} e N_A}{M_o^{\kappa}} \quad (4)$$

where ϵ is the permittivity of the hydrogel, N_A is the Avogadro constant, and M_o^{κ} is the molar mass of species κ . Solving this coupled system provides a continuum-level description of piezoionic transduction. It accurately predicts

complex temporal dynamics, such as the transient recovery peak observed upon stress release, which is mechanistically attributed to the backward advective flow restoring equilibrium[31]. For specific applications in vibrational energy harvesting, this continuum theory is often abstracted into vibro electrochemomechanical models utilizing resistive capacitive transmission line circuits, which effectively map the distributed strain along a cantilever to charge accumulation dynamics[32].

To rigorously validate these theoretical predictions against experimental reality, novel characterization methods have been developed. The advective transport mechanism postulated in Eq. (2) has been substantiated through spatiotemporal mapping using multi-electrode arrays, which reveals a distinct temporal latency in voltage peaks recorded at spatially separated electrodes[31]. This propagation delay confirms that the electrical signal travels at the speed of pore fluid diffusion rather than the instantaneous speed of electron conduction. Complementing this, frequency domain analysis has been employed to extract transfer functions under open circuit and short circuit conditions, effectively decoupling the intrinsic transduction efficiency from the mechanical resonances of the device structure[33]. Furthermore, experimental validation in structural engineering using geometrically asymmetric hydrogels has shown that structural inhomogeneity amplifies local Darcy velocity and stress concentration, thereby enhancing convective ion flux. Crucially, these experiments also corroborated the differential mobility theory (Eq. (1)) by substituting salts with varying ionic radii—validating that mobility scales with bare ionic radius for alkali metals ($\text{Li}^+ < \text{Na}^+ < \text{K}^+$) while being significantly constrained by steric hindrance in bulky organic anions like (TFSI^-) to modulate and even reverse the signal polarity[34].

While continuum models successfully describe macroscopic transport, elucidating the thermodynamic origins of interaction parameters such as the hindrance factor β^c necessitates a molecular level perspective. By probing the ion-polymer interface through coarse-grained molecular dynamics, researchers have established that the pressure-induced potential is fundamentally a perturbation of the Donnan equilibrium[35]. The simulation results reveal a direct linear relationship between the generated Nernst-Donnan potential and the lateral pressure gradient offering a molecular level validation of the macroscopic phenomenon. However, capturing the physicochemical intricacies of ion specific behaviors requires higher fidelity approaches beyond coarse grained models. Recent multiscale

simulations combining density functional theory with all atom molecular dynamics have delved into the electric double layer dynamics revealing that structural asymmetry dictates adsorption kinetics[36]. The sequential collapse of the outer and inner Helmholtz planes demonstrates how hydronium ions facilitate polarization while chloride anions drive current generation through a unipolarization process providing an atomistic mechanism that explains the high energy conversion efficiency observed in specific electrolytes. However, the atomistic fidelity of these simulations comes at a prohibitive computational cost, restricting their application to nanosecond timescales and nanometer length scales.

To overcome these spatiotemporal limitations, the field is embracing data-driven modeling as a high-efficiency alternative to traditional multiphysics solvers (**Fig. 3(c)**). Deep Operator Networks (DeepONets) have emerged as surrogate models capable of learning the nonlinear operators that map sparse sensor measurements to full spatiotemporal fields[37]. Trained on high fidelity datasets generated from experimentally calibrated finite element analysis these networks can predict pressure and ion concentration distributions orders of magnitude faster than conventional methods enabling real time analysis for tactile imaging. Beyond computational innovations theoretical exploration has also expanded to novel mechano-transduction mechanisms such as the interfacial ionic p-n junction. In contrast to bulk transport models, simulations based on Poisson-Nernst-Planck equations in this paradigm demonstrate that the electrical signal arises not from bulk ion migration but from the mechanical modulation of the depletion layer at the contact interface[38]. Notwithstanding these methodological strides current theoretical frameworks remain constrained by the disconnect between macroscopic and microscopic descriptions. In continuum models key parameters like the hindrance factor are often treated as empirical fitting constants rather than being derived from their thermodynamic origins established by molecular simulations. Bridging this divide requires the development of unified models that rigorously link molecular interactions to macroscopic transport. Collectively these evolving theoretical frameworks ranging from continuum equations to atomistic simulations alongside novel spatiotemporal characterization techniques provide a robust foundation for designing next generation piezoionic devices.

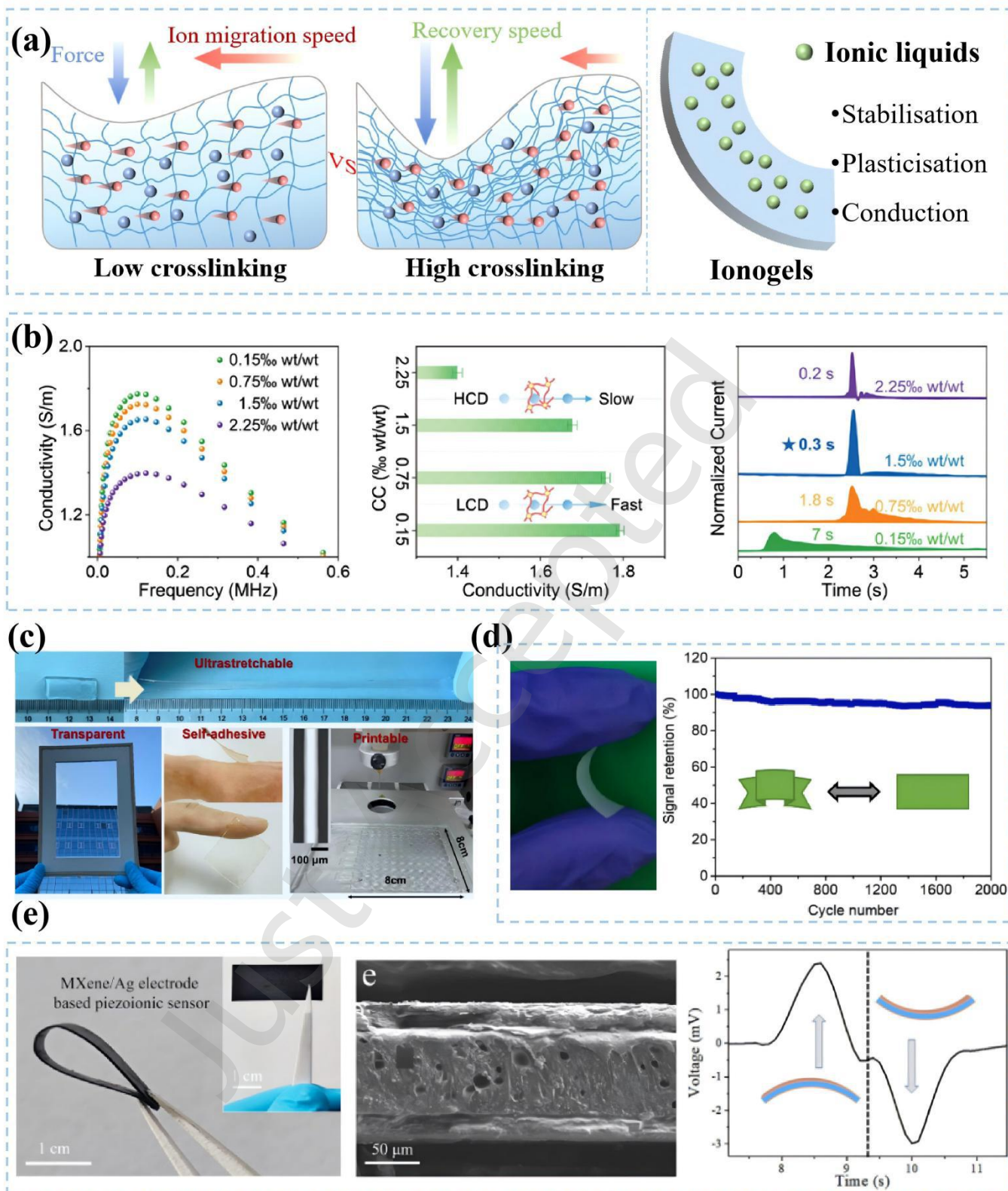


Figure 4 Evolution and performance-enhancement strategies of ionic matrix systems. (a) Effects of hydrogel crosslinking and ionic liquids on ion mobility and matrix stability. (b) Crosslink density regulates electrochemical performance. Reprinted with permission from Ref. [39], Copyright 2024 Wiley-VCH GmbH. (c) Stretchable, transparent, and adhesive hydrogels for dual force and temperature sensing. Reprinted with permission from Ref. [40], Copyright 2021 American Chemical Society. (d) Solution-processed ionogel film retaining a stable signal after 2,000 deformation cycles. Reprinted with permission from Ref. [41], Copyright 2022 Elsevier. (e) Laminated three-layer elastomer-based ionogel for vectorial sensing with opposing electrical signals. Reprinted with permission from Ref. [42], Copyright 2024 Elsevier.

3 Multiscale Material Engineering Enhances Piezoionic Transduction Performance

Elevating the piezoionic effect from a fundamental physicochemical phenomenon to a viable technological platform necessitates a concerted evolution in material engineering. Performance optimization relies on the deliberate modulation of intrinsic properties across multiple length scales, ranging from molecular network topology to macroscopic device architecture. Strategies such as the rational design of polymer crosslinking densities and the incorporation of non-volatile ionic liquids into elastomer matrices address critical challenges regarding environmental stability and signal fidelity. Further enhancement is achieved through the integration of functional nanocomposites and the construction of bio-inspired gradient structures, which collectively amplify mechano-ionic coupling and direct ion transport. Advanced fabrication techniques ultimately translate these sophisticated molecular and structural designs into integrated, robust systems capable of precise signal transduction.

3.1 Material component design for intrinsic kinetics and operational stability

The evolution of ionic matrix systems underpins the advancement of piezoionic devices, transitioning from simple hydrogels to sophisticated, environmentally resilient architectures. Functional hydrogels leverage tunable network topologies and chemical modifications to optimize electromechanical coupling and bio-interfacing capabilities. To overcome aqueous limitations, ionogels and ionomers incorporate non-volatile ionic liquids, ensuring long-term stability and mechanical robustness (**Fig. 4(a)**). Furthermore, the integration of functional nanocomposites and molecular recognition elements enhances mechanical toughness and charge selectivity, improving mechanical toughness and signal transduction efficiency (**Fig. 5(a)**).

3.1.1 Crosslinking density controls ion mobility and signal recovery

Hydrogels possess an inherent advantage in bio-interfacing due to their high water content and tissue-like mechanical compliance, yet the precise modulation of their electromechanical response remains a complex challenge governed by the polymer network topology. The efficacy of hydrogels in piezoionic transduction originates in tight coupling between a viscoelastic polymer network and a mobile ionic phase confined within interstitial water. Regulation of electromechanical kinetics therefore depends on precise control of network topology, with crosslinking density governing both mechanical relaxation time and ionic mean free path (**Fig. 4(b)**). Recent theoretical and experimental studies converge on a central trade off, a densely crosslinked network strengthens the elastic restoring force and accelerates signal recovery, yet steric constraints within the tightened mesh simultaneously impede ion migration[39]. Such mesh size modulation operates as a frequency selective element, enabling discrimination between transient impacts and sustained static pressure through the temporal evolution of ionic

gradients[43]. By tuning the monomer to crosslinker ratio, the hydrogel can shift from a passively deformable solid to a programmable transduction medium that encodes temporal information into electrical output[44].

