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Review Article

Electroactive materials for bioelectronics and regenerative medicine: mechanisms, interfaces, and applications

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ABSTRACT

Electroactive materials, capable of generating, transmitting, and modulating electrical signals in physiological environments, have emerged as a cornerstone for bioelectronic devices and regenerative medicine. Recent advancements in conductive hydrogels, piezoelectric, triboelectric, thermoelectric, and optoelectronic systems have provided novel approaches for the development of flexible biological interfaces, self-powered sensing, and low-power electrical stimulation. However, as applications transition from short-term experimental prototypes to long-term wearables and chronic implants, the mere pursuit of high conductivity or output power is no longer sufficient to meet practical demands. Factors such as interface impedance, signal noise, environmental stability, stimulation safety, and scalability in manufacturing have become critical limiting factors in their widespread adoption. This review systematically examines the mechanisms and fundamental properties of various electroactive materials through the lens of biological responses to electrical signals at multiple

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scales, proposing an integrated framework for defining requirements, selecting materials, fabricating devices, and validating performance. It also summarizes the current research progress and key challenges faced in typical biological application scenarios. Finally, the paper offers insights into the future development directions of electroactive materials in bioelectrical interface engineering, system-level integration, and intelligent manufacturing.

1. Introduction

Biological systems inherently process and regulate information, with electrical signals playing a pivotal role in numerous physiological functions.[1–4] From neuronal firing and cardiac excitation to tissue repair and inflammation modulation, electrical activity operates across multiple scales-from molecules and cells to tissues and organs-dictating life processes through the interplay of membrane potentials, ion channels, and localized electrochemical microenvironments.[5–7] Concurrently, the ability of materials and devices to interface with and manipulate biological electrical signals has become a cornerstone for next-generation wearable health monitoring, implantable therapies, and regenerative medicine.[8–13] Electroactive materials, which generate, modulate, or transmit electrical signals in response to external stimuli or physiological conditions, are thus recognized as key mediators between biological systems and electronic technologies.[14,15]

Over the past decade, electroactive materials have advanced rapidly. Flexible conductive networks and hydrogels have improved electrode-tissue coupling,[16–18] while piezoelectric and triboelectric systems have enabled self-powered sensing and bioinspired electrical stimulation.[19–22] Meanwhile, photoelectric materials support light-responsive recording and optically triggered stimulation,[23–26] and thermoelectric materials offer routes for temperature-gradient energy harvesting and low-power operation.[27–29] However, as these technologies progress from laboratory demonstrations toward long-term wearables, chronic implants, and closed-loop therapies, fundamental and structural challenges are becoming increasingly evident.

Firstly, while many studies continue to emphasize intrinsic material properties such as high conductivity or output power, real-world biological environments reveal that factors like interface impedance, signal-to-noise ratios, temporal drift, polarization effects, and environmental coupling ultimately dictate device performance.[30] Secondly, the composition, microstructure, and fabrication processes of electroactive materials are highly interdependent, resulting in a complex and tightly coupled parameter space. Consequently, experience-driven optimization and trial-and-error approaches are insufficient for rapid device iteration or consistent manufacturing. Lastly, long-term exposure to warm, wet physiological environments accelerates material aging, causes interfacial contamination, packaging failures, and triggers evolving biological responses such as inflammation and fibrotic encapsulation, factors that erode the performance benefits observed in short-term experiments and pose significant barriers to long-term reliability and clinical translation.

In this context, the field is shifting from a phase focused on material performance to one that emphasizes bioelectrical interface quality and system-level integration. The central question is no longer whether a material can achieve high performance, but whether its electrical activity can be reliably generated, transmitted, and interpreted within soft, wet, and ion-dominated environments. Equally crucial is the ability of devices to maintain calibrated and interpretable outputs amidst noise and motion-induced perturbations, as well as the integration of material selection, device architecture, packaging strategies, and validation protocols into a cohesive, systematic framework. Moreover, the advent of artificial intelligence and data-driven methodologies offers powerful new tools for learning, inverse design, and adaptive fabrication across the materials, structures, processes, and performance dimensions. These innovations have the potential to transform the research paradigm of electroactive materials, expediting their transition from conceptual demonstrations to reproducible, scalable engineering systems.

This review systematically addresses key issues in electroactive materials for bioelectronics and regenerative medicine, with a focus on the journey from biological needs to material mechanisms and device realization. We begin by summarizing biological responses to electrical signals at molecular, cellular, tissue, and organ levels, establishing a multiscale framework for understanding bioelectrical interactions. We then delve into the mechanisms of electrical activity generation and transduction in conductive, piezoelectric, thermoelectric, triboelectric, and photoelectric materials, analyzing their performance metrics, operational limitations, and application-specific challenges in biological settings. Building on this foundation, we propose an implementation framework that spans demand analysis, material selection, device fabrication, packaging, and hierarchical validation, with a particular emphasis on long-term reliability and system safety. Finally, drawing from representative application scenarios, including wearable monitoring, electrical stimulation, and tissue repair, we summarize current progress, assess the levels of evidence, and outline future directions for electroactive materials in bioelectrical interface engineering, system-level design, AI-driven fabrication, and clinical translation.

2. Multiscale biological responses to electrical signals

The perception and response of living systems to electrical signals span multiple hierarchical levels, from molecules and cells to tissues and organs (Fig. 1). This multilevel responsiveness constitutes the fundamental biological basis that enables electroactive materials to interface with biological systems and achieve functional regulations.[3,31] Across different length scales, the relevant response variables, time scales, and safety windows associated with electrical stimulation differ substantially. This intrinsic multiscale heterogeneity dictates that the design of materials and devices must be explicitly matched to

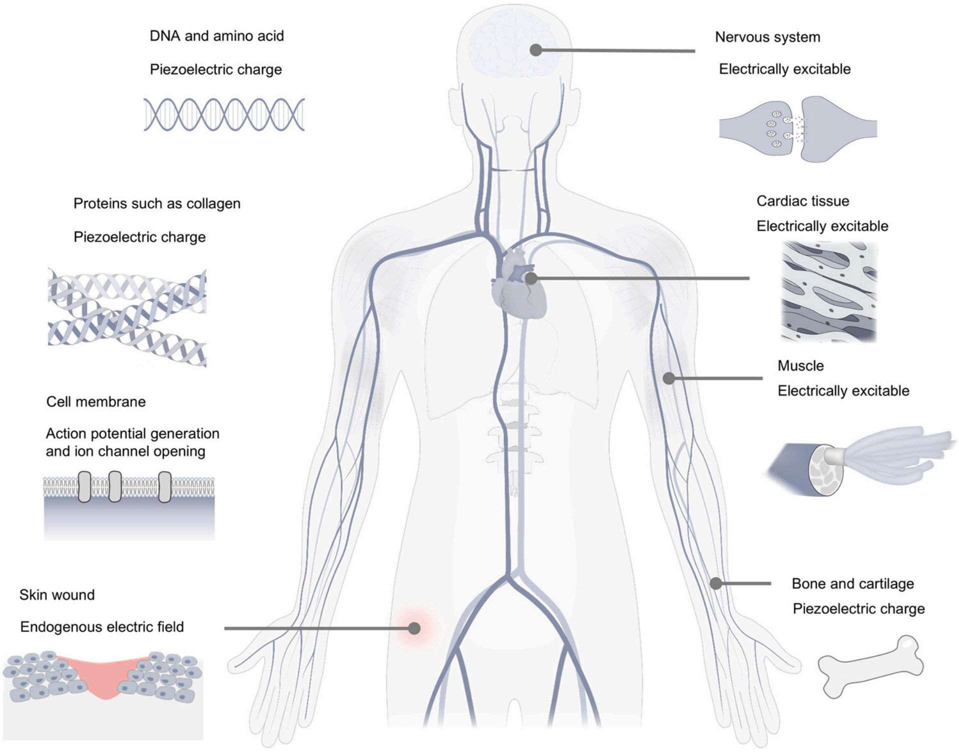


Fig. 1. Electrical signaling cues in biological systems. Illustration of representative electrical signaling mechanisms in the human body spanning multiple length scales. Several biological tissues and biomolecules, including bone, cornea, structural proteins such as collagen, nucleic acids, and certain amino acids, exhibit piezoelectric responses when subjected to mechanical deformation. At the cellular level, ion pumps and transmembrane ion gradients establish membrane polarization, while the activation of voltage gated ion channels enables the initiation and propagation of action potentials. Electrically excitable cells, such as neurons and myocytes, support rapid electrical communication in the nervous system, skeletal muscle, and cardiac tissue. In epithelial tissues, polarized ion transport generates endogenous electric field gradients at wound sites, which guide directional cell migration and contribute to tissue repair processes.

the targeted biological scale. In this section, biological responses to electrical signals are systematically reviewed at the molecular and membrane, cellular, and tissue or organ levels, providing a biological foundation for the selection of material performance metrics and device parameters discussed in later sections.

