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Research Progress on Multimodal Physiological Sensing and System Integration of Flexible Bioelectronic Devices

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Abstract. Flexible bioelectronic devices provide mechanically compliant interfaces for acquiring, processing, and modulating physiological information across skin, organ, and neural systems. Their development has moved from single-parameter wearable sensors toward integrated platforms that combine electrophysiological, mechanical, thermal, and biochemical measurements with wireless communication, soft power modules, and algorithm-assisted interpretation. This review summarizes recent progress in the material basis, interface construction, multimodal sensing mechanisms, and system-level integration of flexible bioelectronics. Emphasis is placed on conductive hydrogels, elastomeric composites, liquid metals, laser-induced graphene, organic electrochemical transistors, porous soft structures, and adhesive interfaces that support low-impedance coupling, strain tolerance, and long-term operation. The review further discusses device designs for electrocardiography, electromyography, electroencephalography, pressure, strain, temperature, sweat metabolites, electrolytes, and inflammatory biomarkers, followed by integration strategies for crosstalk control, energy supply, wireless data transfer, intelligent analysis, and closed-loop feedback. It is demonstrated by current evidence that clinically oriented flexible bioelectronics require coordinated optimization of biointerface mechanics, signal fidelity, biochemical selectivity, manufacturing reproducibility, and data reliability. Future research is anticipated to focus on standardized validation, durable encapsulation, patient-specific algorithms, and therapeutic systems capable of linking continuous sensing with adaptive intervention.

Keywords: Flexible bioelectronics, multimodal physiological sensing, wearable devices, soft interfaces, system integration

1. Introduction

Flexible bioelectronic devices have become an important technological route for continuous physiological monitoring and personalized biomedical intervention. Conventional rigid electronics provide high electrical performance, but their mechanical mismatch with soft tissues can cause motion artifacts, unstable contact impedance, tissue irritation, and limited tolerance to dynamic deformation.These constraints can be addressed by flexible bioelectronics through the use of stretchable conductors, soft substrates, ultrathin device geometries, and bioadhesive interfaces to

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establish intimate coupling with skin or internal tissues. With this design principle, physiological signals can be acquired under daily motion, organ deformation, and long-term wearing conditions. Recent reviews and representative devices show that the field has shifted from isolated materials development toward integrated systems for connected healthcare, organ monitoring, neuroengineering, and closed-loop therapy [1, 2].

The concept of multimodal physiological sensing refers to the simultaneous or coordinated acquisition of different biological signal classes,which include electrophysiological signals such as electrocardiography, electromyography, and electroencephalography, mechanical signals such as pulse wave, respiration, joint motion, and tissue strain, thermal signals that reflect local metabolic or inflammatory states, and biochemical signals including sweat electrolytes, lactate, glucose, cortisol, uric acid, and cytokine-associated markers. Physiological interpretation can be improved by combining these signals because most disease states do not alter a single signal dimension. For example, cardiovascular assessment benefits from concurrent electrical, mechanical, and hemodynamic information, whereas stress monitoring benefits from integrated endocrine, autonomic, and behavioral markers [3].

System integration has become a defining challenge in this area in recent years. A flexible sensor can only serve biomedical use when it maintains mechanical conformability, electrochemical stability, signal selectivity, power autonomy, data communication, and interpretability within a compact platform.Increasing emphasis has therefore been placed on multifunctional porous materials, conductive hydrogel interfaces, printed sensor arrays, wireless modules, and machine-learning-assisted data analysis [4]. The translational value of these systems is determined by whether the recorded signals can be related to clinical decisions, rehabilitation protocols, or individualized risk assessment under conditions that include sweat, repeated motion, skin renewal, and variable user behavior. Recent progress in this field is organized around material and interface construction, multimodal sensing mechanisms, and integrated system design.