Beyond physical confinement, chemical functionalization of the polymer backbone enables dynamic intermolecular interactions that enhance ionic conductivity and improve interfacial compatibility. Introducing zwitterionic moieties into polysaccharide networks establishes electrostatic interactions that dissipate fracture energy under deformation while maintaining high ionic conductivity[40]. Such molecular architectures can also confer conformal adhesion across diverse substrates and suppress crystallization, thereby sustaining high optical transparency for unobtrusive wearable implementations (**Fig. 4(c)**). More broadly, chemically engineered matrices can alleviate impedance mismatch at bioelectronic interfaces, promoting high fidelity signal transmission from compliant soft tissues to rigid electronic components.

Macroscopic assembly of heterogeneous hydrogel layers enables complex functional architectures for advanced signal transduction and energy harvesting. Biomimetic designs that alternate cation selective and anion selective hydrogels can rectify stress driven ion flux to produce additive potentials, illustrating how spatially programmed ionic gradients amplify energy conversion efficiency[45]. In parallel, integration of piezoionic transduction with potentiometric sensing within a single interface enables concurrent readout in which physical pressure signals are distinguished from biochemical concentration information[46]. Collectively, these advances demonstrate that the hydrogel's tunable architecture, spanning its physical network, chemical composition, and functional integration, establishes it as the leading material for advanced piezoionic systems.

3.1.2 Ionic liquids and solid-state architectures for piezoionic performance retention

Ionogels and ionically conductive elastomers offer a robust material platform engineered to overcome the intrinsic environmental limitations of aqueous gel systems. Their composition involves a polymer matrix, physically encapsulating a non-volatile ionic liquid. Scalable fabrication methods, including solution casting, yield uniform, solid films suitable for device integration[47, 48]. Intrinsic non-volatility of the ionic liquid safeguards the hydrogel against solvent depletion, forestalling compositional drift and perpetuating a stable ionic inventory throughout protracted operation. Under 1.5% strain, an ionogel-based piezoionic sensor generated 2.11 mV and retained 94% of its signal after 2,000 cycles in air (**Fig. 4(d)**) [41]. Comparable cyclic durability was observed for an externally driven hybrid PVDF/ionic-liquid actuator, with peak-to-peak displacement remaining stable over 300 cycles at 10 Vpp and 0.2 Hz[49]. Elastomer-based ionogels also enable laminated solid-state architectures in which an ionic polymer layer is placed between flexible electrodes (**Fig. 4(e)**) [42]. Opposing bending directions generate voltage signals of opposite polarity, supporting directional mechanical sensing. Introducing Ag nanoparticles between MXene sheets increased the interlayer spacing and suppressed electrode restacking. Resulting MXene/Ag sensors produced 11.1 mV

at 0.7% bending strain and retained 95% of their signal over 13,000 s of cyclic bending. VHB encapsulation further protected the device against unintentional damage and ambient humidity.

Damage-tolerant molecular networks provide additional routes to maintaining function after repeated deformation. UiO-66-NH₂/PAA-reinforced TPU ionogels reached 850% elongation and showed negligible signal deterioration beyond 3,000 bending cycles[47]. Following recycling,

elongation remained at 766%, whereas ionic conductivity decreased from 44.1 to 20.8 $\mu\text{S}/\text{cm}$ because of ionic-liquid loss[50]. Mechanical recovery therefore did not fully restore ion-transport performance. Cl-functionalized polyurethane iontronic material reached 91% self-healing within 60 min at room temperature and 20-40% relative humidity. Electrical conduction recovered within 1 min after a partial-thickness cut, while mechanical durability was assessed separately over 250 pressure cycles[51].

Table 1 Nanocomponent functions and principal performance enhancements in piezoionic and hybrid composites

Matrix system	Nanocomponent	Function of nanocomponent	Principal performance enhancement	Ref.
Nanostructured interfaces for signal amplification				
Nafion/ionic-liquid membrane	Graphene/CNT porous electrode	Increase interfacial area and conductivity	Increased voltage output (from 1.3 to 4.5 mV)	[14]
TPU ionogel	MXene/Ag heterostructure	Increase ion storage and transport	Increased voltage output (to 11.1 mV)	[42]
PVA/H ₂ SO ₄ electrolyte	gel Coiled CNT yarn	Create asymmetric ion squeezing	Increased voltage output and bandwidth (to 15 mV; 0.1–10 Hz)	[28]
PVDF-HFP ionogel	Ultrathin nanosheets	MXene Provide ion channels and storage sites	Increased voltage output (to 219 mV)	[52]
Multilayer polyelectrolyte hydrogel	Aligned microchannels	MXene Direct ion transport	Increased voltage and power output (to 1.41 V; 2.9 mW/m ²)	[53]
TPU ionogel	CNT/graphene electrode	porous Open ionic and electronic pathways	Improved current response and sensing speed (0.62 μA ; 0.10 s response)	[54]
Nanocomponents for mechanical reinforcement and multifunctionality				
PAAm/PVA double-network ionogel	Graphene	Reinforce the network and ion pathways	Increased ionic conductivity and storage (0.186 mS/cm; 213 F/g)	[55]
PAA/TPU ionogel	UiO-66-NH ₂ metal-organic framework	Provide reversible crosslinks	Increased stretchability and recyclability (850% elongation)	[50]
PAA hydrogel film	Chitin nanofibres	Reinforce the matrix	Increased tensile strength and modulus (32 and 166 MPa)	[21]
PAA hydrogel	Liquid-metal nanoparticles/CNC	Initiate polymerization and toughen the network	Increased stretchability and toughness (approximately 2,000%; approximately 1.8 MJ/m ³)	[56]
PVA/H ₂ SO ₄ electrolyte	gel AgNW/graphene aerogel	Provide an elastic conductive framework	Improved pressure sensing and storage (2.54 kPa ⁻¹ ; 146.6 F/g)	[57]
PVA/PAM/PSSNa hydrogel	MXene/CNF composite with silane/PFPE coating	Reinforce and limit solvent loss	Improved environmental resistance (33.4% water loss at 7 d; stable output to -80 °C)	[58]
Nanocomponents for anisotropic or hybrid transduction				
Chemically crosslinked ionogel	BaTiO ₃ nanoparticles	Add directional ferroelectric polarization	Enabled directional low-frequency sensing (0.1-1 Hz)	[59]
Double-network hydrogel	SnSe nanosheets	Concentrate stress and add polarization	Increased piezoionic response and strength (1,780 nV/Pa; 1,273 kPa at 90% strain)	[60]
Porous TPU/ionic-liquid matrix	Silica nanoparticles	Stabilize anisotropic pores	Expanded sensitivity and pressure range (0.23 mV/kPa; up to 634 kPa)	[61]
Porous TPU/WPU bilayer film	Single-walled carbon nanotubes	Enable ionic and electronic transfer	Enabled multimodal pressure sensing (1.2 kPa ⁻¹ ; 45-625 kPa)	[62]

Ionomers constitute a distinct class of solid ionic materials in which ionic groups are covalently tethered to the polymer

backbone. Within EMITFSI-swollen Aquivion composites, signal generation depended strongly on mechanical

matching across the electrode-electrolyte assembly[47]. Electrode modulus, rather than electronic conductivity alone, governed the efficiency of stress transfer to the ionomeric core. Repeated stimulation nevertheless caused delamination of pristine PEDOT:PSS electrodes, identifying interfacial integrity as an additional determinant of operational stability. Across these material and device configurations, reported stability remains specific to the applied loading mode, test duration and environmental condition. Ambient cycling, encapsulation and self-healing measurements establish short-term operational durability, whereas retention of electrical output, ionic composition and interfacial integrity during prolonged physiological exposure remains insufficiently evaluated.

3.1.3 Nanocomposites improve hydrogel toughness and piezoionic efficiency

The integration of nanoscale fillers into piezoionic polymer matrices represents a pivotal strategy for transcending the performance limitations of single-component systems and imbuing them with multifunctionality (Table 1). A key

manifestation of this strategy is the engineering of the polymer matrix to achieve superior mechanical properties. Liquid metal nanoparticles stabilized by cellulose nanocrystals (CNC) exemplify this approach by acting as both polymerization initiators and dynamic cross-linking agents[56]. The resulting hydrogels exhibit a combination of high stretchability, sustaining strains up to 2000%, and efficient self-healing, recovering nearly all of their original toughness after being severed and rejoined. While such dynamic, non-covalent bonds impart high resilience and healability, they may also introduce challenges such as viscoelastic creep under prolonged static loads, a trade-off when compared to covalently cross-linked systems. Nanofillers can also be selected to impart additional functionalities directly into the matrix, as seen in graphene-reinforced ionogels that function as both sensing elements and energy storage units[55]. These advancements in matrix engineering provide a mechanically robust and functionally versatile foundation, which is a prerequisite for developing reliable signal transduction capabilities.

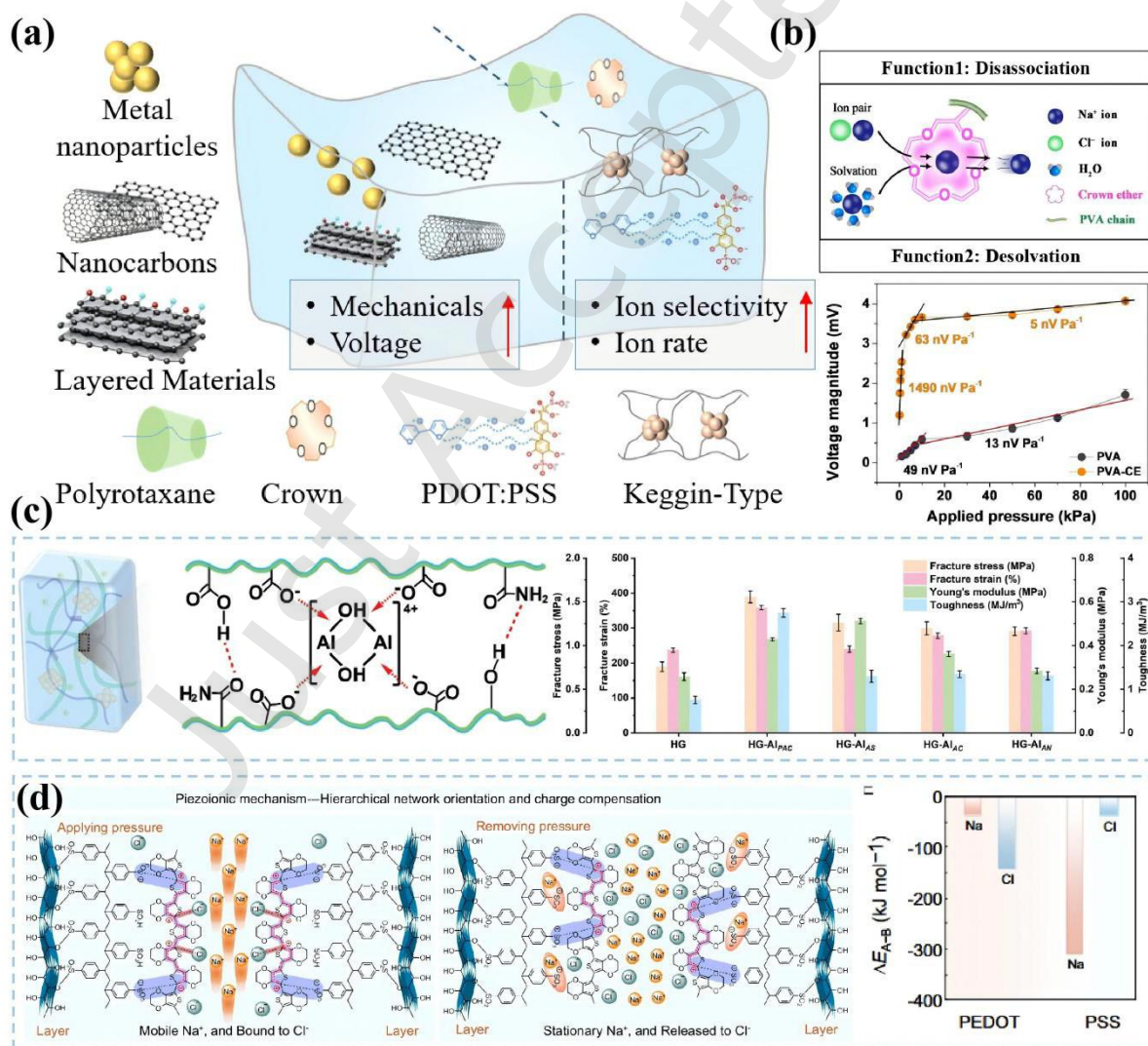


Figure 5 Nanocomposites and molecular interactions enhance hydrogel toughness and piezoionic performance. (a) Nanocomponent and molecular regulation strategies. (b) Crown-ether-based ion-selective mobility amplification and the corresponding approximately 30-fold increase in the piezoionic coefficient. Reprinted with permission from Ref. [12]. Copyright 2024 Wiley-VCH GmbH. (c) Stress-strain response and structure of spider-web-inspired aluminum-coordination clusters. Reprinted with permission from Ref. [63]. Copyright 2025 Wiley-VCH GmbH. (d) Dynamic charge compensation in conductive eutectogels for sustained ion streaming. Reprinted with permission under a Creative Commons CC BY License from Ref. [64]. Copyright 2026 Springer Nature.