2.1. Molecular and membrane scale

At the molecular and cell membrane scale, biological sensing of electrical signals is primarily manifested through the establishment, maintenance, and dynamic regulation of the transmembrane potential.[7,32,33] Electrochemical gradients formed by asymmetric ion concentrations across the cell membrane give rise to a stable resting membrane potential.[34] The opening and closing of voltage-gated ion channels induce rapid local charge redistribution, thereby driving the generation and propagation of action potentials as well as synaptic signal transmission. External electric fields or electrical stimulation can perturb membrane potential distributions, modulate ion channel conformations, and regulate calcium ion influx, triggering a cascade of downstream signaling events.[35–38]

Importantly, at this scale, electrical signals perceived by biological systems do not exist in isolation but are strongly coupled to the local chemical microenvironment.[39] Electrical stimulation is often accompanied by changes in local pH, fluctuations in ionic strength, variations in dissolved oxygen concentration, and shifts in redox state.[11,40–43] If electroactive materials induce significant electrochemical side reactions during operation, these accompanying effects may superimpose on or even dominate the biological response, complicating mechanistic interpretation and potentially leading to misattribution. Therefore, at the molecular and membrane scale, clearly distinguishing between electric field effects and electrochemical effects is a critical prerequisite for understanding biological response mechanisms and assessing material safety.

2.2. Cellular scale

At the cellular level, electric fields influence a range of behaviors, including migration, adhesion, cytoskeletal dynamics, and cell growth or differentiation, with effects typically emerging over minutes to hours as changes in morphology or cell fate.[44–46] Increasing attention has been given to electromechanical coupling, reflecting the strong sensitivity of cells to mechanical cues such as stiffness, strain, and shear stress. Piezoelectric materials can convert small mechanical deformations into localized electrical stimuli, providing self-powered and physiologically relevant signals for stem cell modulation and tissue repair. However, the weak mechanical loads present under physiological conditions limit the achievable electrical output, and the resulting cellular responses are closely intertwined with simultaneous mechanical, structural, and chemical cues. Disentangling these effects and establishing clear causal links, therefore, requires integrated electrophysiological measurements and targeted biological interventions.

2.3. Tissue and organ scale

At the tissue and organ scale, biological responses to electrical signals are strongly tissue dependent and can be broadly classified into excitable and non-excitable tissues, which differ fundamentally in response time scales, activation thresholds, and safety windows. Excitable tissues, such as neural and cardiac tissues, are highly sensitive to electrical stimulation and generate rapid responses on the millisecond time scale.[2,3] For these systems, precise control of stimulation parameters is critical, as charge injection density, interfacial polarization, and local temperature rise directly affect functional safety, placing stringent demands on interfacial stability, signal fidelity, and long-term device reliability.

In contrast, soft load-bearing tissues, including skin, blood vessels, tendons, and ligaments, primarily exhibit electrical effects in slower regulatory processes such as regeneration, inflammation modulation, and angiogenesis.[47] Their electrical responses are often tightly coupled to the mechanical environment, enabling conductive and piezoelectric materials to offer distinct advantages in combined electrical and mechanical modulation. Bone tissue represents a special case, as its intrinsic piezoelectricity confers direct biological relevance to electrical signals in bone physiology and remodeling, thereby establishing a clear mechanistic connection between piezoelectric materials and bone repair and motivating sustained research into piezoelectric ceramics and composite scaffold systems.[48]

3. Electroactive materials and their fundamental characteristics

For electroactive materials used at biointerfaces, the primary value does not lie in simply achieving higher electrical conductivity or energy conversion efficiency. Rather, it lies in their ability to support stable, low-noise, low-impedance, and low-power electrical signal exchange under soft, wet, and ion-dominated biological environments over extended time periods. As a result, the advantages and limitations of different classes of electroactive materials in biological applications arise mainly from their underlying physicochemical mechanisms of electrical activity generation and transport, rather than from any single material metric. In this section, we discuss the fundamental electroactive mechanisms of representative material systems and analyze their key advances and remaining challenges in relevant biological contexts (Fig. 2 and Table 1).

3.1. *Conductive materials*

Conductive materials play foundational roles in bioelectronics as electrodes, interconnects, and media for signal acquisition and stimulation delivery.[68] Their electroactivity is rooted in the continuous transport of charge carriers, primarily electrons. Conventional metals and carbon-based materials rely on electronic conduction and offer high conductivity and chemical stability. However, their high elastic modulus and often hydrophobic surfaces tend to induce mechanical mismatch at biointerfaces, leading to elevated interfacial impedance and motion-induced artifacts.[69–71]

In recent years, conductive hydrogels and organic conductors have emerged as mainstream choices for biointerfaces, accompanied by a significant shift in electroactive mechanisms.[71–73] Conductive hydrogels typically construct continuous conductive networks using conducting polymers, ionic conductors, or conductive fillers, while their high-water content enables coupled ionic and electronic transport. This mixed conduction mechanism facilitates smoother signal transduction between materials and biological tissues, thereby markedly reducing interfacial impedance and polarization effects.

Key advances of conductive hydrogels at biointerfaces stem from the synergistic optimization of electroactive mechanisms and interfacial structures. On one hand, uniformly distributed and stable conductive networks, combined with highly hydrated interfaces, effectively lower contact impedance between electrodes and skin or tissues, improving the signal-to-noise ratio of weak bioelectrical signals such as ECG, EMG, and EEG.[74–77] On the other hand, the introduction of adhesion mechanisms, including covalent bonding, hydrogen bonding, or topological entanglement, enables robust attachment in wet environments, minimizing impedance fluctuations and signal drift caused by interfacial micromotion.[78,79]

3.2. *Piezoelectric materials*

The electroactivity of piezoelectric materials originates from their non-centrosymmetric crystal structures. Under mechanical loading, internal dipoles reorient and generate measurable polarization charges, enabling direct conversion of mechanical energy into electrical signals.[57,58,80–82] In biological environments, this mechanism allows piezoelectric materials to transduce daily motion, tissue deformation, or micro vibrations into localized electrical stimulation, forming self-powered electroactive systems without external energy input.[57,58,83]