2. Material basis and interface construction of flexible bioelectronic devices

2.1. Flexible and stretchable functional materials

Flexible bioelectronic materials must preserve electrical, ionic, or electrochemical function during bending, stretching, compression, and repeated contact with hydrated biological surfaces. Conductive hydrogels have received extensive attention because their water-rich networks resemble soft tissue mechanics and can support ionic transport, tissue adhesion, and local biochemical exchange. Recent hydrogel systems incorporate polyacrylamide, gelatin, alginate, zwitterionic polymers, dynamic covalent networks, metal coordination, conductive polymers, carbon nanomaterials, and MXene-based fillers to balance softness, conductivity, toughness, and interfacial adhesion [5, 6]. Oxidative cross-linking and biomimetic catechol chemistry have also been used to construct ionically conductive interfaces that resist dehydration and preserve low contact impedance during long-term wearable operation [7].

Elastomeric composites and ultrathin polymer films provide another material class for soft devices. Polydimethylsiloxane, thermoplastic polyurethane, styrene-ethylene-butylene-styrene, Ecoflex, polyimide, and parylene-based structures can host metal nanowires, carbon nanotubes, graphene, liquid metals, conductive polymers, or microcracked metallic films. Their mechanical behavior can be adjusted by serpentine interconnects, island-bridge layouts, kirigami structures, porous networks, and strain-isolation layers [8]. Liquid metals such as eutectic gallium-indium provide high conductivity and intrinsic deformability, allowing strain sensors and stretchable

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interconnects to retain electrical continuity under large deformation.Sensitivity to motion and physiological strain is further increased by fractal microchannel designs while maintaining a soft contact profile [9].

The mechanical selection of functional materials is therefore constrained by the modulus and strain range of target tissues, as summarized in Figure 1.

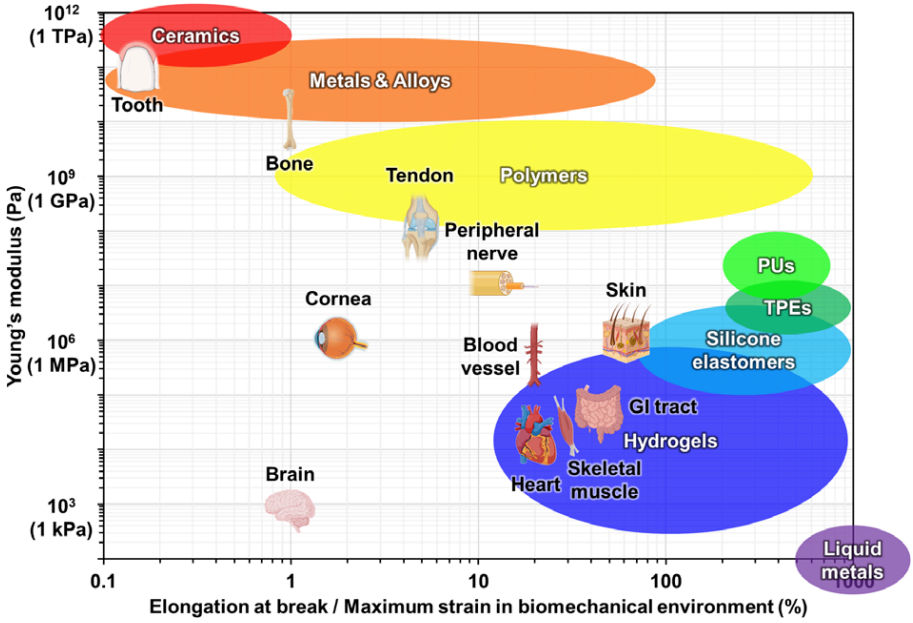


Figure 1. Mechanical matching between soft functional materials and biological tissues [8]

Organic mixed ionic-electronic conductors have expanded the material basis of tissue-interfaced electronics. Ionic signals from biological environments are amplified by organic electrochemical transistors through volumetric ion penetration and electronic transport within conducting polymers. This operating principle is suited for low-amplitude electrophysiological recordings and biochemical sensing in aqueous media [10]. Laser-induced graphene has also become a scalable material for flexible multimodal platforms because direct laser writing can generate porous conductive carbon patterns on polymer substrates without complex lithography. Laser-induced graphene electrodes have been applied to electrophysiological, strain, temperature, and biochemical sensing, and recent all-laser fabrication methods have integrated multilayer interconnects for compact multimodal arrays [11].