Beyond matrix mechanics, the signal transduction efficiency of piezoionic composites is critically dependent on the engineering of the electrode-electrolyte interface. A composite electrode fabricated from graphene and carbon nanotubes exhibits a highly porous, interconnected network architecture[14]. This microstructural design, when compared to a standard gold electrode, results in a near fourfold increase in output voltage under identical strain conditions, from approximately 1.3 mV to 4.5 mV. The principle of performance enhancement through nanostructuring is further extended by the use of two-dimensional materials, where the exfoliation of bulk MXene into ultrathin nanosheets unlocks a pronounced piezoionic effect, yielding voltage outputs orders of magnitude higher than their bulk counterparts[52]. The enhanced performance is attributed to the highly accessible, layered structure of the nanosheets, which provides efficient ion migration channels in contrast to the tortuous pathways within bulk materials. Although these nanostructured interfaces significantly enhance signal transduction, the long-term chemical stability of certain nanomaterials like MXene in ambient, oxidative environments, alongside the scalability of uniform electrode fabrication, remain pertinent considerations for practical applications[14, 53]. While optimizing a single transduction pathway yields substantial gains, the integration of multiple physical principles or complex structural designs offers a route to more sophisticated functionalities.

The integration of nanomaterials can also be leveraged to introduce hybrid transduction mechanisms or to engineer anisotropic responses, enabling functionalities beyond simple strain detection. One approach involves creating hybrid systems that merge the isotropic piezoionic effect of an ionogel matrix with the anisotropic piezoelectric effect from dispersed ferroelectric nanoparticles like BaTiO₃[59]. The synergistic integration of ion redistribution and dipole alignment under pressure generates a direction-dependent electrical signal. The integration of 2D nanosheets with piezoelectric properties, such as SnSe, into a robust double-network hydrogel similarly enables high-fidelity force transduction. The resulting composite exhibits a fracture strength of 1273 kPa at 90% strain, while generating a non-linear but highly sensitive voltage and current output that scales with the applied force, reaching a piezoionic voltage coefficient of 1780 nV/Pa[60]. However, the development of such hybrid or multi-layered systems often introduces fabrication complexities, such as the need for high-voltage poling steps that may affect the ionogel matrix, or the challenge of ensuring robust adhesion between functionally distinct layers[61]. These composite-based approaches thus represent a significant shift from simple material enhancement to the deliberate design of integrated, multifunctional systems.

3.1.4 Molecular interactions enable ion selectivity

Precise manipulation of ion transport kinetics at the molecular level necessitates strategies that go beyond simple physical confinement, creating a paradigm where ionic mobility is dictated by host guest interactions. Grafting 15-crown-5-ethers onto polymer backbones exemplifies a

specific cation trapping mechanism where the cavity size matches sodium ions to strip their hydration shells and accelerate transport[12]. Such molecular precision yields an exceptional piezoionic coefficient of 1490 nV/Pa and an ultralow detection limit of 0.2 Pa, making the material ideal for high sensitivity detection (**Fig. 5(b)**). Distinct from this acceleration mode, polyrotaxane structures employing alpha cyclodextrin rings utilize a steric hindrance mechanism. Threading cyclodextrin rings onto polyacrylic acid chains forms a slide ring architecture that allows the rings to move along the polymer chain under mechanical deformation[65]. These mobile rings selectively impede the migration of larger hydrated ions while permitting smaller species to pass. The resulting signal output is amplified by more than eight times relative to unmodified networks. Crown ether architectures therefore excel in maximizing voltage response through kinetic acceleration, whereas polyrotaxane systems provide a generalized signal amplification strategy via steric gating, offering versatile options for designing high precision sensors.

Complementing the high sensitivity of supramolecular designs, modulating the electrostatic landscape and coordination environment of the polymer backbone addresses the critical requirements for current density and mechanical resilience. Incorporating inorganic ligands to form Keggin type aluminum clusters creates stable cationic nodes that electrostatically separate chloride ions (**Fig. 5(c)**). These polynuclear clusters form stable crosslinks with carboxyl groups through hydrogen and coordination bonds, which significantly elevates toughness to 2.75 MJ/m³ [63]. For applications prioritizing power output, acidifying polyacrylamide networks to protonate amide groups creates a dense positive field. The resulting high electrostatic potential effectively attracts anions to retard their transport, generating a substantial current output of 610.5 μ A[66]. Furthermore, dynamic charge compensation using conductive polymers like poly(3,4-ethylenedioxythiophene) doped with poly(styrenesulfonate) (PEDOT:PSS) bridges the gap between transient and continuous sensing. Strong interaction energy between PSS chains and sodium ions drives the inactivation kinetics (**Fig. 5(d)**), enabling a sustained response duration of 200 s via the reversible charge compensation mechanism[64]. These molecular level modifications serve as fundamental building blocks for high performance piezoionics. Yet, translating such molecular efficiencies into macroscopic devices necessitates the synergistic application of integrated fabrication strategies to construct hierarchical architectures.

3.2 Structure engineering directs piezoionic transport and integration

The optimization of piezoionic transduction necessitates a transition from intrinsic material synthesis to precise structural engineering across multiple length scales. Gradient architectures serve as a fundamental strategy to break centrosymmetry by employing spatial variations in charge density, modulus, and geometry to rectify ion transport and amplify signal output. Microstructural control and surface patterning strategies complement this macroscopic directionality by leveraging phase separation

and hierarchical textures to define efficient ionic pathways and modulate interfacial capacitance. Specific host-guest interactions and steric gating mechanisms at the molecular level are engineered to dictate charge selectivity and

transport kinetics. The realization of these sophisticated designs relies on integrated fabrication strategies where additive manufacturing and in-situ synthesis enable the seamless construction of robust, high-fidelity devices.

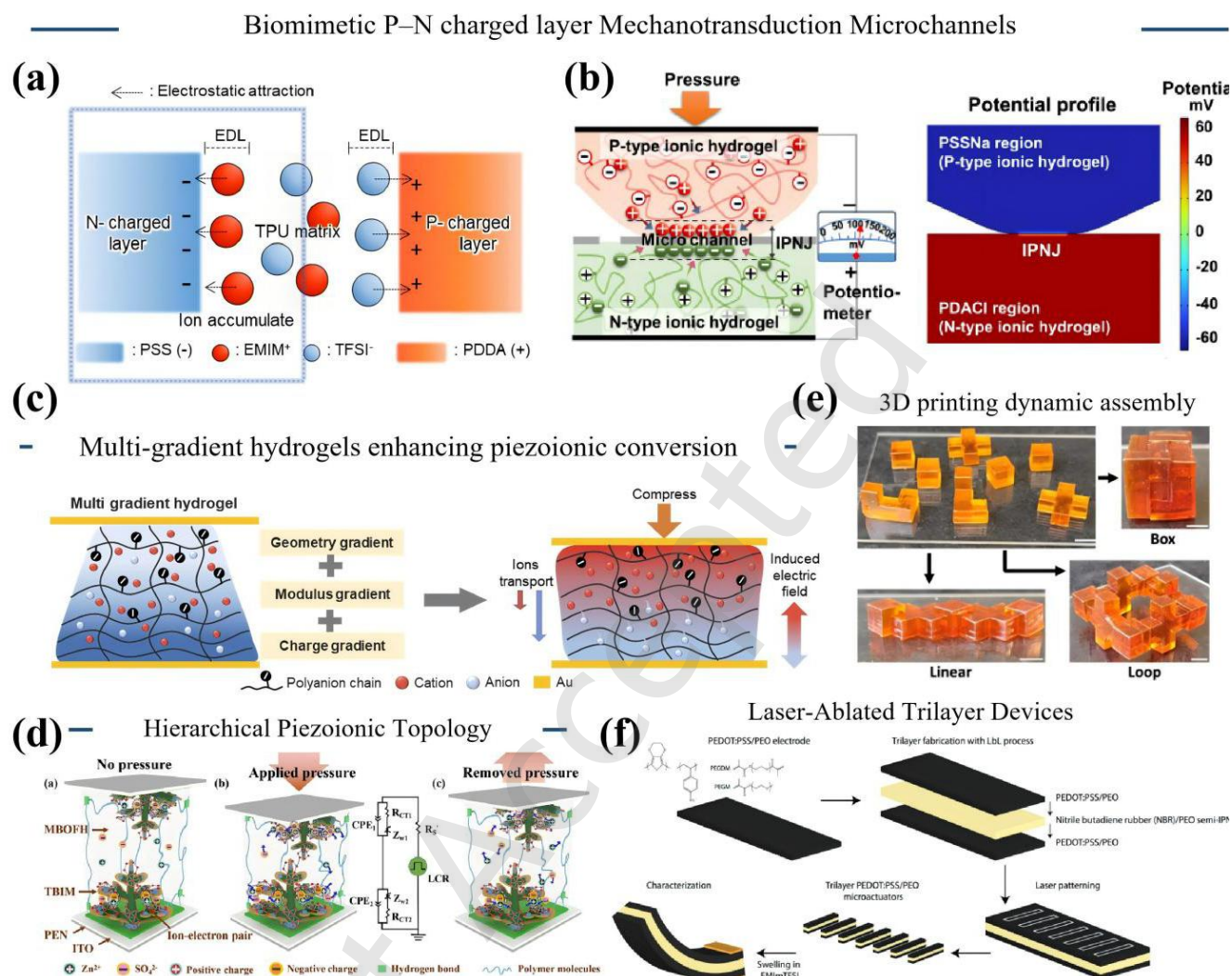


Figure 6 Structural engineering directs piezoionic transport and device integration. (a) Charge gradients in multilayer sensors enhance directional ion mobility. Reprinted with permission under a Creative Commons CC BY License from Ref. [67]. Copyright 2025 The Royal Society of Chemistry. (b) Interfacial potential-gradient modulation in ionic p–n junctions. Reprinted with permission from Ref. [38]. Copyright 2025 American Chemical Society. (c) Geometric and modulus gradients drive longitudinal ion flux. Reprinted with permission from Ref. [68]. Copyright 2025 Elsevier. (d) Interstitial gaps in microleaves facilitate piezoionic transfer for sensing. Reprinted with permission from Ref. [69]. Copyright 2022 Elsevier. (e) Vat photopolymerization creates modular components for customized sensor architectures. Reprinted with permission under a Creative Commons CC BY License from Ref. [70]. Copyright 2024 The Royal Society of Chemistry. (f) Layer-by-layer assembly combines sequential deposition with laser patterning to fabricate integrated microsystems. Reprinted with permission from Ref. [71]. Copyright 2019 Wiley-VCH GmbH.