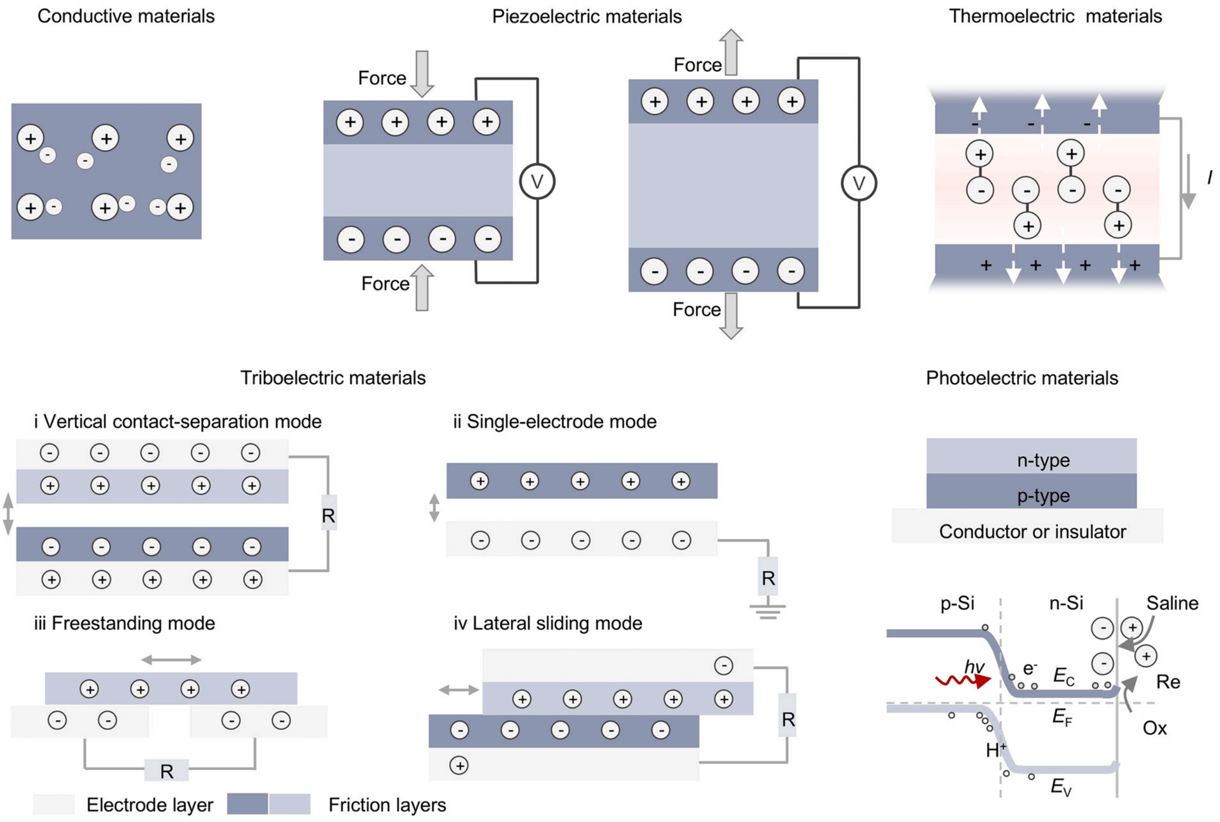


Fig. 2. Mechanisms of electroactive materials. Conductive materials enable electrical signal transmission through the continuous transport of charge carriers, including electrons and ions, within the material and across interfaces. Piezoelectric materials generate electrical polarization in response to mechanical deformation due to their non-centrosymmetric structures, allowing direct conversion of mechanical stimuli into electrical signals. Thermoelectric materials produce electrical output via the Seebeck effect, in which temperature gradients drive carrier diffusion and voltage generation. Triboelectric materials convert mechanical motion into electrical signals through contact electrification and electrostatic induction during contact, separation, or sliding processes. Photoelectric materials generate or modulate electrical signals upon light absorption by creating charge carriers or altering electronic band structures, thereby transducing optical stimuli into electrical responses.

In bone tissue engineering, piezoelectric ceramics such as barium titanate and their composites have been widely employed to construct electroactive scaffolds due to their relatively high piezoelectric coefficients and mature fabrication processes.[56] Their electrical output mechanisms closely resemble the endogenous electrical signals generated in bone under mechanical loading. In load-bearing soft tissues, including tendons, ligaments, and cartilage, piezoelectric materials are often combined with conductive components to create force-electric coupled microenvironments. In such systems, electroactivity evolves from a passive response into a dynamic factor actively involved in regulating cellular behavior.

The major limitations of piezoelectric materials in biological applications arise not from the piezoelectric effect itself, but from the effectiveness and controllability of electrical activity under realistic physiological conditions.[6] Mechanical loads *in vivo* are typically low in frequency and amplitude, making it challenging to generate sufficient and predictable electrical outputs. In addition, exposure to physiological fluids can lead to polarization decay, resulting in time-dependent drift of piezoelectric activity. More importantly, biological responses induced by piezoelectric stimulation are often accompanied by concurrent changes in mechanical cues and surface morphology.[84] Establishing clear causal mechanisms, therefore, requires integrated studies combining ion channel blocking, electrophysiological measurements, and signaling pathway analysis.

Table 1
Electroactive materials for bioelectronics and regenerative medicine.[26,28,48–67]

Material Type	Examples	Electroactive behavior	Young's modulus	Interface role	Device function	Advantages	Degradation	Application
Conductive materials								
Polymers	PEDOT, PPy	10^5 S m^{-1}	~ 1–100 MPa	Low-impedance biointerface; charge transfer	Signal acquisition, stimulation	Excellent mechanical	-	Nerve; Heart; Bone; Skin; Motion sensor; Disease surveillance
Biodegradable-metals	Mg, Zn, Fe, Mo, W	> 10^6 S m^{-1}	~ 10–50 GPa	Temporary conductive interface	Implantable electrodes	Biodegradable; High mechanical strength;	Days to years	
Non-biodegradable metals	Au, Ag, Cu, Ti	> 10^6 S m^{-1}	~ 50–120 GPa	Stable electrode interface	Signal transmission	High mechanical strength;	-	
Two-dimensional materials	MXene, GO, rGO	1–10^4 S m^{-1}	~ 1–10 GPa	High surface area interface	Sensing, stimulation	Good conductivity; Biodegradable	Partial	
Piezoelectric materials								
Non-biodegradable inorganic materials	BaTiO$_3$/ KNN	d_{33} 150–200 pC N^{-1}	~ 50–150 GPa	Mechano-electrical interface	Self-powered stimulation	Self-powered; High piezoelectric coefficient;	-	Nerve; Heart; Bone; Skin; Motion sensor; Disease surveillance
Biodegradable inorganic materials	ZnO	d_{33} 10 pC N^{-1}	~ 50–120 GPa	Mechano-electrical interface	Self-powered stimulation	Self-powered; Biodegradable;	Days to weeks	
Non-biodegradable synthetic polymers	PVDF	d_{33} 30 pC N^{-1}	~ 1–3 GPa	Flexible transducer interface	Sensing, stimulation	Self-powered; Soft; Biocompatible;	-	
Biodegradable synthetic polymers	PLLA	d_{14} 10 pC N^{-1}	~ 0.1–4 GPa	Temporary interface	Regeneration stimulation	Self-powered; Biodegradable; Soft	Months to years	
Natural polymers	β-glycine	d_{16} 190 pC N^{-1}	~ 1–10 GPa	Temporary interface	Self-powered sensing	Self-powered; Biodegradable;	Minutes to hours	
Thermoelectric materials								
Organic thermoelectric materials	TPU/ FeSO$_4$: Fe$_2$(SO$_4$)$_3$	1.7–3.6 mV K^{-1} 1.84 S m^{-1}	~ 1–50 MPa	Flexible thermal interface	Energy harvesting	Self-powered; Soft; Highly integrated; Biocompatible	-	Skin; Motion sensor; Disease surveillance
Inorganic thermoelectric materials	Bi$_2$Te$_3$/ Bi$_{0.5}$Sb$_{1.5}$Te$_3$	10 K 10 mV	~ 30–80 GPa	Thermal-electric interface	Power supply	Self-powered; Soft; Biocompatible	-	

(*continued on next page*)

Table 1 (*continued*)

Material Type	Examples	Electroactive behavior	Young's modulus	Interface role	Device function	Advantages	Degradation	Application
Triboelectric materials								
Inorganic non-metallic materials	ZnO/$MgSiO_3$	0.9–2.7 μC m^{-2}	~10–100 GPa	Contact interface	Self-powered sensing	Excellent capability; Self-powered; High biological safety	-	Nerve; Heart; Bone; Skin; Motion Sensor; Disease surveillance
Synthetic polymers	PTFE/PDMS/Kapton/PVDF	87–113 μC m^{-2}	~0.5 MPa–1 GPa	Flexible contact interface	Energy harvesting	Strong organizational adaptability; Self-powered; Soft	-	
Natural polymer materials	Gelatin/HA	4–165 mW m^{-2}	~10 kPa–1 MPa	Biointerface	Self-powered sensing	Biodegradable; Self-powered; Soft	Weeks to months	
Photoelectric materials								
Organic materials	PTCDI/H_2Pc	300-320 mV	~1–5 GPa	Light-responsive interface	Optical stimulation	Soft	-	Neuromodulation; Cardiac Pacing; Bone; Skin
Inorganic material	p-type Si	100 nA	~100–170 GPa	Light-responsive interface	Optical stimulation	Soft; Biocompatibility	5–100 nm/day	

PEDOT: poly(3,4-ethylenedioxythiophene; PPy: polypyrrole; KNN: potassium sodium niobate; PVDF: polyvinylidene fluoride; PLLA: poly(L-lactic acid); TPU: thermoplastic polyurethane; PTFE: polytetrafluoroethylene; PDMS: polydimethylsiloxane; HA: hyaluronic acid; PTCDI: perylene-3,4,9,10-tetracarboxylic diimide.

3.3. *Thermoelectric materials*

The electroactivity of thermoelectric materials is based on the Seebeck effect, in which a temperature gradient drives carrier diffusion and generates an electrical voltage. In biological settings, available temperature differences on or within the body are typically limited to only a few kelvin or less.[85,86] Consequently, the electroactivity of thermoelectric materials is generally manifested as low-power, continuous, or intermittent output rather than high-efficiency energy conversion.