2.2. Device structural design and micro/nanofabrication technologies

The performance of flexible bioelectronic devices depends not only on material composition but also on structural design. Ultrathin device thickness reduces bending stiffness and improves conformal contact with curved or moving surfaces. Strain is distributed away from active regions by serpentine conductive traces, mesh layouts, buckled films, and neutral mechanical plane design, reducing mechanical failure during repeated deformation. Porous soft bioelectronics further decrease effective modulus, enhance breathability, and support fluid transport, making them suitable for long-term skin contact and wound-related monitoring [12].

Microfabrication technologies for flexible bioelectronics include photolithography, transfer printing, screen printing, inkjet printing, aerosol jet printing, electrospinning, soft lithography, laser writing, and three-dimensional printing. Printing methods are useful for large-area and low-cost

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manufacturing because they allow conductive inks, enzymatic layers, ion-selective membranes, and encapsulation materials to be deposited directly onto flexible substrates. Fully printed multimodal systems have shown continuous monitoring during exercise by integrating sensing elements for mechanical and biochemical measurements within a wearable format [13]. Laser-based processes provide spatially defined carbonization, multilayer interconnection, and three-dimensional microstructured electrode fabrication, which can simplify the production of integrated physiological monitoring systems [14].

Sensitivity is improved by micro/nanostructuring through increased effective surface area, stress concentration, analyte accessibility, and interfacial charge transfer. Porous electrodes enhance sweat capture and electrochemical reaction kinetics, while nanowire networks and graphene structures support percolative conductivity under strain. At the same time, structural complexity can introduce batch variability, drift, and inter-sensor interference. Device design therefore requires co-optimization of sensitivity, mechanical durability, manufacturing reproducibility, and encapsulation compatibility. These requirements are particularly important for systems intended to function outside controlled laboratory settings [15].

2.3. Biointerface adaptation and long-term stability regulation

A flexible device can record reliable physiological signals only when the interface with biological tissue remains mechanically and chemically compatible. Skin-mounted devices require adhesion that resists sweat, motion, and repeated detachment, while implantable devices require minimized fibrotic response, reduced inflammatory irritation, and stable encapsulation in fluid-rich environments. Hydrogel and bioadhesive interfaces reduce modulus mismatch and improve ion exchange, but water evaporation, swelling, enzymatic degradation, and bacterial contamination can compromise long-term use. Antibacterial conductive hydrogels, zwitterionic hydration layers, dynamic adhesive networks, and selectively damping materials have been developed to improve contact quality and reduce motion artifact [16].

The biointerface also determines signal quality. For electrophysiological sensing, low impedance and stable electrode contact are essential for detecting microvolt- to millivolt-level signals. For mechanical sensing, the interface must transmit strain without slippage or excessive constraint. For biochemical sensing, the interface must allow analyte transport while preventing nonspecific fouling and maintaining enzyme or receptor activity. Interfaces for infant cardiovascular monitoring, sleep respiration monitoring, and dynamic organ monitoring illustrate how device mechanics must be matched to the target population and anatomical site [17]. In implantable settings, encapsulation must block water penetration into electronics while preserving flexibility and tissue compliance, which remains a central limitation for chronic deployment.

Long-term stability also depends on calibration. Flexible sensors often operate under varying humidity, temperature, pressure, and strain, so signal drift can arise from material aging, interfacial dehydration, biofouling, enzymatic degradation, or mechanical fatigue. The most robust systems combine material-level stability with algorithmic correction and redundant multimodal readouts. Regenerable sweat sensors, reticular conductive biogel interfaces, and wireless soft systems for mental-state monitoring have shown how device regeneration, durable contact, and multimodal analysis can extend practical use in daily conditions [18].

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3. Sensing mechanisms and device design for multimodal physiological signals

3.1. Flexible sensing of electrophysiological signals

Electrophysiological sensing records bioelectric potentials generated by excitable tissues. Flexible electrocardiography sensors monitor cardiac depolarization and repolarization, electromyography sensors record skeletal muscle activation, electroencephalography sensors capture cortical electrical rhythms, and electrocorticography or peripheral nerve interfaces acquire signals directly from neural tissue. Motion artifacts are reduced by flexible electrodes because they conform to tissue surfaces and maintain contact during deformation. Stretchable electrodes, conformal adhesives, and wireless modules have been integrated intosoft bioelectronics for heart monitoring to improve ambulatory cardiac assessment. Similar principles apply to respiratory muscle monitoring, where multimodal wearable systems combine electromyography with ventilation and cardiovascular signals to characterize respiratory dynamics [19].