3.2.1 Hierarchical architectures enable directional piezoionic transport

Establishing asymmetric physicochemical environments within ionic matrices constitutes a fundamental strategy for breaking the centrosymmetry of ion distribution, thereby enabling directional ion transport and enhanced mechanotransduction[72]. Multilayer architectures incorporating positively and negatively charged surface layers establish controlled charge gradients akin to biological lipid bilayers to modulate ion dynamics (**Fig. 6(a)**). Such biomimetic designs lower electrostatic binding energy between mobile ion pairs and enhance ion mobility via electrostatic interactions that facilitate dissociation under

mechanical stimulation[67]. Utilizing microstructured hydrogels to modulate interfacial contact allows encoding tactile stimuli into ionic potential differences through mechanically regulated ionic p–n junctions which mimic the signal type and intensity of natural skin receptors (**Fig. 6(b)**)[38]. Moreover, engineering gradient polycation and polyanion heterojunctions establishes built-in transmembrane potentials that supplement intrinsic interfacial potentials to boost the open circuit voltage and power density of ionic diodes[13]. Beyond electrochemical gradients, engineering physical heterogeneity through geometry and modulus gradients offers a pathway to amplify piezoionic responses via stress

induced convection. Bioinspired multi gradient structures utilize variations in crosslinking density and geometric shape to intensify internal pore pressure gradients along the stress direction (**Fig. 6(c)**). Simulation results visualize how structural gradients create a significant pore pressure differential along the z axis to physically explain the longitudinal mode capability[68]. Similarly, microphase-separated elastomers containing ionic liquids and plastic crystals leverage the modulus mismatch between hard and soft phases to induce localized stress concentration gradients. Finite element simulations reveal that these microscopic stress gradients promote charge separation within the intermediate phases, enhancing voltage generation without compromising the macroscopic stretchability of the material[73]. At a microstructural level, high-internal phase emulsions can be engineered to form cell-like multicompartments with intercellular ion gradients, where the chemical potential difference between high and low ion-enriched phases drives high-density net ion flux under deformation, mimicking the electrogenic mechanism of electric eels[74].

The strategic manipulation of interfacial interactions within layered architectures further optimizes the coupling between mechanical stress and ionic dynamics. Bilayer structures employing specific elastomer-ionic liquid combinations create distinct ion accumulation interfaces that amplify signal output and response speed while offering self-healing capabilities to maintain gradient integrity[75]. In more complex hybrid systems, sandwiching ion-conducting layers between piezoelectric polymers allows for a synergistic piezo-ionic-electric effect, where bending-induced self-polarization establishes an internal field that directs ion migration within nanochannels. These interface-driven gradient designs not only enhance the magnitude of the generated potential but also improve the temporal resolution of the sensor by facilitating rapid ion relaxation and redistribution[76]. Overall, multilayer design, gradient engineering, phase separation, and multiphysics coupling delineate the current frontier in iontronic materials, enabling high performance devices spanning advanced sensing and sustainable energy systems.

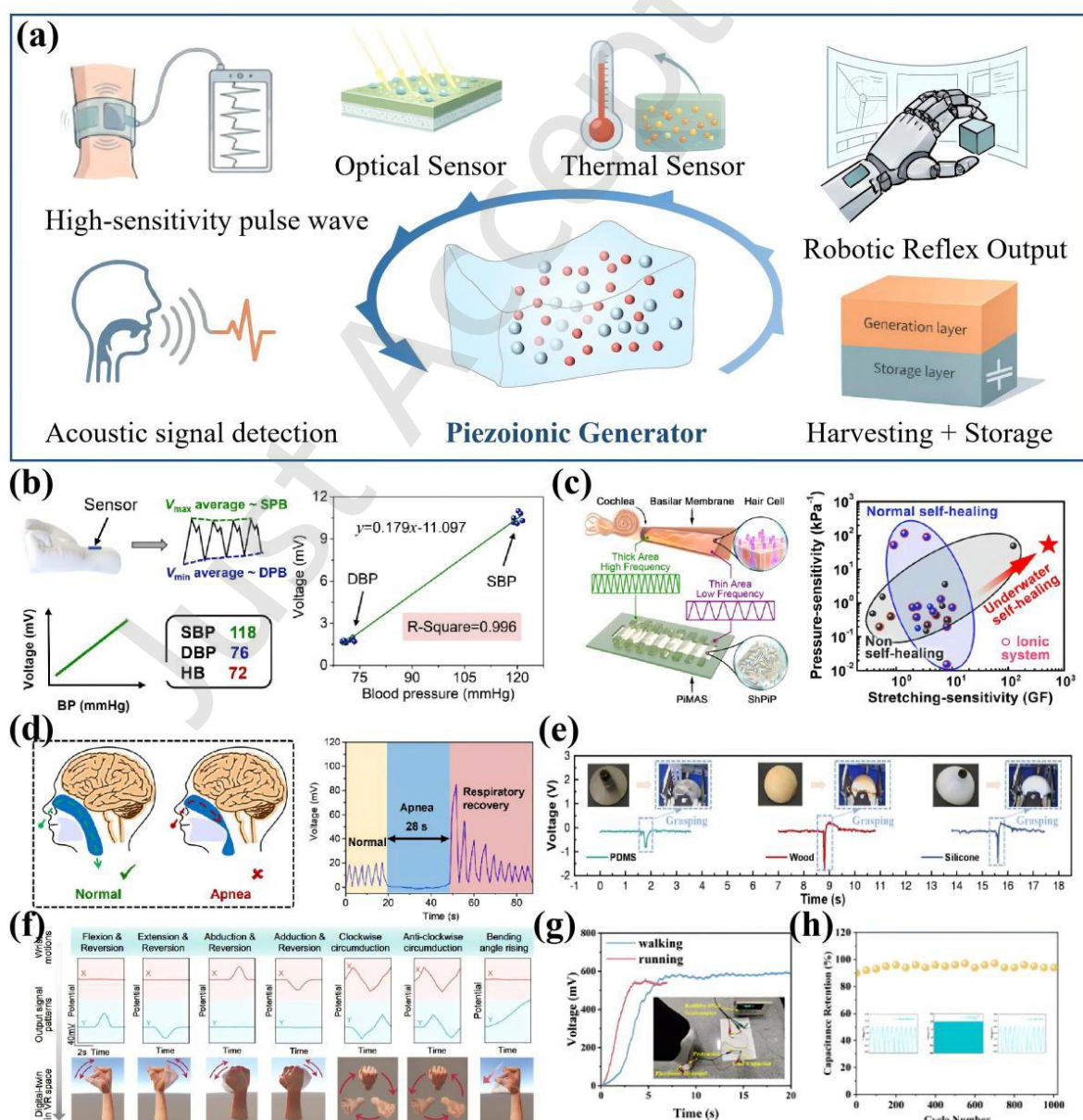


Figure 7 Representative sensing and self-powered systems organized by transduction role. (a) Schematic overview from biomimetic sensing to energy

autonomy. (b) Graphdiyne electrodes enabling cuff-less blood-pressure monitoring through out-of-plane ion transport. Reprinted with permission from Ref. [77]. Copyright 2024 Elsevier. (c) Reconfigurable piezoionic membranes for multiresonance acoustic sensing. Reprinted with permission under a Creative Commons CC BY License from Ref. [78]. Copyright 2025 Springer Nature. (d) Ultrathin MXene nanosheet electrodes resolving simulated respiratory states relevant to sleep-apnea screening. Reprinted with permission from Ref. [52]. Copyright 2023 Elsevier. (e) A porous composite sensor distinguishing object hardness during underwater robotic grasping. Reprinted with permission from Ref. [62]. Copyright 2024 Wiley-VCH GmbH. (f) A multi-degree-of-freedom piezoionic sensor mapping wrist motion into virtual space. Reprinted with permission from Ref. [79]. Copyright 2024 Elsevier. (g) Nanoparticle-enhanced hydrogels charging a capacitor for wearable energy storage. Reprinted with permission from Ref. [80]. Copyright 2025 Wiley-VCH GmbH. (h) A eutectogel combining piezoionic generation and electrochemical storage. Reprinted with permission from Ref. [81]. Copyright 2024 Elsevier.

3.2.2 Microchannels optimize ion diffusion pathways

The deliberate engineering of micro and nanoscopic architectures is a cornerstone strategy for advancing piezoionic materials, leveraging principles such as phase separation to create functionally optimized structures beyond simple compositional blends[82]. One major direction targets bulk structuring to impose well defined ionic pathways[83]. Phase separation techniques can be used to create nanocomposites with distinct hydrophilic and hydrophobic domains, forming tortuous channels that amplify ion separation under stress. A further step change emerges when isotropic disorder is replaced by designed anisotropy. Directional freezing produces aligned parallel microchannels that guide ion movement. Functionalizing these channels can improve ion selectivity and increase piezoionic output by enhancing charge imbalance compared with materials that have disordered pore networks[84]. In a complementary vein, light mediated patterning can generate hierarchical, asymmetric micropatterns that spatially program regions of distinct ionic conductivity, establishing a stable built in potentiometric gradient and providing an additional route to deterministic control of ion transport through predefined structure[85]. These methods demonstrate that meticulous control of internal material architecture through phase separation, directional fabrication and photopatterning critically dictates ion migration pathways and thereby enhances piezoionic performance.

In contrast to strategies that regulate internal phase architecture, surface focused structural engineering offers an alternative route to efficient electromechanical conversion. The hierarchical, multi-scale geometry of intricate, three-dimensional surface structures, such as topological micro-leaves, creates complex interstitial gaps that function as local ion reservoirs. Upon mechanical compression, said gaps expel ions into the adjacent dielectric layer, inducing a rapid and significant change in capacitance that translates to a highly sensitive mechanical response (**Fig. 6(d)**)[69]. Expanding the scope of ionic mechanotransduction beyond mobility-driven phenomena, dynamic surface patterning offers a capacitive-based approach. Inspired by gastric folds, carbon nanotube sheets with microwrinkled surfaces undergo reversible wrinkle unfolding under tensile strain. Surface relaxation increases electrochemically active area and enlarges the effective ion transport volume, enabling additional ion adsorption[86]. Together, these surface architectures couple deformation-driven ion redistribution with electrical-double-layer reorganization, providing an interfacial piezoionic route for transducing multidirectional, low-modulus deformations characteristic of biological

motion.

3.2.3 Integrated manufacturing enables scalable, programmable and robust devices

Additive manufacturing technologies have evolved to permit the direct programming of ionic impedance gradients within three dimensional volumes thereby overcoming the homogeneity limitations of traditional casting. Stereolithography exemplifies this capability by utilizing a sequential resin exchange process during layer by layer construction to embed continuous variations in charge density and crosslinking stiffness directly into the monolithic iontronic body[87]. Such voxel level modulation of the material composition enables the fabrication of devices with built in directional sensing and signal amplification properties that are intrinsic to the printed structure rather than assembled from separate parts. In parallel with monolithic printing strategies the use of vat photopolymerization with resins containing covalent adaptable networks offers a pathway for dynamic reconfigurability where discrete printed modules can be assembled and fused via thermally activated Diels Alder bond exchange (**Fig. 6(e)**)[70]. These complementary additive approaches provide the geometric freedom to tailor the internal ionic architecture for specific electromechanical responses while maintaining structural continuity across the device.