Their practical value lies in synergy with ultralow-power electronics, where they can support energy supplementation, bias maintenance, or state monitoring rather than serving as standalone power sources.[87–89] In such systems, thermal management architectures and packaging-related thermal resistance are often more critical than the intrinsic Seebeck coefficient of the material.

3.4. *Triboelectric materials*

Triboelectric materials generate electrical signals through contact electrification and electrostatic induction, enabling mechanical energy to be converted into electrical output during contact separation or sliding.[66,90] This mechanism grants triboelectric nanogenerators high sensitivity and structural flexibility, making them attractive for wearable motion monitoring and event-driven sensing.[91,92]

However, in wet or fluid-rich biological environments, surface charges are readily neutralized, leading to pronounced degradation of electrical output. In addition, triboelectric signals are strongly dependent on motion dynamics and are easily coupled with motion artifacts. These factors pose challenges to signal authenticity, stability, and calibration in bioelectrical sensing applications.

3.5. *Photoelectric materials*

The electrical activity of photoelectric materials originates from the generation and separation of photo-induced charge carriers, enabling localized electrical stimulation or signal acquisition without direct contact.[93] This characteristic offers unique advantages in neural regulation and high spatial resolution stimulation.[24,25,67]

However, due to the limited light penetration depth in biological tissues and potential photothermal effects, photoelectric materials are more suitable for integration with other electroactive systems to form hybrid systems, such as photoelectric stimulation combined with conductive hydrogels or OECT signal readout, to achieve synergistic regulation of photo-electric-biological signals.

4. Systematic implementation pathway for electroactive materials devices

For electroactive materials to transition from material-level performance demonstration to repeatable, verifiable, and application-potential devices, the core challenge lies not in breakthroughs of individual materials or single performance metrics, but in establishing a systematic implementation pathway that starts with biological needs, spans material design, device realization, and multi-level verification. Without a systematic design approach, material research often remains at the level of parameter comparisons and fails to support stable device-level functionality and long-term application.

This chapter systematically summarizes the key decision-making logic from demand definition, material selection to device fabrication and verification, with a focus on the intrinsic coupling between "demand-material-device-biological validation," providing a reproducible implementation framework for the engineering and transformative application of electroactive materials (Fig. 3).

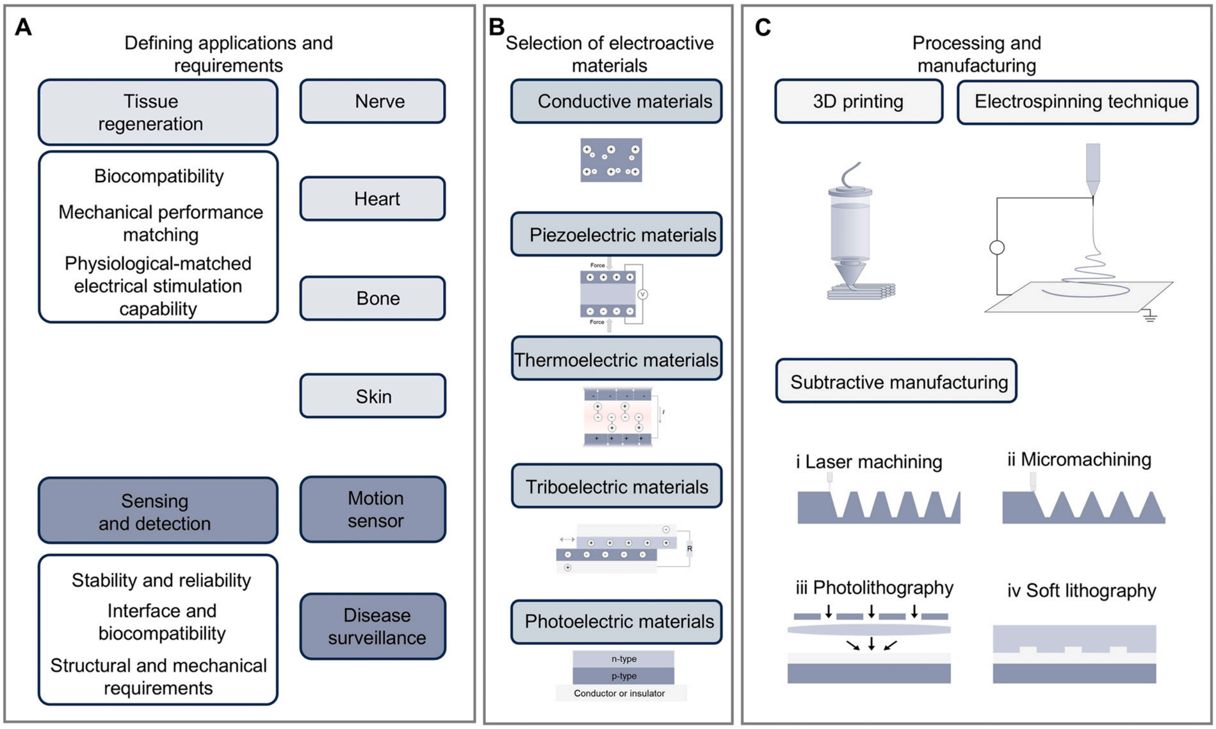


Fig. 3. Design criteria for electroactive device systems. (A) Defining applications and requirements. (B) Selection of electroactive materials. (C) Processing and Manufacturing.

4.1. Engineering specification definition method driven by biological needs

The design of electroactive material devices should start with biological issues, rather than focusing on material properties. Biological systems exhibit significant heterogeneity and contextual dependence. If application goals and environmental conditions are not clearly defined at the early design stage, there is a risk of a disconnect between optimized material performance and actual application needs. Therefore, it is essential to systematically translate complex biological issues into executable engineering specifications.

Firstly, the biological goals need to be clearly defined, focusing on answering the two basic questions:“What to measure?” and “What to control?” “What to measure?” typically involves the acquisition of electrophysiological signals (such as ECG, EMG, EEG), biochemical metabolites, or inflammation-related indicators. “What to control?” includes functional needs such as neural stimulation, muscle activation, electric fields for regeneration promotion, or drug release triggers. Different goals directly determine the signal frequency range, amplitude levels, and tolerance thresholds for noise and interference.

Secondly, application scenarios and environmental constraints must be clearly outlined. Surface-mounted versus implanted applications, short-term use versus chronic service, static monitoring versus continuous operation under high motion states, all impose fundamentally different requirements on materials and devices. Humidity, bodily fluid environments, mechanical loads, as well as ethical and regulatory requirements, directly affect material selection, structural design, and packaging strategies. If these constraints are not considered in the early stages of design, they often evolve into insurmountable bottlenecks during the subsequent translation phase.

Finally, biological needs should be translated into quantifiable engineering metrics, including sensitivity, specificity, noise levels, signal drift, service life, safety working window, and manufacturability. It is important to emphasize that material choices must serve the target signal characteristics and overall system power consumption budget, rather than solely aiming to push a single material performance metric to its extreme.

4.2. Material selection and material-interface-system mapping relationship

Once application needs are clear, material selection should not be based solely on material type or single performance parameters, but should establish a “material-interface-system function” mapping relationship from a system perspective, i.e., clarifying the interface role of the material in the device and its actual contribution to overall performance.

For high-quality electrophysiological signal acquisition and electrical stimulation electrodes, the design focus is on reducing biological interface impedance and noise levels, while ensuring long-term stable adhesion in dynamic physiological environments.[94,95] Conductive hydrogels and other soft interface materials, due to their low modulus, high water content, and good wettability, effectively mitigate the mismatch between soft and hard interfaces and are essential materials for constructing high-performance bioelectric interfaces. However, their potential risks of dehydration, aging, and biological contamination still need to be addressed through synergistic optimization of material system design and packaging strategies.

In passive or self-powered event sensing applications, piezoelectric and triboelectric materials demonstrate unique advantages. These materials do not aim for a continuous power supply, but instead, they convert mechanical disturbances into recognizable electrical signals to trigger events or monitor states. In such applications, the key to material selection lies not in maximizing instantaneous output amplitude, but in the repeatability of signal output, environmental stability, and calibratability under moist physiological conditions.