Electrophysiological electrodes usually rely on ionic-electronic transduction at the electrode-tissue interface. Conductive hydrogels provide hydrated ionic pathways, while conducting polymers and organic electrochemical transistors improve charge transfer and local amplification [15, 19]. In neural applications, soft interfaces reduce mechanical strain on tissue and may lessen inflammatory responses compared with rigid probes. Flexible neural bioelectronics have been explored for epilepsy monitoring, brain tumor-related electrophysiology, and neuroengineering platforms that combine recording with stimulation or drug delivery. The signal amplitude and spatial scale differ markedly across electrocardiography, electromyography, electroencephalography, and neural recordings, so electrode geometry, impedance, noise shielding, and placement must be tailored rather than generalized across applications.

OECT-based systems further illustrate how ionic biochemical inputs, analog amplification, digital processing, wireless communication, and power supply can be combined within tissue-compatible bioelectronic platforms, as shown in Figure 2.

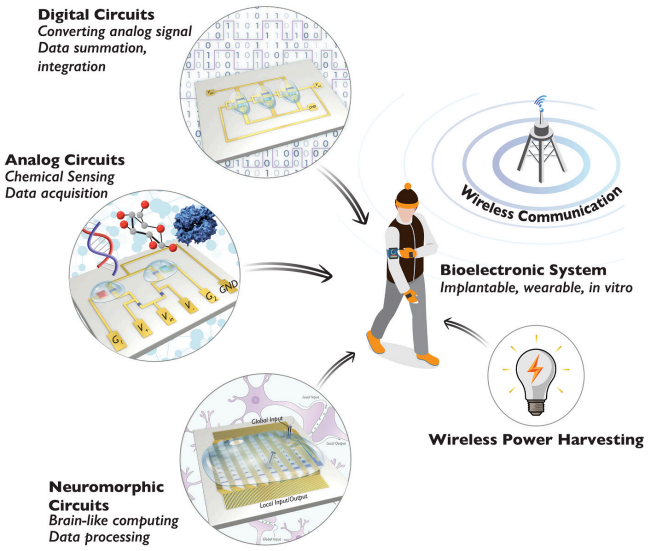


Figure 2. Integrated OECT-enabled bioelectronic system for sensing, processing, communication, and power management [10]

Signal contamination remains a core limitation. Motion artifacts, electrode displacement, sweat-induced impedance change, and electromagnetic noise can mask electrophysiological features.

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Device-level solutions include ultraconformal epidermal antennas, damping layers, soft adhesives, differential recording, and shielded interconnects [20]. System-level solutions use multimodal compensation, for example combining inertial or strain signals with electrophysiological recordings to identify motion-correlated noise. These approaches have particular value in ambulatory monitoring, where laboratory-grade stillness cannot be assumed.

3.2. Flexible sensing of mechanical and thermal physiological signals

Mechanical signals provide information on body movement, pulse wave, respiration, phonocardiography, tissue deformation, gait, tremor, swallowing, and wound status. Flexible strain and pressure sensors translate deformation into resistance, capacitance, piezoelectricity, triboelectricity, optical change, or electrochemical response. Resistive sensors often use conductive networks in elastomers or hydrogels, where strain changes percolation pathways. Capacitive sensors measure changes in electrode distance or dielectric properties. Piezoelectric and triboelectric devices generate charge under dynamic deformation and can be used for self-powered sensing. Reviews of flexible strain sensors emphasize that sensitivity, working range, hysteresis, response time, and mechanical durability must be evaluated together for physiological monitoring [21].