Establishing a mechanically and chemically stable boundary between the ionic matrix and external electrodes is as critical as defining the bulk geometry for ensuring long term operational fidelity under harsh conditions. In situ chemical synthesis strategies effectively address the modulus mismatch at the electrode electrolyte interface by reducing metallic precursors directly within the polymer scaffold to grow conductive networks that mechanically interlock with the matrix like biological roots[88]. Surface initiated chemical bonding techniques utilizing sequential plasma treatment and double layer coatings of silanes and perfluoropolyethers further construct a robust barrier that prevents dehydration and freezing while maintaining strong interfacial adhesion[58]. Complementing these chemical bonding approaches are physical integration strategies such as thermocompression which allow for the lamination of pre formed conducting polymer films onto ionomeric membranes to yield interfaces with higher conductivity and mechanical stiffness compared to solution based drop casting methods[47]. Similarly the fabrication of fluoropolymer based actuators benefits from hot press lamination processes where gold leaf electrodes are bonded to solvent cast ionic liquid polymer composite films under controlled heat and pressure to ensure consistent electrical

contact across the entire active area without compromising ionic mobility[49].

Scalable solution processing techniques leverage the rheological properties of functional inks to offer versatile fabrication routes for engineering both the internal microstructure and the macroscopic architecture of iontronic devices. Solvent exchange induced phase separation provides a route to generate highly porous elastomeric matrices with interconnected microchannels that facilitate ion migration and enhance compressibility particularly when combined with replica molding to create hierarchical sensor architectures[61]. For large area applications a monolithic architecture free from discrete pixelation can be realized through the facile solution casting of ionogel films bridging peripheral electrodes which

eliminates the structural complexity and extensive wiring associated with conventional sensor arrays[89]. In contrast, for microscale actuation and sensing layer by layer fabrication processes enable the precise construction of trilayer devices by sequentially casting conducting polymer composite electrodes and semi interpenetrating polymer network electrolytes followed by laser ablation (**Fig. 6(f)**)[71]. While current fabrication strategies have successfully demonstrated the ability to engineer ionic systems from the molecular interface to the macroscopic device level future efforts must focus on integrating these diverse processing techniques into a unified high throughput manufacturing platform capable of producing high density iontronic arrays with sub micron precision.

Table 2 Piezoionic sensors for physiological and biomechanical monitoring: mechanisms, performance and operational stability

Sensing material	Structural design and mechanism	Performance and operational stability	Physiological or biomechanical signal	Ref.
Cardiovascular Monitoring (Pulse or Blood Pressure)				
Graphdiyne	Graphdiyne nanopores enable out-of-plane ion transfer	116 mV; 94.7% retained after 4,000 cycles	Blood pressure and pulse	[77]
Graphene/solid polymer electrolyte	Piezoionic transduction with graphene field-effect amplification	Approximately 5 mV; gauge factor 16-30; approximately 250 ms; >2,000 cycles	Joint motion, pulse and touch	[90]
PAA/liquid-metal nanoparticle/CNC hydrogel	Nanoparticle-reinforced dynamic ionic network	10 $\mu\text{A}/\text{cm}^2$; approximately 2,000% strain; full current recovery after healing; aging not reported	Speech, breathing, pulse and touch	[56]
Hydrogel/ion-selective-electrode interface	Dual interfaces decouple pressure and ion concentration	Pressure-ion concentration decoupling; stability not reported	Simultaneous pulse and sweat analysis	[46]
p-type/n-type hydrogel junction	Deformation-driven interfacial ion redistribution at an ionic p-n junction	Approximately 120 mV; 0.01 N detection limit; >100,000 cycles; temperature and humidity dependent	Pulse and contact-force discrimination	[38]
Voice, Breath, or Facial Expression				
Fluorinated polyurethane/ionic liquid	Ion hitching-in-cage enables frequency discrimination	20-3,300 Hz; 530 kPa^{-1} ; self-healing in air and water; long-term retention not reported	Voice discrimination and cochlea-mimetic sensing	[78]
UiO-66- NH_2 @PAA/TPU ionogel	Reversible interactions dissipate energy	850% elongation; stable over >3,000 cycles; recyclable	Voice, facial expression and joint motion	[50]
Graphene/PAAm/PVA double network	Graphene reinforces ionic and conductive pathways	213 F/g; 89% capacitance retention after 30,000 cycles; piezoionic retention not reported	Breathing-state monitoring	[55]
Ultrathin MXene ionogel	MXene channels and interfacial ion storage amplify output	219 mV; 98% retained after 10,000 ambient cycles	Respiratory and sleep-apnea monitoring	[52]
Au/Nafion bio-inspired interface	In situ interface growth suppresses interfacial slip	Approximately 26 mV; >90% retained after 3,000 cycles in air	Skin touch, eye movement, cheek bulging and finger motion	[88]
Complex Kinematics or High-Impact Force				
Directionally frozen cellulose-nanofibril organohydrogel	Anisotropic channels direct ion transport	199.45 mV within 150 ms under 5 N; stability not reported	Finger, wrist and foot motion	[84]
TPU/ionic liquid/silica nanoparticle composite	Interlocked pores decouple shear and normal loading	0.23 mV kPa^{-1} ; up to 634 kPa; 5,000 cycles; long-term retention not reported	Gait and plantar shear or slip	[61]
MXene/Ag heterostructure	MXene/Ag lamellae enhance ion storage and transport	11.1 mV; 95% retained after 13,000 s; VHB encapsulated	Pulse and high-impact pressure during CPR training	[42]
Charge-gradient hydrogel membrane	Salinity-gradient-assisted piezoionic output with pressure-dependent ion transport	Initial salinity-gradient output: approximately 290 mV and 1.46 mA/cm^2 ; soft at -20 $^{\circ}\text{C}$; retention period not reported	Pulse, blowing and joint motion; gradient-assisted output	[91]

PVA/ionic-liquid ionogel	Force-voltage coupling drives ion redistribution	2.11 mV at 1.5% strain; 94% retained after 2,000 cycles in air	Subtle-pulse detection	[41]
Aluminium-coordination hydrogel	Aluminium coordination stabilizes ion separation	0.89 mV kPa ⁻¹ ; 1.29% author-reported energy-conversion efficiency; long-term cycling not reported	Tactile-force monitoring and injury prevention	[63]

4 Piezoionic transduction enables biomimetic sensing and autonomous powering

Piezoionic systems are advancing from passive transducers to autonomous platforms integrating sensing, perception, and power generation. Molecular and structural engineering enable high-precision physiological monitoring and complex environmental interaction, mimicking biological sensory fusion[92]. Concurrently, innovations in power density and monolithic storage integration are establishing self-sustaining energy solutions, bridging the gap between signal detection and autonomous operation (**Fig. 7(a)**).

4.1 Piezoionic devices enable sensitive, stable physiological monitoring

The precision of physiological monitoring is fundamentally determined at the molecular level, where the modulation of ion mobility and electrode carrier concentration dictates detection limits and signal linearity[15]. Creating specific ion traps within the polymer matrix serves as an effective strategy to suppress noise and enhance sensitivity (**Table 2**). For instance, polyurethane chains functionalized with electronegative chlorine groups establish strong ion-dipole interactions that confine mobile cations, yielding a high-pressure sensitivity of 7.36 kPa⁻¹, which is sufficient to resolve the fine features of arterial pulse waves[51]. Alternatively, precision can be achieved by facilitating rapid ion flux through engineered nanopores. Graphdiyne membranes featuring intrinsic triangular pores enable ultrafast out-of-plane ion transport and provide expanded ion storage, thereby establishing a direct linear correlation between voltage output and blood pressure values without the need for cuff-based calibration (**Fig. 7(b)**)[77]. Beyond structural confinement, the coupling of piezoionic potentials with semiconductor properties allows for the precise modulation of the Fermi level in graphene channels, this interaction causes a shift in the Dirac point that significantly amplifies the gauge factor for strain detection[90]. Coupling the piezoionic potential to a graphene channel shifts its Dirac point and amplifies the strain gauge factor, while ion redistribution remains the source of the transduction signal. To ensure signal fidelity during the repetitive mechanical stress of cardiac cycles, hydrogel networks incorporating liquid metal nanoparticles stabilized by cellulose nanocrystals provide the necessary viscoelastic toughness to resist motion artifacts[56]. Signal purity is further enhanced by decoupling physical stimuli from biochemical interference. Innovative dual-mode platforms separate pulse-induced pressure variations from sweat electrolyte changes, ensuring that physical vital signs are recorded with high selectivity[46]. Additionally, robust interfaces inspired by tree root structures establish intimate contact with the skin,

preventing delamination and ensuring consistent charge transfer efficiency during long-term monitoring[88].

Capturing rapid transient bio-signals, ranging from high-frequency acoustic vibrations to dynamic facial muscle movements, necessitates materials with optimized microstructural ion pathways and fast interfacial kinetics (**Fig. 7(c)**). Biomimetic architectures based on fluorinated polyurethanes utilize a dynamic ion “hitching” mechanism to mimic the frequency selectivity of the basilar membrane, enabling the discrimination of sounds ranging from 20 to 3300 Hz[78]. In throat-mounted applications, signal attenuation is minimized through anisotropic channels created via directional freezing, which align ion transport pathways to enhance the voltage response to vocal cord vibrations[84]. Ultrathin Ti₃C₂Tx MXene electrodes enhanced interfacial ion transport, enabling a below-nose sensor to distinguish normal breathing, simulated apnea, recovery, rapid breathing, and deep breathing (**Fig. 7(d)**). Because apnea was simulated by a 28s breath hold, the study demonstrates proof-of-concept respiratory monitoring rather than clinical diagnostic performance[52]. Furthermore, the optimization of charge transfer rates at the electrode interface is vital when transitioning from acoustic vibrations to transient facial muscle tracking. Nanocomposites integrating carbon nanotubes and graphene provide hierarchical porosity that expedites ion exchange, facilitating the real time recognition of dynamic facial expressions[54]. To enable inconspicuous monitoring, the incorporation of polyelectrolytes into alginate networks significantly improves optical transparency and adhesiveness, creating imperceptible patches for tracking swallowing and speaking activities[40]. Sustainability concerns are addressed by reversible molecular interactions within ionogels, which permit the recycling of sensors used for motion tracking without compromising their dynamic sensing performance[50].

Translating molecular precision into complex kinematic monitoring requires macroscopic architectures capable of decoupling multidirectional forces and resisting environmental drift. Hierarchically structured porous thermoplastic polyurethane films serve this purpose by separating normal pressure from shear forces, which enables the detailed mapping of gait patterns and foot slip within smart insoles[61]. While continuous monitoring is often plagued by signal decay due to ion concentration polarization, self-powered sensors based on gradient polyelectrolyte membranes mitigate this effect to maintain linear pressure sensing even after the initial ion gradient dissipates[91]. In high impact scenarios such as cardiopulmonary resuscitation training, heterostructures combining MXene and silver nanoparticles provide the requisite conductivity and mechanical robustness to accurately monitor compression depth and frequency[42].

For large scale body movements, graphene-enhanced double-network ionogels offer the fracture toughness required to withstand thousands of deformation cycles while monitoring joint bending and respiration[55]. At the system level, smart bracelets leverage these robust mechanisms to identify specific athletic postures by analyzing vector forces[14]. Ultimately, the optimization of the electrode-electrolyte interface remains the foundational element for maximizing charge transfer efficiency in these mechanically demanding applications.