Thermoelectric materials are primarily used for energy supplementation and state maintenance in ultra-low-power systems, with their electrical activity derived from small temperature differences on the skin surface or inside the body. Because the temperature difference available is often very limited, thermoelectric materials are unlikely to serve as independent power sources. Therefore, material selection should focus on their synergistic match with low-power electronic systems, long-term stable output capabilities, and thermal management and packaging design at the device level.

Photoelectric materials are suitable for applications requiring non-contact control or spatially selective stimulation, such as light-induced neural regulation or localized signal triggering. During the material selection process, attention should be paid to their spectral response range, biological tissue penetration depth, potential photothermal side effects, and stability and biocompatibility *in vivo*, rather than simply pursuing high photoelectric conversion efficiency.

In addition to functional matching at the material–interface level, achieving practical system operation also requires careful consideration of energy supply and consumption at the system level. In practice, electroactive materials such as piezoelectric, triboelectric, and thermoelectric systems typically generate intermittent, low-frequency, and environment-dependent outputs, whereas backend modules for signal acquisition, processing, and wireless transmission require continuous and stable power. This inherent mismatch represents a key bottleneck in translating material-level energy conversion into functional devices.

To address this issue, system-level integration strategies are essential. Hybrid energy harvesting approaches can improve energy availability under varying physiological conditions, while power management circuits-including rectification, impedance matching, and voltage regulation-are required to convert irregular outputs into usable electrical energy. Energy storage components, such as micro-supercapacitors or micro-batteries, can buffer fluctuating outputs and support intermittent high-power operations. In addition, energy-aware operation strategies, such as duty-cycled sensing, event-triggered data acquisition, and local signal processing, can significantly reduce overall energy consumption.

Overall, these considerations highlight that material selection should not only focus on local interface performance but also on its role within the system-level energy architecture, enabling coordinated optimization across materials, devices, circuits, and operation strategies.

4.3. Manufacturing and multi-level verification pathway for electroactive materials devices

Once the material system is determined, whether the device can achieve stable, reliable, and repeatable functional output depends on the complete closed-loop design spanning fabrication, interconnection integration, encapsulation, and verification. In particular, the transition from electroactive materials to functional devices inevitably involves the integration of mechanically dissimilar components, such as soft interfacing materials, rigid chips, metallic conductors, and packaging layers. As a result, soft-rigid junctions often become the most vulnerable sites under chronic physiological loading.

During long-term operation in dynamic biological environments, repeated deformation, tissue motion, and environmental fluctuations can induce stress concentration at these heterogeneous interfaces, leading to interfacial delamination, conductor fracture, contact instability, and moisture or ion-induced electrical failure. To mitigate these risks, current device engineering strategies increasingly rely on structural and materials co-design. Strain-isolation architectures, such as island–bridge layouts, serpentine interconnects, and three-dimensional or helical configurations, are widely adopted to redistribute mechanical strain away from rigid functional regions. In parallel, compliance engineering strategies-including soft substrates, intrinsically stretchable conductors, and modulus-gradient or buffer layers-are used to reduce abrupt mechanical mismatch across interfaces. Furthermore, interfacial adhesion can be enhanced through surface activation, adhesion promoters, bioadhesive layers, and mechanical interlocking structures, thereby improving resistance to delamination under cyclic loading.

Encapsulation is equally critical for long-term device reliability, as even mechanically robust systems may fail due to gradual penetration of water and ions into active regions or interconnects. Advanced encapsulation strategies typically employ conformal multilayer barriers, such as polymer/oxide or organic/inorganic hybrid thin films, which combine flexibility with improved resistance to moisture and ion ingress. Importantly, encapsulation design must be integrated with interconnect geometry and interface engineering to ensure barrier integrity under chronic deformation and physiological exposure.

To systematically evaluate device performance under realistic conditions, the verification process can be divided into three progressive levels: material level, device level, and biological level.

Material-level verification primarily focuses on the fundamental performance and stability of the material in the target service environment, including mechanical properties (elastic modulus, stretching and fatigue behavior, interface adhesion energy), electrical properties (conductivity, Seebeck coefficient, piezoelectric coefficient, etc.), and stability in moist and ionic environments, such as swelling behavior, dehydration characteristics, and salt solution aging. Additionally, the biological safety of the material must be systematically assessed, including cytotoxicity and the potential biological impacts of leachable or degradation products.

At the device level, the verification focus shifts to functional reliability and determining safety boundaries. Impedance spectroscopy (EIS) and noise spectral density analysis can be used to assess the quality of biological interfaces; signal drift and calibration characteristics under temperature and humidity variations, mechanical stress, or motion disturbance reflect the device’s stability in real working conditions. For devices involving electrical stimulation functions, charge injection density, polarization window, and local temperature rise must also be systematically evaluated, especially in neural and myocardial applications, where these parameters directly define the device's safe operating range.

Biological-level verification should follow a clear evidence-based pathway, progressing from *in vitro* experiments to small-animal acute models and then to sub-chronic or chronic implantation studies. The evaluation should assess not only functional effectiveness, but also the temporal evolution of inflammation, fibrotic encapsulation, interface stability, and long-term functional maintenance.

In physiological environments, the long-term degradation of electroactive devices often arises from the coupled evolution of material properties, interfacial chemistry, and host responses. After implantation, rapid protein adsorption forms an initial biointerface, followed by acute inflammation and immune-cell recruitment. With prolonged implantation, chronic inflammation, fibroblast activation, extracellular matrix remodeling, and collagen deposition may lead to fibrotic capsule formation.

For electroactive materials and bioelectronic interfaces, these processes are particularly important because they increase the separation between the device and target tissue and alter ionic transport, interfacial impedance, polarization behavior, and charge transfer. As a result, signal attenuation, noise increase, stimulation-threshold drift, and reduced therapeutic performance may gradually occur. These effects can further couple with material aging, swelling, dehydration, ion adsorption, and packaging defects, accelerating long-term instability.

Therefore, biological-level validation should go beyond endpoint assessments of efficacy or histological compatibility and include time-dependent evaluation of inflammation, fibrotic encapsulation, interface integrity, impedance changes, signal stability, and stimulation safety during long-term implantation.

5. Biological applications of electroactive materials devices

Broadly speaking, the interaction between electroactive materials and biological systems can be summarized into two basic and complementary functional modes: the first is as a "sensing and translation unit" for physiological information, which accurately converts mechanical, bioelectric, or behavioral signals from the human body into interpretable electrical signals for continuous monitoring and quantitative analysis of life states; the second is as an "active regulation unit" for biological processes, outputting controllable electrical signals as a non-pharmacological physical stimulation means to directly intervene and reshape cellular and tissue functional behaviors, thus promoting repair and regeneration. Importantly, the integration of these two modes enables the formation of closed-loop systems, in which real-time physiological sensing is coupled with feedback-controlled stimulation, allowing dynamic and adaptive regulation of biological processes. Together, these functional modes provide the fundamental basis for electroactive materials in physiological sensing, electrically mediated tissue repair, and emerging closed-loop theranostic applications.

5.1. Application of electroactive materials in human motion sensing and detection

In the field of human motion sensing and detection, the core function of electroactive materials lies in passively sensing and accurately translating the mechanical behaviors of the human body.[96–99] When such materials are constructed into flexible or stretchable electronic devices that closely adhere to the skin, or further integrated into smart textile structures, mechanical activities ranging from macroscopic joint flexion and muscle contraction to microscopic movements such as pulse beats and vocal cord vibrations can induce corresponding physical deformations in the material.[100] The key advantage of electroactive materials is their ability to convert these complex, multi-scale deformation processes into electrical signal outputs in real-time, with high sensitivity and repeatability, establishing a direct and stable interface between the physical world of the human body and digital information systems.[52]

Based on different physical mechanisms, mechanical deformation can be converted into measurable electrical signals via various pathways. For example, piezoelectric and triboelectric materials can directly generate voltage or current during mechanical force or relative movement, making them naturally suitable for building self-powered sensing systems to capture periodic dynamic behaviors such as gait, heartbeat, and breathing.[20,101] Meanwhile, flexible conductive materials based on the piezoresistive effect (such as conductive hydrogels, carbon-based or composite conductive networks) undergo changes in internal conductive pathways due to deformation, allowing a quantitative correlation between resistance changes and deformation magnitude.[102,103] These material systems, based on different mechanisms, have driven the development of various novel device forms, including "electronic skin" for fine monitoring of joint motion and facial expressions, "smart textiles" for long-term, imperceptible monitoring of breathing and gait, and human-machine interfaces for prosthesis control and immersive virtual reality.[104–107]