Thermal sensing reflects local skin temperature, heat flux, inflammation, vascular perfusion, and thermoregulatory responses. Flexible temperature sensors commonly use thermoresistive materials, thermoelectric elements, or ionic thermoelectric hydrogels. Temperature measurement can also correct biochemical sensor outputs because enzymatic and electrochemical reactions are temperature dependent. A wireless closed-loop thermoregulation platform demonstrated how flexible temperature sensing can be combined with feedback control to support decoupled multimodal health monitoring [22]. Thermal devices require careful isolation from mechanical strain, because deformation-induced resistance changes can be misinterpreted as temperature variation.

Mechanical and thermal sensors increasingly appear as components of broader physiological systems rather than standalone devices. Exercise monitoring, chronic wound assessment, infant cardiovascular follow-up, and sleep respiration evaluation benefit from integrated readouts that combine motion, pressure, temperature, and electrophysiology. Such multimodal designs provide contextual information that can distinguish physiological change from sensor disturbance. For instance, increased skin temperature during exercise has different interpretation when accompanied by elevated strain, sweat secretion, and cardiac rhythm compared with the same temperature increase at rest.

3.3. Biochemical signal sensing and multimodal cooperative detection

Biochemical sensing extends flexible bioelectronics beyond physical signals by monitoring metabolites, electrolytes, hormones, and inflammatory markers in sweat, interstitial fluid, saliva, tears, or wound exudate. Sweat sensors are widely studied because sweat can be accessed noninvasively and contains lactate, glucose, chloride, sodium, potassium, cortisol, uric acid, pH, and hydration-related indicators. Electrochemical detection uses enzymatic reactions, ion-selective membranes, molecularly imprinted polymers, redox probes, or catalytic nanomaterials. Simultaneous monitoring of lactate and sweat secretion rate has been demonstrated by remote sweat biosensors, indicating that biochemical concentration must be interpreted alongside local fluid dynamics [23].

Microfluidic integration improves biochemical sensing by guiding sweat collection, controlling sample volume, delaying evaporation, and separating detection zones. Multiplexed sweat analysis is

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provided by integrated microfluidic electrochemical and colorimetric platforms within a compact wearable format. Resettable electrochromic biosensors and sweat-activated microbial fuel cells show that sweat can also support visual readout or power generation, expanding the design space for low-power wearable systems [24]. Nevertheless, sweat composition differs from blood composition and is influenced by gland physiology, sampling rate, skin contamination, and environmental conditions. Calibration against physiological context and validated correlation with disease-relevant endpoints are therefore required for direct clinical interpretation.

Multimodal cooperative detection is central to reliable biochemical interpretation. Stress assessment platforms that combine sweat cortisol with physiological signals use machine learning to relate endocrine, autonomic, and behavioral information. Sweat chemistry is combined with temperature, motion, and cardiovascular indicators in exercise systems to differentiate metabolic demand from local sweat dilution. Wound monitoring systems use temperature, pH, uric acid, impedance, and pressure-related signals to evaluate healing microenvironments. These examples show that flexible bioelectronics are moving toward integrated physiological state estimation rather than isolated molecular readout.

4. Integration and intelligentization of flexible bioelectronic systems

4.1. Multisensor unit integration and signal crosstalk suppression

Multisensor integration requires spatial arrangement, material compatibility, and signal separation across electrical, mechanical, thermal, and biochemical units. When different sensors share a substrate, mechanical deformation, temperature variation, humidity, sweat accumulation, and electromagnetic coupling can influence multiple channels at the same time. Crosstalk can be reduced by mechanical decoupling structures, strain-isolation islands, selective encapsulation, shielding layers, differential circuit design, independent reference electrodes, microfluidic routing, and algorithmic compensation.

Printed and laser-fabricated platforms have accelerated multisensor integration because they allow patterned electrodes, interconnects, microfluidic channels, and dielectric layers to be fabricated with fewer alignment steps. How scalable processes can support multichannel detection is illustrated by fully printed systems for exercise monitoring and laser-induced graphene devices for physiological-electrophysiological monitoring [11]. The possibility of multilayer interconnects in compact soft systems is further demonstrated byall-laser fabricated three-dimensional bioelectronic platforms. Despite these advances, integrated devices still require rigorous validation of channel independence, because apparent multimodal performance can be confounded when one physical stimulus drives multiple sensor outputs.