4.2 Multimodal signal integration enables complex perception

Synergistic integration of mechanical sensing with optical, thermal, and chemical modalities enables the emulation of sophisticated biological sensory fusion for comprehensive environmental awareness. Biomimetic synapse architectures incorporating MXene nanosheets facilitate the concurrent processing of tactile and visual signals where pressure drives

piezoionic potentials while near infrared light induces ionic thermodiffusion for robotic reflex control[18]. Beyond optical fusion, decoupling thermal stimuli from mechanical inputs is achieved via thermochromic microcapsules embedded within ionic liquids which provide visual thermal feedback alongside piezoionic pressure sensitivity even under freezing conditions[93]. For extreme environments such as deep sea exploration, multi hierarchical composite films distinguish object hardness and conductivity by coupling work function induced electron transfer with ion mediated pressure sensing (**Fig. 7(e)**)[62]. Visualizing mechanical stress directly through electrochemical luminescence offers another dimension of interaction where visco poroelastic relaxation in ion doped thermoplastic polyurethanes regulates the distribution of ionic luminophores to map stress spatially[94]. Furthermore, transparency in ionic liquid polymer composites permits the seamless integration of pressure sensing into optical systems without compromising visual transmission[95].

Table 3 Piezoionic systems for multimodal perception and human-machine interaction: mechanisms, performance and environmental stability

Material system	Coupled mechanism	Performance and environmental stability	Perception or interaction function	Ref.
Multimodal and Environmental Perception				
Bilayer asymmetric ionic hydrogel synapse	Hybrid piezoionic-thermodiffusive response	Detection limits: 3.6 kPa and 35.7 mW/cm ² ; near-constant output over 8,000 s with gradual attenuation; encapsulation limited evaporation	Tactile-visual fusion and robotic reflex control	[18]
PVA/PEG/ionic-liquid/thermochromic hydrogel	Piezoionic pressure sensing with independent thermochromic readout	Decoupled electrical and visual outputs; >90% water retained after 7 d; frost resistant below -70 °C	Bimodal electronic skin and extreme environments	[93]
SWNTs-TPU/C-WPU film	Electronic conductivity recognition with piezoionic pressure sensing	1.2 kPa ⁻¹ ; 10.54% signal loss at simulated 100 m depth	Deep-sea robotics and material recognition; hybrid mechanism	[62]
TPU/[Ru(bpy) ₃] ²⁺ /ionic-liquid composite	Piezoionic transduction with externally powered electrochemiluminescent readout	Stress-dependent luminance; operation below 4 V; stability not reported	Visual tactile skin and stress mapping	[94]
SEBS/[Bmim][N(CN) ₂] film	Compression-dependent ionic conductivity with externally biased iontronic readout	Approximately 25 kΩ/N over 0-10 N; nonvolatile ionogel; long-term cycling not reported	Transparent touchpad; piezoresistive boundary system	[95]
Dynamic Tactile and Texture Recognition				
PVDF-HFP/EMIM-TFSI bilayer	Ion accumulation at a self-healing interface	95 mV; 30 ms response; approximately 100% self-healing; 8,000 cycles	Braille and texture discrimination	[75]
TPU/PSS/PDDA multilayer	Charge gradients accelerate interfacial ion transport	19 ms; 1.2 μA; 5,000 cycles; stable after 3 months in air without encapsulation	Airflow mapping and voice recognition	[67]
Gelatin/KCl hydrogel	Hybrid triboelectric-piezoionic response	Switchable contact and deformation signals; stability not reported	Wireless robot control and texture recognition; hybrid mechanism	[96]
PVA/MXene microneedle hydrogel	Stress concentration directs proton transport through MXene channels	165.6 mW/m ² ; stable over 10,000 cycles; PDMS limits dehydration and oxidation	Shape and texture recognition	[97]
Zwitterionic copolymer/LiTFSI hydrogel fibre	Dipole-ion interactions decouple multi-axis bending	3.2 mV degree ⁻¹ ; stable over 10,000 bending cycles	Metaverse control and digital twins	[79]
CNT yarn/PVA gel	Coiled fibres generate asymmetric ion squeezing	15 mV; 0.1-10 Hz; stable over approximately 10,000 stretching cycles	Smart textiles and gesture recognition	[63]
Intelligent Processing or Interaction				

PAAm/salt asymmetric hydrogel	Stress-driven ion migration performs mechano-ionic logic	AND/OR logic; current drift and waveform reversal after approximately 700 cycles	Robotic logic control and human-machine interaction	[34]
PVDF-HFP ionogel	Externally driven impedance mapping (iontronic readout)	Up to 455 kPa; approximately 10% current loss over >3,300 s static load; stable after 60 d ambient storage	Handwriting and piano interfaces; boundary readout	[89]
NaCl/PAM hydrogel	Cross-link density tunes the ion-migration time constant	0.1-3 s tunable response; 500 cycles; swelling equilibrium at 1 week	Security authentication and pattern unlocking	[39]

Discriminating between static pressure and dynamic tactile features such as texture or slip remains a critical challenge for artificial skins requiring high spatiotemporal resolution. Bilayer architectures utilizing ion dipole interactions facilitate the formation of ion accumulation interfaces which significantly amplify output signals and enable the detection of both static bending and dynamic vibrations for Braille recognition[75]. Similarly, charge modulated multilayer structures create controlled charge gradients that enhance ion mobility and allow for precise airflow mapping and surface texture differentiation[67]. To further refine dynamic perception, hybrid systems combining triboelectric and piezoionic effects allow for the distinction between initial contact and subsequent deformation thereby mimicking the adaptation rates of biological mechanoreceptors[96]. Coupling piezoelectric and piezoionic mechanisms within all polymer sandwich structures enhances the discrimination of weak physiological signals and mechanical vibrations by maximizing interfacial polarization[76]. Structural innovations such as stress concentrated hydrogel microneedles further amplify proton transport gradients and enable the system to recognize object categories based on multimodal feedback including texture and shape[97]. Additionally, multi degree of freedom sensors utilizing square prism shaped fibers and symmetric nanomesh electrodes can decouple complex joint motions to facilitate intuitive control in virtual reality environments (**Fig. 7(f)**)[79].

The progression from passive sensing to active information processing involves the integration of advanced signal decoupling and energy autonomy directly into the sensing loop. For large area scalability, monolithic iontronic sensors employ machine learning to decouple complex pressure and position signals from a minimal electrode configuration and eliminate the need for pixelated arrays[89]. Additionally, modulating the crosslinking degree of the hydrogel network allows for the tuning of ion migration rates and enables precise trajectory recognition for security authentication applications[39]. Highly compressible aerogel springs integrated with supercapacitors further demonstrate the potential for self-powering multifunctional devices that combine energy storage with pressure sensitivity[57]. Such integration of intelligent processing capabilities transforms simple transducers into cognitive interfaces capable of complex interaction (**Table 3**), yet achieving high resolution recognition and complex decision making in extreme environments remains a challenge for future integrated systems.

4.3 Piezoionic transduction enables energy harvesting and integrated storage

Conversion of low frequency mechanical inputs into electrical power underpins the appeal of piezoionic materials for self powered electronics and energy harvesting iontronics[98]. Realizing this potential requires simultaneous improvements in voltage and current output, load-matched power delivery, mechanical-to-electrical energy-conversion efficiency, and charge-accumulation kinetics. Microphase-separated elastomers exploit stress concentration and directional ion transport to reach a peak power density of $1.3 \mu\text{W}/\text{cm}^3$ and an energy-conversion efficiency of approximately 1.8%[73]. Aluminum coordination within the hydrogel network yielded a piezoionic coefficient of 0.89 mV/kPa and a mechanical-to-electrical energy-conversion efficiency of 1.29%[63]. Gradient ionic heterojunctions further combine transmembrane potentials with interface-dependent charge collection, producing 306.53 mV and a peak power density of $50.16 \mu\text{W}/\text{cm}^2$. Under quasi-static compression, a thickness-dependent generator produced 2.00 mJ of electrical energy from 3.17 mJ of mechanical work, corresponding to an efficiency of 63.09%[13]. Its markedly higher value than those reported for the phase-engineered and aluminum-coordinated networks also reveals the strong dependence of calculated efficiency on loading mode and energy-accounting method.

Beyond increasing instantaneous output, practical energy harvesting requires rapid charge accumulation and resilience to intermittent mechanical input. Surface-functionalized nanoparticles regulate ionic mobility within hydrogel networks, enabling outputs of 827.90 mV and 1.28 mA and charging a 1 mF capacitor at 146 mV/s over an operating frequency range of 0.1–10 Hz (**Fig. 7(g)**)[80]. Coupling ionic thermoelectric and piezoionic effects provides a complementary strategy by maintaining a continuous voltage component when mechanical excitation is absent[99]. In this hybrid configuration, thermodiffusion sustains a voltage component between mechanical events, whereas deformation-driven ion redistribution generates the piezoionic component. By extending material design from maximizing peak output towards regulating the temporal availability of harvested energy.

Integration of generation and storage further reduces the functional separation between piezoionic transducers and electrochemical power units. Cationic-chitosan eutectogels can operate as both piezoionic generators and solid-state electrolytes, retaining 94% of their initial capacitance during repeated cycling while powering an electronic timer (**Fig. 7(h)**)[81]. Polyzwitterionic composite eutectogels provide a complementary route. Their piezoionic output reached 80 mV under a 2 N load and remained repeatable over approximately 400 cycles. The same material family

supported quasi-solid-state supercapacitors with a specific capacitance of 4.62 F/g at 7.36 mA/g, an energy density of 1.03 Wh/kg, and a power density of 7.36 W/kg[100]. The chitosan platform demonstrates energy generation and storage within the same electrolyte formulation, whereas the polyzwitterionic system establishes compatibility across distinct generator and supercapacitor configurations. Together, these approaches move piezoionic energy harvesting beyond transient voltage generation towards integrated energy management for self-powered electronics.

5 Emerging therapeutic applications of piezoionic transduction

Beyond sensing and energy harvesting, piezoionic materials convert mechanical inputs into localized electrical or electrochemical activity at soft tissue interfaces. This coupling underpins emerging applications in force-triggered neuromodulation, therapeutic delivery, and tissue repair. **Table 4** consolidates the material design, actuation and electrical output, biological evidence, and limitations of the therapeutic and regenerative piezoionic and hybrid systems covered in this section.

5.1 Piezoionic artificial nerves enable neuromodulation

The creation of seamless bioelectronic interfaces demands the resolution of mechanical impedance disparities between

rigid electronic components and soft biological tissues. Conductive hydrogels possessing physiological modulus values minimize chronic inflammatory responses and optimize interfacial impedance, defining the requisite coupling standards for bioelectronic devices[101]. Distinct from passive conductive interfaces, structured piezoionic hydrogels introduce an autonomous modality by converting physiological mechanical stresses directly into regulatory ionic currents. The alignment of poly(ethylene terephthalate) microfibers within a poly(acrylic acid) matrix guides pressure-induced ion migration. This structured artificial nerve produced 30 mV and 65 $\mu\text{A}/\text{cm}^2$ during device characterization; during sciatic-nerve stimulation, the output remained above 21 mV and reached 66 $\mu\text{A}/\text{cm}^2$, evoking electromyographic signals and downstream muscle contraction in rodents (**Fig. 8(a)**)[19]. The direct coupling between quantified output and a physiological response establishes acute neuromodulation under the reported interface. The architecture also mimics the spatiotemporal integration functions of biological synapses, a capability further elucidated by nonlinear ionic gating in hydrogel systems[102]. Differences in cation and anion diffusivity can consequently be used to emulate threshold-dependent sensory responses and construct autonomous artificial reflexes[16].