Although electroactive sensors have demonstrated significant potential in human motion sensing, several challenges remain as they transition from laboratory prototypes to large-scale, reliable applications. First, in terms of signal fidelity and long-term stability, the inherent hysteresis, creep, and signal drift of materials, combined with electromagnetic interference and complex motion artifacts in real-world applications, make the accurate extraction of high-quality physiological information highly dependent on advanced signal processing and modeling algorithms. Second, regarding material durability and biocompatibility, long-term attachment or wearable devices not only need to meet basic requirements such as non-irritation, breathability, and skin-friendliness but must also maintain electrical performance and mechanical integrity after enduring thousands of stretching, bending, and washing cycles.[108–111] Finally, in terms of system-level integration and intelligence, how to reliably integrate rigid signal processing, wireless communication, and energy management modules with flexible sensing units into a unified package and ensure long-term operation under ultra-low-power conditions remains a core engineering challenge.[112] Furthermore, given the significant physiological and motion differences between individuals, there is an urgent need to develop rapid personalized calibration strategies and, in conjunction with machine learning methods, achieve adaptive interpretation of sensor data and high-level semantic extraction (Fig. 4).[113–115]

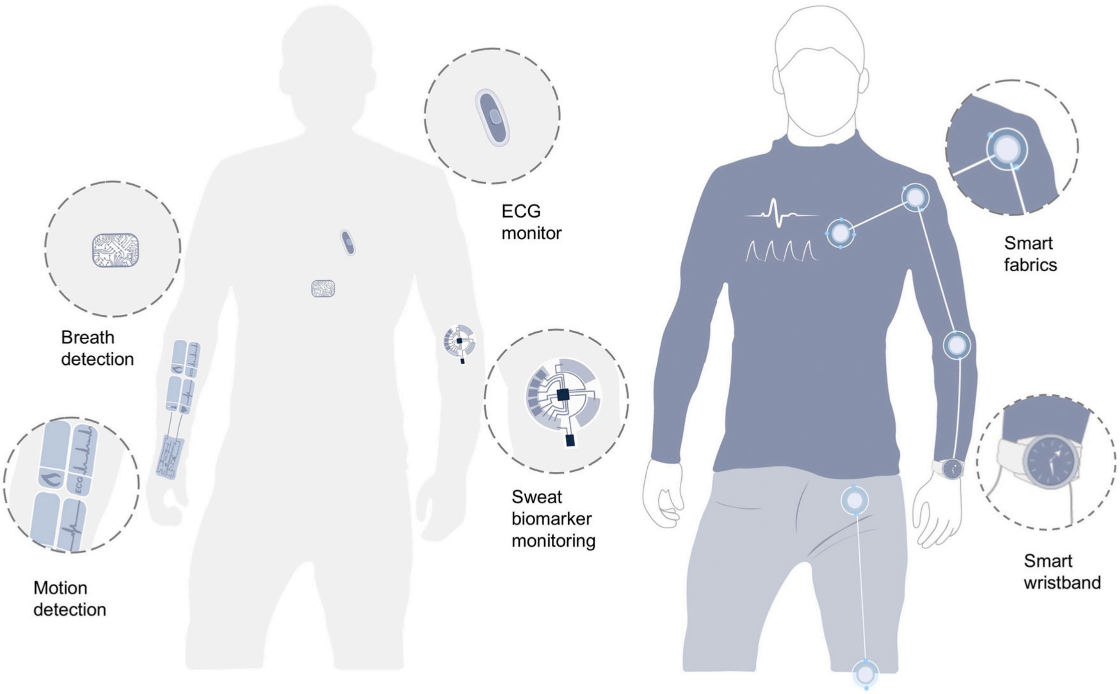


Fig. 4. The application of electroactive devices in human motion sensing and detection.

5.2. *Applications of electroactive materials in electric stimulation-mediated tissue repair*

Unlike the "passive sensing" role in motion sensing, electroactive materials in tissue repair serve as an active platform for outputting functional electrical signals (Fig. 5).[83] In this application paradigm, precisely controlled electrical stimulation is regarded as a non-pharmacological physical therapy that directly intervenes and guides cell proliferation, migration, differentiation, and tissue remodeling processes, thereby accelerating injury repair and promoting functional reconstruction.[38] The biological basis of this approach lies in the intrinsic electrical sensitivity of living systems, where cellular behavior and tissue homeostasis are regulated by endogenous bioelectric signals and potential gradients.[5,52]

In this context, conductive materials (including conductive polymers, conductive hydrogels, and carbon-based or metal nanocomposites) primarily function as flexible electrodes or conductive scaffolds.[16,119,120] Compared to traditional rigid metal electrodes, these materials are mechanically more compatible with soft tissues, significantly reducing interface stress concentration, inflammation responses, and the risk of micro-motion damage. As flexible electrodes, they can transmit electrical signals generated by external stimulation sources to the target tissues with lower energy thresholds and higher spatial uniformity, used for functional electrical stimulation of tissues like nerves, muscles, or the heart.[121,122] As three-dimensional conductive scaffolds, their significance is even more profound. Using 3D printing and other fabrication technologies, porous structures with internal conductive networks can be constructed, providing cells with a biomimetic microenvironment that combines structural support and electrical signal regulation.[123,124] By applying specific electric field distributions, directed potential gradients can be formed inside the scaffold to guide neuronal axon extension, which is crucial for the structural and electrophysiological reconstruction of functional tissues.[125,126]

Thermoelectric materials utilize the temperature gradients that universally exist between the body surface or wound area and the external environment, converting thermal energy directly into continuous, stable, weak electrical signals through the Seebeck effect.[28] Compared to mechanical energy conversion strategies, thermoelectric stimulation does not rely on significant body movement and can continue to work even in a resting state. Therefore, it shows unique advantages in chronic wounds,