Sensor placement is also a biological integration issue. Cardiac, respiratory, neuromuscular, and biochemical signals have distinct anatomical distributions and time constants. Combining them in a single patch improves wearability but may reduce signal specificity if the patch location is not matched to physiological pathways. Distributed systems with multiple soft patches can capture spatially resolved signals, but they increase requirements for synchronization, wireless bandwidth, and power management. The choice between compact and distributed architectures should be determined by the clinical or research question rather than device complexity alone.

DOI: 10.54254/2753-8818/2026.HZ38743

4.2. Energy supply, wireless communication, and system packaging

Energy supply constrains the autonomy, thickness, and wearability of flexible bioelectronic systems. Conventional batteries provide high energy density but introduce rigidity, volume, and safety considerations. Flexible batteries, supercapacitors, energy harvesters, biofuel cells, wireless power transfer, and near-field communication have been developed to support wearable and implantable operation. Sweat-activated microbial fuel cells and sweat-powered electrochromic biosensors show that biofluids can serve as energy sources under selected conditions. In many practical systems, hybrid designs combine a small power unit with low-power circuits, intermittent sampling, and wireless data transmission.

Wireless communication enables continuous monitoring outside clinical settings. Bluetooth, near-field communication, radiofrequency links, and flexible antennas have been used for data transfer, device control, and point-of-care monitoring. Ultra-conformal epidermal antennas improve motion tolerance while supporting multifunctional sensing [25]. Wireless soft electronics for sleep respiration, infant cardiovascular monitoring, and mental-state evaluation indicate that communication design must consider body curvature, motion, tissue absorption, user comfort, and data privacy. For implantable devices, wireless links must also account for depth-dependent attenuation and heating limits.

Packaging determines device lifetime and biological safety. Encapsulation layers must protect circuits from moisture and ionic fluids while allowing the sensor interface to contact the biological target. Soft encapsulants, multilayer barrier films, parylene coatings, elastomeric membranes, and hydrogel covers are widely used, but they must be selected according to sensor function. A biochemical sensor cannot be fully isolated from fluid, whereas a wireless circuit requires strong water blocking. Closed-loop and implantable systems place further constraints on packaging because stimulation electrodes, drug reservoirs, and feedback electronics must operate without leakage or signal drift.

4.3. Multimodal data fusion, intelligent analysis, and closed-loop feedback

Multimodal physiological data require analysis methods that can handle different sampling rates, amplitudes, noise sources, and biological time scales. Signal preprocessing usually includes filtering, normalization, artifact removal, calibration, and time synchronization. Feature extraction can quantify rhythm intervals, frequency bands, strain amplitude, temperature gradients, metabolite trends, and cross-channel relationships. Machine learning has been applied to sweat sensing, stress assessment, exercise monitoring, and mental-state evaluation, where multimodal data provide richer inputs than single-signal models [26].

Data fusion can occur at signal, feature, or decision level. Signal-level fusion uses synchronized raw or minimally processed data, feature-level fusion combines extracted descriptors, and decision-level fusion integrates outputs from separate models. Flexible bioelectronics often benefit from feature-level fusion because each sensor class has distinct physical units and noise structures. Model reliability depends on training data quality, population diversity, calibration strategy, and external validation. Algorithms developed from small laboratory cohorts may fail when applied to broader populations with different age, skin properties, sweating patterns, disease states, medications, and activity levels.

Closed-loop feedback is an emerging direction that links sensing with adaptive intervention. Examples include thermal regulation, neurostimulation, wound therapy, drug delivery, and adhesive bioelectronics for closed-loop treatment. A closed-loop system must define a physiological target,

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detect a deviation, decide an intervention, deliver therapy, and evaluate response. Low-latency sensing, reliable actuation, failsafe logic, and transparent clinical endpoints are required for this sequence. Integration with artificial intelligence can improve pattern recognition and personalization, but stricter validation are required for closed-loop biomedical devices when compared with passive monitors because algorithmic errors can directly influence treatment.