Table 4. Electrical outputs, biological outcomes, stability evidence and evidence boundaries of therapeutic piezoionic and hybrid systems

Material composition	Actuation and electrical output	Biological outcome	Stability and degradation	Principal limitation	Ref.
PET-microfibre/PAA/LiCl hydrogel	Pressure pulses, 30 mV and 65 $\mu\text{A}/\text{cm}^2$, with up to 66 $\mu\text{A}/\text{cm}^2$ during neural stimulation	Acute sciatic-nerve activation and muscle contraction	Not reported	Regeneration and chronic implantation were not evaluated	[19]
Polycationic hydrogel/organogel biphasic gel with a KCl gradient	Intermittent tapping, about 200 mV and nearly 400 μA	Vagus-nerve activation and reversible blood-pressure reduction	No attenuation over 20 cycles; gradient current stable for 24 h	Neural stimulation required surgical exposure of the vagus nerve	[74]
Aligned porous PAM/PAMPS hydrogel	Pressure gradient, up to 33 mV and 35 μA	Peripheral-nerve modulation and EMG activation	96% water loss at 48 h; 7.14-fold swelling in PBS	Long-term implantation was not evaluated	[103]
LiCl-loaded PVA hydrogel with asymmetric carbon electrodes	80 kPa at 0.1 Hz, 4 mA, 916 mC/m ² per cycle and 475 mW/m ²	Self-powered cefazolin release and wound treatment	No output loss over 7,500 cycles; stable at high humidity	Healing was mediated by drug release rather than direct bioelectrical stimulation	[20]
N-acryloyl-glycinamide/NaCl hydrogel	30% compression, 7.9 mV and 120 nA, with 3 mV and 40 nA under biological loading	Piezo1 activation and cartilage repair	Approximately 1,000 cycles; stable output and conductivity for four weeks in PBS; no inflammation at eight weeks in vivo	Small cohort; mechanical and electrical effects not separated	[104]
AETA or SPA-modified GelMA hydrogel	Compression coefficients of -0.24 and +0.28 mV/kPa	High cell viability and maintained myotube formation	Enzymatic degradation within 244–282 min	Active stimulation and in vivo repair were not evaluated	[105]
Chitin-nanofibre/PAA film	Horizontal strain of 2–10%, generating 10–40 mV	Enhanced bone-tendon interface regeneration	100 tensile cycles; minimal subcutaneous inflammation	The acute rabbit model does not fully reproduce chronic or degenerative tears in older patients	[21]
Glycine/PCL module with Li ⁺ -releasing hydrogel	Ultrasound from 100 kHz to 9 MHz, reaching 260 mV peak-to-peak at 5 MHz	Complete bone bridging within eight weeks	Complete degradation within 120 days in vitro	The in vivo design did not isolate piezoionic stimulation from Li ⁺ release	[106]
GelMA-polypyrrole/MXene hydrogel with PVA ionic layers	Compression at 8 kPa, generating 8.29 $\pm$ 1.26 mV	Osteogenic differentiation and ALP sensing in vitro	Conductivity stable for 60 days; voltage stable over 500 cycles; approximately 80% degradation at 14 days	Self-powered osteogenesis and in vivo efficacy were not evaluated	[63]

Mineral/calcium-alginate biphasic scaffold	Ultrasound at 1 MHz and 30 mW/cm ² , generating 80 mV after mineralization	Homogeneous bone ingrowth throughout the scaffold	Integrity retained for seven days; output decreased after mineralization	Mineralization reduced the piezoionic output	[23]
Acrylic acid/NIPAM/quaternary-ammonium-salt/tannic-acid hydrogel	Ultrasound at 1 MHz and 0.1-0.5 W/cm ² , generating 38-75 mV	Near-complete infected-wound closure by day 14	More than 700% swelling at 72 h	The in vivo design did not isolate piezoionic stimulation from antibacterial and antioxidant effects	[107]

Advanced material architectures have further expanded the functional scope of piezoionic neuromodulation beyond basic stimulation to include logic processing and autonomic regulation. Geometrically asymmetric hydrogels can perform mechanically driven AND and OR logic operations, enabling complex mechanical inputs to be pre-processed into defined stimulation signals[34]. An aligned artificial-ion-pump hydrogel generated approximately 33 mV and 35 μ A during characterization, motion-induced millivolt signals subsequently modulated the peroneal nerve and elicited tibialis-anterior electromyographic responses in mice[103].

Extending this concept from somatic to autonomic regulation, piezoheterogated biphasic gels containing engineered intercellular ion gradients enhance ionic transmission through distinct transport-energy barriers[74]. During vagus-nerve stimulation, the device generated approximately 200 mV and nearly 400 μ A and reduced rodent blood pressure from approximately 110 to 90 mmHg (**Fig. 8(b)**). These results extend the direct validation of piezoionic neuromodulation from somatic motor pathways to autonomic circuits.

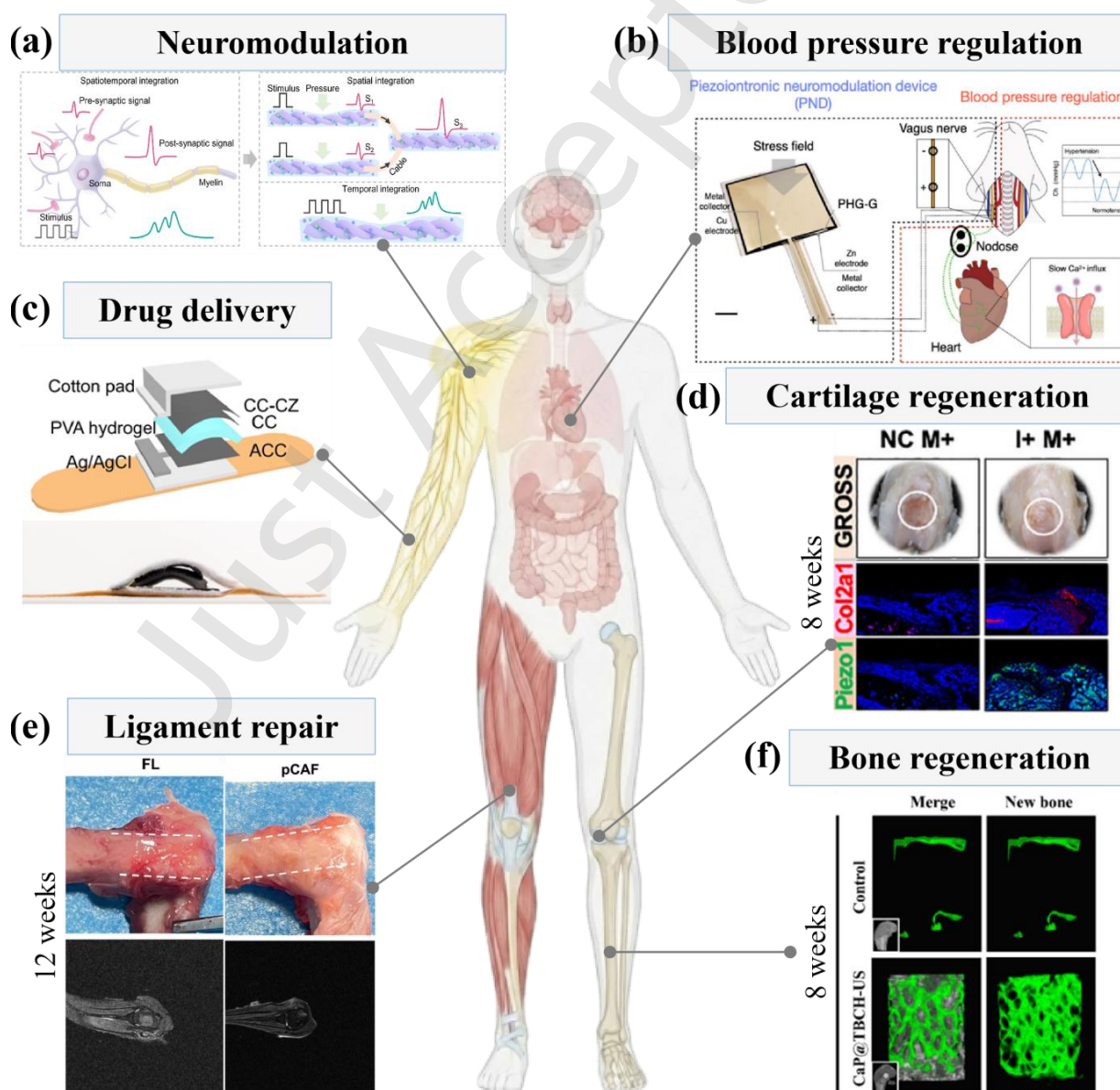


Figure 8 Mechanism-resolved therapeutic and regenerative evidence. (A) Pure piezoionic artificial nerve stimulating sciatic nerve and evoking muscle electromyographic activity. Reprinted with permission from Ref. [19]. Copyright 2024 Elsevier. (b) Piezoheterogated gel modulating vagus nerve for in vivo blood pressure regulation. Reprinted with permission from Ref. [74]. Copyright 2025 American Chemical Society. (c) Pure piezoionic generator driving electrochemical drug release. Reprinted with permission under a Creative Commons CC BY License from Ref. [20]. Copyright 2024 Springer Nature. (d) Pure piezoionic hydrogel reproducing cartilage-scale bioelectric signals during cartilage repair. Reprinted with permission from Ref. [104]. Copyright 2025 Wiley-VCH GmbH. (e) Chitin-nanofibre/poly(acrylic acid) film combining mechanical reinforcement and mechanoelectrical stimulation during tendon-bone repair. Reprinted with permission under a Creative Commons CC BY License from Ref. [21]. Copyright 2025 Elsevier. (f) Pure piezoionic biphasic mineral-hydrogel scaffold associated with homogeneous bone regeneration under acoustic actuation. Reprinted with permission from Ref. [23]. Copyright 2025 Elsevier.

Complementary iontronic strategies further broaden the therapeutic scope, although their driving mechanisms should be distinguished from piezoionic transduction. Microporous, phase-separated hydrogels combining hydrophilic and hydrophobic domains can couple electrical regulation of neural activity with active protein adsorption, thereby integrating electrophysiological and biochemical functions[83]. Bioinspired soft ionic sources driven by concentration gradients can also modulate neuronal networks through intracellular calcium waves, providing a chemically driven route for regulating neural activity and plasticity[108, 109]. Piezoionic logic interfaces and complementary ionic modulation strategies therefore provide distinct but potentially cooperative routes for targeting peripheral nerves, neuronal networks, and autonomic circuits.

Importantly, the available evidence establishes acute neuromodulation through the reported device-tissue interfaces but does not demonstrate axonal regeneration or long-term target reinnervation. Electrical stimulation that has promoted peripheral-nerve repair has instead been delivered as defined regimens. Supramaximal 3 V, 100 μ s pulses at 20 Hz for 1 h accelerated motor-axon regeneration in a rat femoral-nerve model[110], the same 20 Hz, 1 h protocol accelerated median-axon regeneration and thenar muscle reinnervation after carpal tunnel release[111] and enhanced sensory reinnervation after digital-nerve repair in a randomized controlled trial[112]. A shorter regimen of 0.5 mA, 100 μ s pulses at 16 Hz for 10 min also accelerated early axonal outgrowth and functional recovery after rat tibial-nerve repair[113]. These studies define effective, interface-specific protocols rather than a universal minimum energy threshold, because none titrated the delivered dose to treatment failure. Accordingly, the outputs of current piezoionic artificial nerves are sufficient for the acute responses reported above, whereas their sufficiency for nerve regeneration remains unproven.