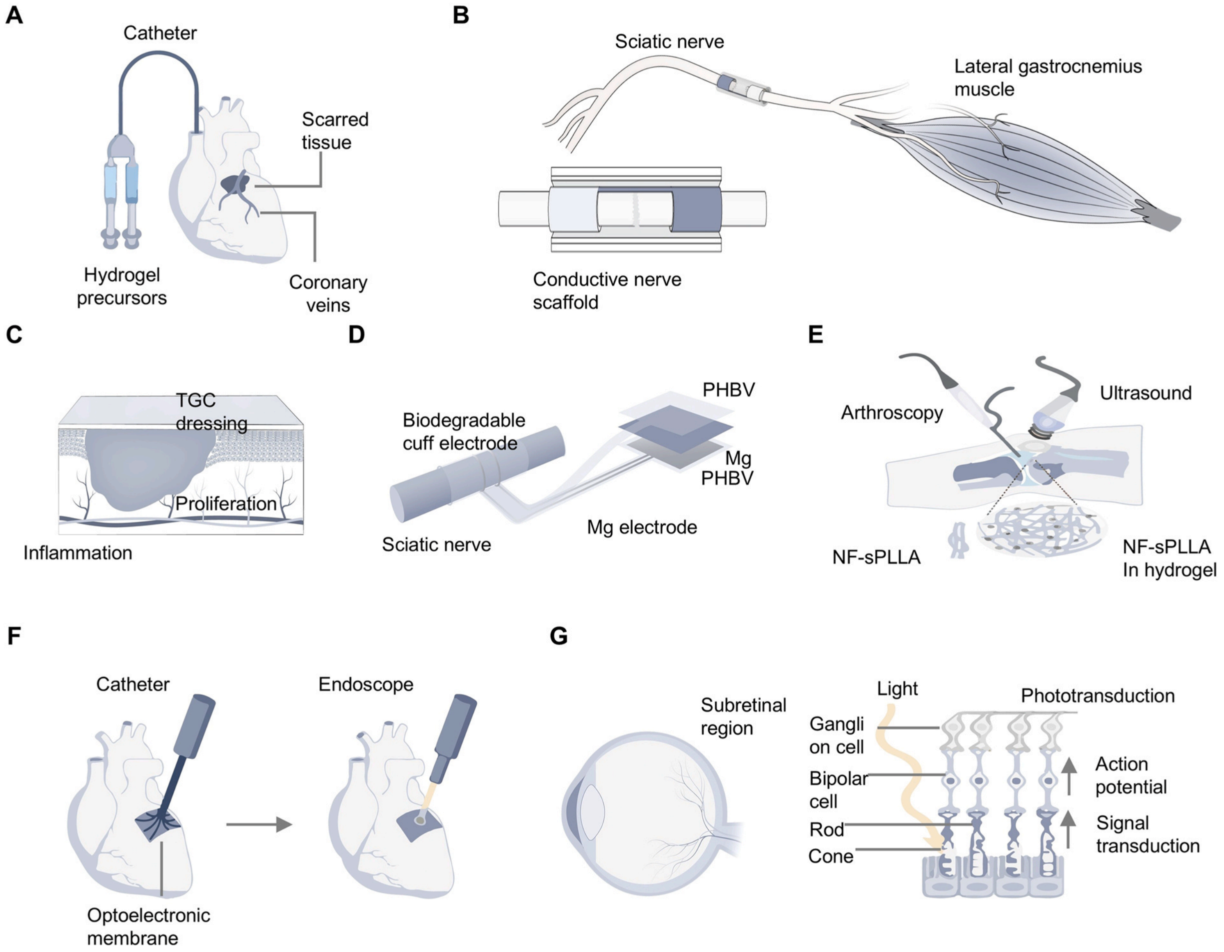


Fig. 5. The application of electroactive devices in biological tissues. (A) Injectable conductive hydrogel for myocardial infarction treatment.[16] (B) Conductive nerve scaffolds are used for peripheral nerve repair. (C) Thermoelectric hydrogel as a dressing material for wound healing.[28] (D) On-demand-driven biodegradable TENG for nerve repair.[116] (E) Ultrasound-driven piezoelectric hydrogel accelerates bone repair.[117] (F) Flexible photovoltaic silicon films are used in cardiac pacing.[25] (G) Optoelectronic nanomaterials for visual restoration.[118].

burns, and diabetic ulcers, among other long-term repair scenarios. When thermoelectric materials are integrated into flexible dressings or wound coverings, they can establish low-intensity electric fields *in situ* in the wound microenvironment without external energy supply, thereby regulating fibroblast migration, epithelial regeneration, and angiogenesis processes.[29,127] This temperature-difference-driven, self-powered stimulation mode provides a new material path for developing long-term, low-burden, and patient-compliant smart wound repair systems.

Furthermore, piezoelectric, triboelectric, and optoelectronic materials represent a class of more intelligent stimulation strategies, with the common goal of elevating the electric stimulation model for tissue repair from “wired intervention” dependent on external power sources to *in situ* energy conversion and wireless precise control.[24,25,116] Unlike traditional stimulation systems continuously powered by external devices, these materials can directly utilize the physical energy that is commonly present in the human body or the environment, achieving more biologically adaptive electrical signal output.

Ultrasound-driven on-demand neural scaffolds and ultrasound-responsive piezoelectric hydrogels have been developed for nerve and cartilage repair, respectively.[116,128] By converting external mechanical energy into localized microcurrents, these materials enable self-powered, on-demand electrical stimulation that synergistically combines mechanical and electrical cues to promote tissue repair and accelerate healing.

In contrast, optoelectronic materials exhibit unique advantages in stimulation precision, especially in nerve regulation and biomedical fields. With highly controllable optical techniques, optoelectronic silicon membrane technology can precisely regulate local electrical signals on a micrometer spatial scale and millisecond time scale. This characteristic is particularly prominent in the applications of pacemakers and artificial retinas: in pacemaker applications, optoelectronic silicon membranes can provide precise electrical stimulation to ensure stable heart rhythms; while in artificial retina research, optoelectronic materials regulate local currents through the photoelectric effect, achieving self-powered visible and near-infrared vision restoration in retinal prosthetics, with good biocompatibility and functional validation, offering a new approach for treating retinal degenerative diseases.[25]

Despite the promising prospects of the above strategies, their clinical translation still faces key scientific challenges, including the precise matching of long-term biocompatibility, degradation behavior, and functional lifespan of materials, as well as the safety and efficacy windows of stimulation parameters in different physiological environments.

5.3. *Closed-loop theranostics*

Beyond the conventional classification into passive sensing and active regulation, electroactive material-based systems are increasingly evolving toward closed-loop theranostics, where real-time physiological monitoring is seamlessly integrated with on-demand therapeutic intervention. Such systems establish a feedback loop linking signal acquisition, processing, and actuation, enabling adaptive regulation of biological functions.

A typical closed-loop system involves high-fidelity sensing interfaces, real-time data processing, and localized stimulation modules. Electroactive materials play a central role in both signal transduction and functional actuation. Reliable operation requires stable, low-noise biointerfaces for accurate signal acquisition, as well as precise and controllable stimulation to avoid interference and ensure effectiveness.

However, several challenges remain. Long-term interface stability, biofouling, and fibrotic encapsulation can degrade signal quality. At the device level, soft–rigid integration and encapsulation reliability are critical under chronic physiological loading. At the system level, response latency, energy efficiency, and the integration of sensing, processing, and actuation modules remain key bottlenecks.

Future progress will rely on co-design across materials, interfaces, devices, and system architectures. Closed-loop theranostic systems are expected to enable intelligent, self-adaptive bioelectronics for precision medicine and long-term health management.

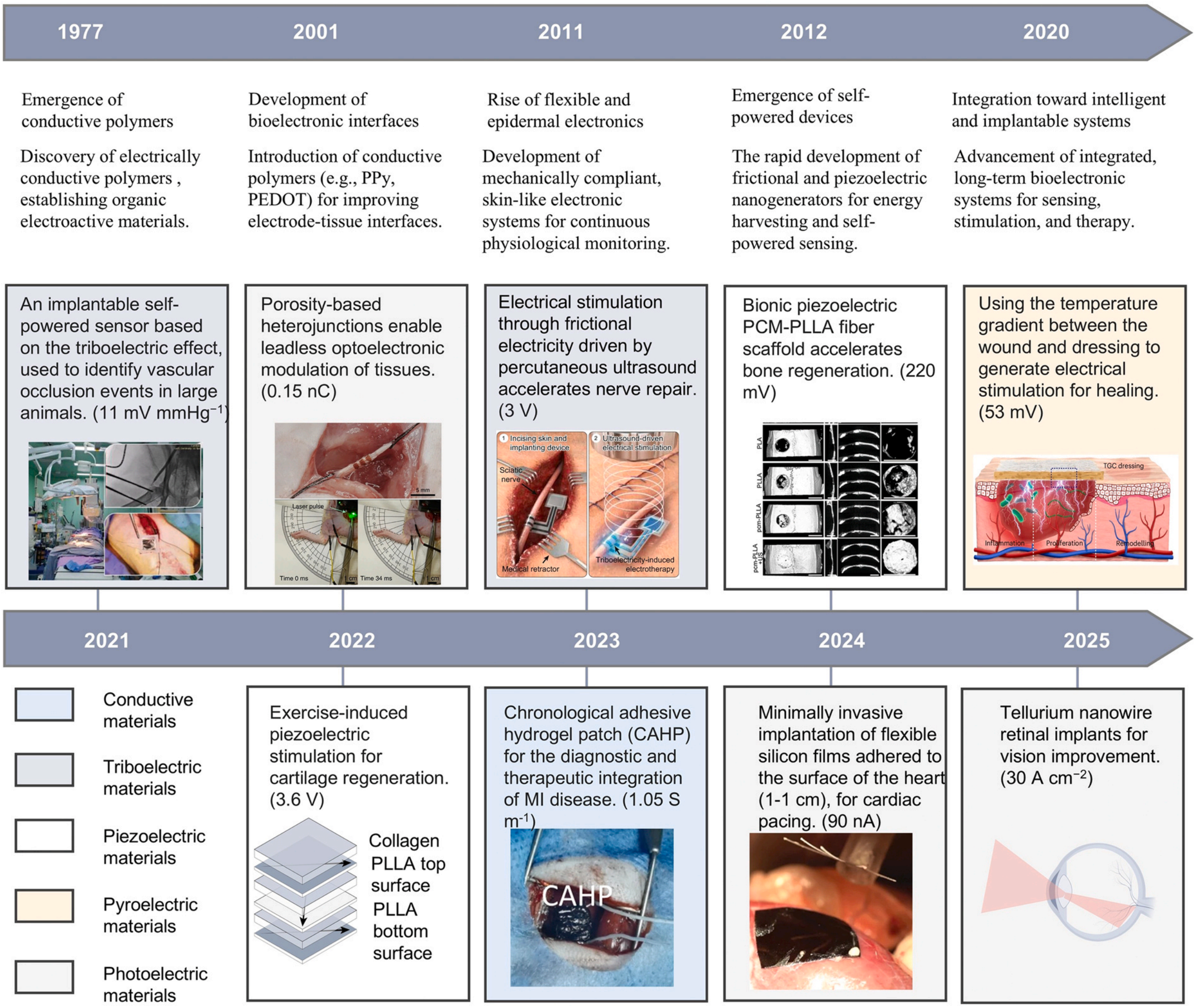
6. Future development directions

From the discovery of conducting polymers in 1977, the field of electroactive materials gradually evolved from material-level conductivity studies to biointerface engineering in the early 2000s, flexible epidermal electronics in 2011, self-powered devices enabled by triboelectric nanogenerators after 2012, and finally toward integrated, chronically stable, and even bioresorbable bioelectronic systems by 2020. Together, these milestones mark the transition of electroactive materials from fundamental functional materials to system-level platforms for sensing, stimulation, and regenerative bioelectronics.