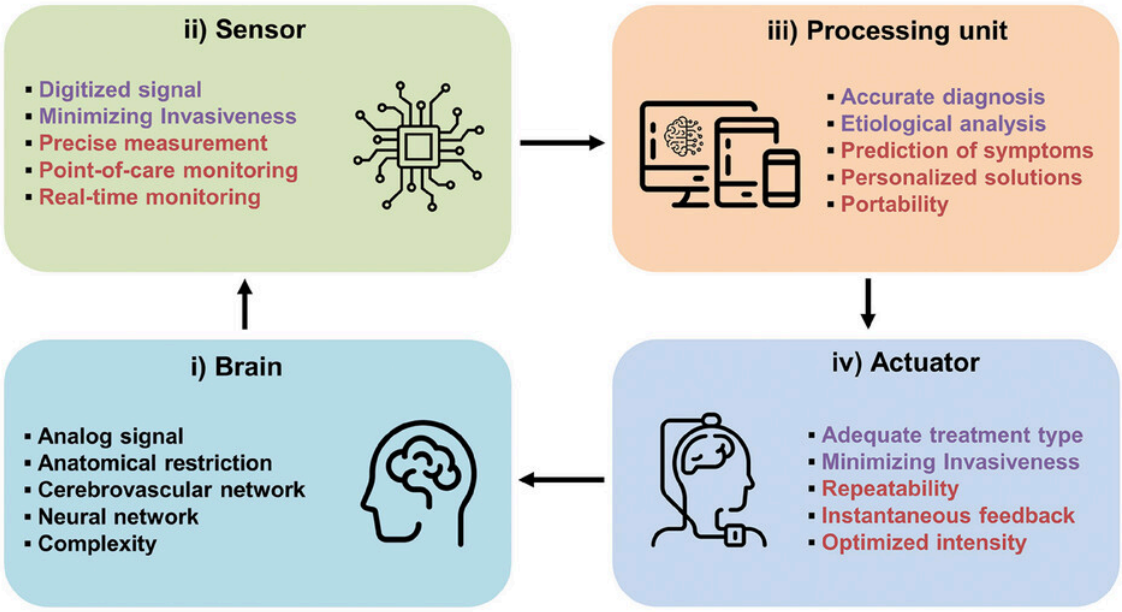


Figure 3. Closed-loop soft bioelectronic framework linking sensing, processing, and actuation for brain disease intervention [27]

This closed-loop architecture can be organized as a recurrent sequence connecting brain-state acquisition, sensor digitization, computational interpretation, and adaptive actuation, as illustrated in Figure 3.

5. Conclusions and perspectives

Flexible bioelectronic devices have progressed from mechanically compliant sensors toward integrated platforms capable of multimodal physiological sensing, wireless communication, intelligent analysis, and feedback control. The mechanical and interfacial compatibility of devices with skin and soft tissues has been improved by recent advances in conductive hydrogels, organic mixed conductors, porous soft structures, liquid metals, laser-induced graphene, printed electronics, and bioadhesive interfaces. Multimodal sensing expands physiological interpretation by integrating electrophysiological, mechanical, thermal, and biochemical information, thereby reducing dependence on a single signal channel and improving context awareness.

Several scientific and translational challenges remain. Materials must retain conductivity, adhesion, hydration, and biocompatibility during long-term motion and exposure to sweat or tissue fluids. Integrated systems must suppress crosstalk while preserving high sensitivity across heterogeneous signal types. Improved selectivity, anti-fouling performance, and clinically meaningful calibration are required for biochemical sensors. Wireless and powered devices must balance autonomy, miniaturization, data security, and user comfort. Algorithms must be trained and

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validated across diverse populations and real-world use conditions rather than relying only on controlled laboratory datasets.

Future flexible bioelectronics are expected to develop along four linked directions. The first direction is tissue-adaptive materials that combine mechanical compliance with durable electrical and biochemical function. The second part is scalable manufacturing that supports reproducible sensor arrays and integrated circuits. Equally important is clinically interpretable multimodal data fusion, with models designed for uncertainty estimation and patient-specific calibration. Finally, closed-loop integration should enable continuous sensing to guide adaptive stimulation, thermoregulation, wound management, or drug delivery.Progress in these directions will determine whether flexible bioelectronic systems can move from engineering prototypes to reliable biomedical platforms for long-term monitoring, disease management, and individualized therapy.

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