5.2 Piezoionic signals regulate intelligent therapeutic agents

Eliminating bulky power sources remains a major objective in implantable therapeutics because reducing device volume and dependence on batteries can improve tissue compatibility and decrease the risks associated with repeated surgical replacement and infection[5]. Piezoionic hydrogels offer a self-powered alternative by converting physiological mechanical energy into electrical signals through stress-induced ionic redistribution. Introducing coupled structural and chemical asymmetries into the hydrogel matrix further promotes directional ion transport and increases the output to the milliampere level. Under a

compressive pressure of 80 kPa at 0.1 Hz, an engineered mechanoionic hydrogel generator delivered a current of 4 mA (5.5 A/m²), a charge density of 916 mC/m² per cycle, and a peak power density of 475 mW/m² across a load resistance of 122 Ω [20]. When integrated into a wearable patch, the mechanically generated current drove the electrochemical reduction of polypyrrole electrodes and the consequent release of anionic cefazolin sodium, enabling motion-regulated drug delivery and supporting wound treatment (**Fig. 8(c)**). Relief structures that reduce internal resistance, together with selective adsorption at the electrode interface, facilitate ion transport and improve the coupling between mechanical input and electrochemical actuation.

Beyond releasing pre-loaded agents piezoionic materials possess the capability to actively manipulate biological factors within the local environment for therapeutic purposes. Porous hydrogels featuring hydrophilic-hydrophobic phase blending generate substantial electric fields that actively absorb and enrich proteins from the surrounding fluid[83]. Microscopic porosity and phase separation within the matrix create efficient ion transport pathways to facilitate the accumulation of functional enzymes like horseradish peroxidase while preserving catalytic activity for potential reactive oxygen species therapies. Harnessing the traction forces exerted by adherent cells on piezoionic substrates induces localized potential differences that modulate cell behavior for the endogenous production of therapeutic factors[22]. Deforming the charged polymer matrix translates mechanical strain from cellular focal adhesions into millivolt-level electrical signals to activate voltage-gated calcium channels and downstream signaling pathways including the PI3K/AKT cascade. These diverse approaches collectively illustrate the potential of piezoionic platforms to function as versatile bio-interfaces that not only release synthetic drugs but also enrich environmental enzymes and stimulate the production of endogenous bio-therapeutics.

5.3 Piezoionic bioelectricity promotes tissue repair

The paradigm in biointerface engineering is shifting from providing passive structural cues to designing biomimetic matrices that actively reprogram cellular metabolism and fate through endogenous bioelectric signaling[7, 114–117]. Piezoionic hydrogels can provide such local cues by recapitulating aspects of the electromechanical microenvironment. In cartilage regeneration, native tissue generated up to approximately 2 mV and 37 nA, whereas a mechano-iontronic hydrogel reached 7.9 mV and 120 nA at 30% compression. Under a 20 min/day loading regimen, the hydrogel generated approximately 3 mV and 40 nA *in vitro*, activated Piezo1, reprogrammed glutamine metabolism, and

promoted cartilage repair *in vivo* (**Fig. 8(d)**)[104]. By linking loading, quantified output, cellular signalling, and a regenerative endpoint within the same model, this study provides direct evidence of therapeutic sufficiency for that configuration rather than a transferable voltage or current threshold.

Skeletal muscle regeneration is associated with a broad range of stimulation regimens rather than a single electrical threshold. In mice, microcurrent stimulation at 10 μ A, 0.3 Hz, and 250 ms for 60 min/day promoted regeneration of cardiotoxin-injured tibialis anterior when applied three days per week for three weeks[118] and facilitated regrowth of unloading-atrophied soleus when applied on 1, 3, and 5 days[119]. In chronically denervated human quadriceps, long biphasic pulses of 150–300 ms at $\pm$ 250 mA and 2 Hz, followed by tetanic training, restored muscle structure, mass, and force over 2.4–9.3 years[120]. In healthy older adults, stimulation at 75 Hz with 400 μ s pulses for 18 min per session, three times per week for eight weeks, increased myogenic-precursor-cell proliferation and satellite-cell fusion[121]. These markedly different protocols indicate that the biological response depends on waveform, intensity, treatment duration, and cumulative dose. Within this context, grafting cationic or anionic monomers into gelatin methacryloyl hydrogels regulated ion mobility and generated polarity-dependent piezoionic responses of -0.24 and +0.28 mV/kPa, respectively[105]. The modified hydrogels maintained more than 95% C2C12 myoblast viability after seven days and preserved myotube fusion, demonstrating the compatibility of ionic functionalization with myogenic culture. These results support ionically modified hydrogels as myocompatible mechanoelectrical scaffolds, while the relationship between their piezoionic output and regenerative efficacy remains to be established in injured skeletal muscle models.

Beyond skeletal muscle, scaffold design for load-bearing tissues such as tendon and bone increasingly seeks to couple mechanical reinforcement with electromechanical signalling. A chitin nanofiber reinforced poly(acrylic acid) film generated stable outputs of 10–40 mV as tensile strain increased from 2% to 10%, which was attributed to the differential displacement of Na^+ and Cl^- . When combined with a fascial autograft, the film promoted tenogenic differentiation *in vitro* and improved collagen organization and tendon maturation at the tendon-bone interface in a rabbit model of massive rotator cuff repair (**Fig. 8(e)**). Although the original study described the film as piezoelectric, the proposed ion displacement mechanism indicates a substantial piezoionic contribution. Nevertheless, the repair outcome likely arose from the combined electrical, mechanical, and antibacterial functions of the composite, and the specific contribution of the electrical signal was not independently resolved. Complementing this therapeutic platform, bioinspired multigradient hydrogels spatially regulate geometry, modulus, and charge density to intensify pressure driven convective ion transport and preserve robust electrical outputs under mechanically demanding conditions, providing a general design principle for piezoionic scaffolds in load bearing environments[21]. In parallel, bioinspired multigradient engineering sustains

signal fidelity within mechanically robust scaffolds by spatially modulating modulus and charge density to intensify convective ion transport and produce robust electrical outputs essential for effective stimulation[68]. Complementary biodegradable scaffoldoids couple physical orchestration with chemical signaling by synergizing piezoelectric fields with bioactive lithium ions to co activate PI3K/AKT and Wnt signaling pathways, thereby accelerating bone regeneration kinetics[106]. Embedding ionic liquids into piezoelectric polymers establishes a hybrid electroactive interface in which deformation induced ion migration generates a piezoionic potential that augments the intrinsic piezoelectricity of the polymer matrix, amplifying electromechanical cues that upregulate osteogenic gene expression while physicochemical toxicity associated with the ionic phase concurrently inhibits bacterial biofilm formation, together offering a dual mechanism strategy against orthopedic implant failure[122]. While promising, the therapeutic efficacy of such mechanoresponsive systems remains intrinsically tethered to a patient's capacity for physical activity, constraining applicability in clinical scenarios that necessitate immobilization.

Ultrasound triggered piezoionic transduction provides a remote route to bioelectric therapy when endogenous mechanical loading is insufficient, particularly in deep or immobilized tissues. Here, ultrasound supplies the mechanical input, while electrical generation remains governed by the scaffold's ionic transduction. A microscopically biphasic scaffold comprising calcium alginate hydrogel channels within a mineralized bone framework facilitated the transmission of low intensity pulsed ultrasound throughout the construct. Under 1 MHz ultrasound at 30 mW/cm², the mineralized scaffold generated a surface potential difference of approximately 80 mV, compared with approximately 120 mV for the unmineralized hydrogel scaffold. Ultrasound activation increased bone volume relative to tissue volume by 62% compared with the same scaffold without ultrasound and promoted homogeneous bone ingrowth throughout the construct (**Fig. 8(f)**)[23]. In infected diabetic wounds, the poly(acrylic acid) piezoionic hydrogel generated 38–75 mV under 1 MHz ultrasound as the intensity increased from 0.1 to 0.5 W/cm²[107]. Daily treatment at 0.5 W/cm² with a 50% duty cycle for 3 min reduced the residual wound area to approximately 1% by day 14 and produced a collagen density of 75%, accompanied by reduced inflammatory marker expression and increased vascular endothelial growth factor expression. These studies demonstrate that ultrasound can remotely activate piezoionic scaffolds and that the resulting electrical outputs are associated with improved bone and wound repair. However, because both systems combine electrical stimulation with scaffold architecture, ultrasound effects, and additional biochemical functions, the specific contribution of the piezoionic signal remains unresolved. Therapeutic sufficiency can therefore be assessed only when electrical output, loading conditions, and biological outcomes are reported within the same model and supported by appropriate controls.

Conclusion and outlook

The field of piezoionic materials has progressed from the

observation of force-induced ionic currents to the control of ion transport through molecular, structural, and interfacial design. Asymmetric ion migration is increasingly supported by theoretical models and experimental evidence[11, 35]. Strategies that regulate polymer-ion interactions, selective ion transport, and hierarchical microstructures have improved sensitivity, electrical output, and durability[12, 52, 123]. These advances have supported physiological sensing, energy harvesting, neuromodulation, mechanically regulated drug delivery, and tissue repair. Together, they establish a materials and device framework for coupling mechanical deformation to sensing, energy conversion, and localized biological function.

Further progress is constrained by closely related challenges in material stability, mechanistic understanding, and device engineering. Repeated deformation can redistribute ions and relax concentration gradients, while solvent exchange, electrode polarization, and interfacial failure can progressively attenuate electrical output. Increasing mobile-ion density and transport asymmetry must therefore be balanced against mechanical integrity and long-term retention of the ionic distribution. Existing models provide important descriptions of force-induced ion transport, but continuum treatments largely assume quasi-static loading, and the atomistic simulations that resolve polarization dynamics remain restricted to nanosecond and nanometer scales. At the device level, sensitivity to temperature and humidity, encapsulation under repeated deformation, mechanical and electrochemical matching at electrode-electrolyte interfaces, and fabrication of well-defined ionic channels continue to limit miniaturization, array integration, and stable operation in physiological environments[4, 124, 125]. Concurrently, a fundamental trade-off often exists between mechanical properties and ionic response. For instance, increasing crosslinking density enhances mechanical robustness but can impede ion transport, slowing the response time[39]. Overcoming these limitations requires the development of new polymer chemistries and composite structures that can maintain hydration and structural integrity without compromising ion mobility. Furthermore, the lack of standardized testing protocols and performance metrics makes direct comparison between different material systems difficult[30, 31]. Establishing universal frameworks for characterization is essential for guiding systematic material optimization and for the reliable assessment of device performance.

Therapeutic applications place additional demands on the relationship between material output and biological response. Acute neuromodulation, electrochemical drug release, and tissue repair involve different signal amplitudes, exposure times, and interface conditions, making peak voltage or current alone insufficient for evaluating efficacy. Because output further depends on loading and circuit conditions, reported voltages, currents, power densities, and conversion efficiencies cannot yet be compared across studies. Long-term studies must determine how the ionic signal delivered to tissue changes with material swelling, degradation, and host response. In multifunctional regenerative systems, the contribution of piezoionic stimulation should also be distinguished from accompanying

mechanical, acoustic, or chemical effects. Future research should therefore determine how mechanical input generates ionic electrical output, how much of that output reaches the tissue interface, and how the resulting stimulus influences biological responses under physiologically relevant conditions. With this foundation, piezoionic materials may evolve into integrated sensing-and-treatment systems that monitor tissue status and, in response, provide electrical stimulation or localized therapy tailored to disease progression or the stage of regeneration.

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Data availability

Not applicable.

Declaration of competing interest

All the contributing authors report no conflict of interests in this work.

Author contribution statement

Y. G. Xue and W. X. Zhou contributed equally to this work. Y. G. Xue and W. X. Zhou performed the literature search, analyzed the data, and wrote the original draft. X. Huang, C. B. Lin, and M. X. Jia assisted in figure preparation and visualization. G. H. Zhang, M. K. Zhu, Y. Liu, R. Bai and Y. Zhang participated in literature collection and discussion. S. S. Xu and Y. Liu conceptualized the topic and supervised the project. All authors have read and agreed to the published version of the manuscript.

Informed consent

Not applicable.

Ethics statement

Not applicable.

Use of AI statement

None.

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