Building upon these foundational advances, recent years have witnessed rapid progress in translating electroactive materials into practical biomedical applications. In 2021, a biodegradable self-powered sensor based on the triboelectric effect was developed for detecting vascular occlusion.[129] In 2022, porous heterojunction materials achieved passive photoelectric regulation, enabling precise control of tissue electrical signals.[26,67,130] By 2023, ultrasound-driven electrical stimulation technology was applied to nerve repair, converting external mechanical energy into electrical current to effectively promote nerve tissue regeneration.[116] In 2024, piezoelectric materials were used for bone repair, accelerating the healing process.[48] Flexible silicon thin films were also successfully applied to pacemakers, providing a more convenient treatment method for patients. By 2025, thermoelectric materials and tellurium nanowire retinal prostheses will drive technological advances in wound healing and vision restoration. These developments demonstrate the broad application potential of electroactive materials in the medical field.[28,118]

Overall, the field of electroactive materials is undergoing a critical transition from being driven by material performance to being guided by system and application needs. As bioelectronics, regenerative medicine, and precision medicine demand higher standards for long-term stability, interface safety, and system synergy, the traditional research paradigm focusing solely on improving conductivity, output power, or energy conversion efficiency is no longer sufficient to support the sustained development of the field. In the future, the core competitiveness of electroactive materials will lie more in their ability to achieve predictable, controllable, and long-term functioning electrical signal interactions in complex biological environments, as well as their deep integration with device systems and biological systems. Based on this overall trend, the future development of electroactive materials can be summarized as the following interconnected key paths (Fig. 6):

Shifting from material performance competition to bioelectrical interface quality dominance. Biological systems are characterized by ion conduction, dynamic reconstruction, and adaptive regulation, which inherently mismatch with traditional material systems that focus on electronic conduction



1977

Emergence of conductive polymers

Discovery of electrically conductive polymers , establishing organic electroactive materials.

2001

Development of bioelectronic interfaces

Introduction of conductive polymers (e.g., PPy, PEDOT) for improving electrode-tissue interfaces.

2011

Rise of flexible and epidermal electronics

Development of mechanically compliant, skin-like electronic systems for continuous physiological monitoring.

2012

Emergence of self-powered devices

The rapid development of frictional and piezoelectric nanogenerators for energy harvesting and self-powered sensing.

2020

Integration toward intelligent and implantable systems

Advancement of integrated, long-term bioelectronic systems for sensing, stimulation, and therapy.

2021

An implantable self-powered sensor based on the triboelectric effect, used to identify vascular occlusion events in large animals. (11 mV mmHg^{-1})

2022

Porosity-based heterojunctions enable leadless optoelectronic modulation of tissues. (0.15 nC)

Exercise-induced piezoelectric stimulation for cartilage regeneration. (3.6 V)

2023

Electrical stimulation through frictional electricity driven by percutaneous ultrasound accelerates nerve repair. (3 V)

Chronological adhesive hydrogel patch (CAHP) for the diagnostic and therapeutic integration of MI disease. (1.05 S m^{-1})

2024

Bionic piezoelectric PCM-PLLA fiber scaffold accelerates bone regeneration. (220 mV)

Minimally invasive implantation of flexible silicon films adhered to the surface of the heart (1-1 cm), for cardiac pacing. (90 nA)

2025

Using the temperature gradient between the wound and dressing to generate electrical stimulation for healing. (53 mV)

Tellurium nanowire retinal implants for vision improvement. (30 A cm^{-2})

Fig. 6. The development process of electroactive devices. Copyright 2021, Wiley-VCH GmbH. Copyright 2022, Springer Nature. Copyright 2023, Springer Nature. Copyright 2023, Springer Nature. Copyright 2024, Science China Press. Copyright 2024, Springer Nature. Copyright 2025, Springer Nature.

and structural stability. As a result, the interface becomes a key bottleneck limiting the biological applications of electroactive materials. Future research will focus more on constructing ion-electron-biological three-phase synergistic interfaces, systematically optimizing interface impedance, polarization behavior, biocompatibility, and long-term stability, and advancing materials from simple functional carriers to active units that can embed and participate in the regulation of the biological microenvironment.

Moving from single physical response to multi-field coupling and system-level design. In the future, electroactive materials will increasingly exist not as “single-function materials” but as multi-physical-field coupling nodes embedded in complex bioelectronic systems. In real biological environments, electrical, mechanical, thermal, optical, and chemical signals are highly intertwined, requiring materials to exhibit predictability, calibratability, and environmental robustness. Accordingly, the research focus will shift from maximizing output to achieving stable, repeatable, and interpretable functional responses under real operating conditions, while obtaining high information-density effective outputs under low-drive conditions through structural design, signal processing, and algorithmic collaboration.

AI-Driven fabrication as a key enabling technology for electroactive materials. As material systems and fabrication processes evolve towards multi-component, multi-scale, and strong path-dependency directions, traditional trial-and-error optimization driven by experience can no longer support rapid iteration. In the future, artificial intelligence will be deeply integrated into the design and fabrication processes of electroactive materials, achieving efficient reverse design and application-customized material development by learning the high-dimensional nonlinear relationships between preparation parameters, microstructures, and electroactive performance. Further combined with *in situ* characterization and adaptive control, electroactive materials will evolve from static products into functional systems that can be “trained” during the fabrication stage.

From short-term functional demonstration to long-term reliability and translation-oriented development. The truly influential research in the future will focus on long-term reliability, system safety, and manufacturability as core evaluation standards. Issues such as material aging, interface contamination, packaging failure, and performance drift will rise from engineering details to key scientific questions determining whether devices can work stably over the long term. In this context, biodegradable and transient electronics, stable bioelectrical interface design for chronic applications, and AI-assisted fabrication and quality control will collectively promote the real-world application and clinical translation of electroactive materials.

Symbiotic bioelectronics will become a new pathway for the development of electroactive materials.[131–133] Symbiotic bioelectronics not only emphasizes the interaction between electroactive materials and biological systems but also focuses on the deep synergy between the two in terms of functionality, adaptability, and self-regulation. Future electroactive materials will not merely serve as tools for biological systems, but rather as system units that evolve alongside the biological body. This means that electroactive materials will achieve adaptive functional responses within the biological body, seamlessly integrating with biological signals to form a dynamic, symbiotic bioelectronic system. Furthermore, this system will not only respond to changes in the external environment but will also actively participate in regulating the biological environment and self-repair, ensuring long-term stability and reliability.

In summary, the future of electroactive materials will not only need to achieve efficient interaction with bioelectrical signals at the functional level but also need to reflect "intelligent" characteristics in interface construction, system collaboration, and fabrication paradigms. As material science, life sciences, medical engineering, and artificial intelligence converge, electroactive materials are expected to evolve from an interdisciplinary research direction into an essential foundational platform for supporting the next generation of bioelectronics and precision medicine.

CRediT authorship contribution statement

Engui Wang: Writing – original draft, Visualization, Data curation, Funding acquisition, Validation. **Xi Cui:** Writing – original draft, Visualization, Data curation, Methodology, Validation. **Lin**

Luo: Visualization, Writing – original draft. **Junwen Zhong:** Conceptualization, Validation, Writing – review & editing. **Han Ouyang:** Writing – review & editing, Supervision, Conceptualization, Funding acquisition, Methodology, Validation. **Zhou Li:** Writing – review & editing, Project administration, Methodology, Funding acquisition, Conceptualization, Resources.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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