Smart wearable and implantable biosensors for continuous health monitoring: materials, biocompatibility, and AI integration

Citation for the original published paper (version of record):

Suryaprabha, T., Choi, C., Wu, Y. et al (2026). Smart wearable and implantable biosensors for continuous health monitoring: materials,
biocompatibility, and AI integration. npj Flexible Electronics, 10(1).
http://dx.doi.org/10.1038/s41528-026-00560-6

(article starts on next page)

npj | flexible electronics

Review

Published in partnership with Nanjing Tech University

https://doi.org/10.1038/s41528-026-00560-6

Smart wearable and implantable biosensors for continuous health monitoring: materials, biocompatibility, and AI integration

Thirumalaisamy Suryaprabha[1], Chunghyeon Choi[1], Yanfang Wu[2], Liyang Liu[3,4] ✉ & Byungil Hwang[5] ✉

Smart wearable and implantable biosensors enable continuous, real-time monitoring of biophysical and biochemical signals for personalized and preventive healthcare. Advances in flexible, stretchable, and biocompatible materials ensure long-term comfort and seamless body integration, while multimodal and multi-analyte sensing improves robustness. AI enhances signal processing and predictive insights, yet challenges remain in motion artifacts, energy autonomy, data privacy, and clinical interpretability. This review summarizes materials, device architectures, and AI-assisted strategies applications.

Significant paradigm shifts are transforming the medical and healthcare industries, fueled by advanced technologies and the growing adoption of services such as telemedicine, wearable diagnostics, remote patient monitoring and personalized treatment strategies[1,2]. Yet several critical challenges persist. These include the need for continuous, real-time health monitoring, risks associated with delayed diagnosis or episodic checkups, limited accessibility for patients in remote or underserved areas, and the lack of user-friendly, noninvasive systems capable of long-term physiological acquisition, particularly for patients with chronic or life-threatening conditions[3,4]. In response to these challenges, smart biosensors, especially those engineered to be flexible, stretchable or implantable, have emerged as next-generation solutions for real-time health monitoring. These devices can continuously record a wide range of physiological signals while conforming intimately to biological tissues without causing discomfort or adverse reactions. Their mechanical compliance, biocompatibility, and seamless integration with the human body make them promising candidates for long-term, noninvasive health tracking in both clinical and personalized healthcare settings[5–7].

Smart biosensors have advanced considerably in terms of functionality, but their design involves much more than the integration of sensing and data transmission. A successful wearable or implantable device requires careful balancing of multiple factors. Beyond biocompatibility and safety, mechanical properties such as flexibility, stretchability, and fatigue resistance are critical to ensure comfortable conformity to the body's soft, dynamic tissues without irritation or structural failure over time. This consideration is especially important for implantable sensors, where inadequate mechanical design can lead to tissue damage, signal degradation, or device malfunction[8,9].

Wearable technologies have progressed far beyond early-generation devices, which were limited to tracking biophysical signals such as heart rate, body temperature, blood pressure, and physical activity. Modern devices, designed as portable and skin-integrated platforms, now provide biochemical sensing, electrophysiological signal monitoring, and continuous real-time insights into health status. In parallel, traditional diagnostic methods such as blood tests, imaging techniques (e.g., MRI and CT scans), and laboratory-based biochemical assays remain highly effective but are often time-consuming, costly, and require specialized infrastructure[10,11]. In contrast, smart biosensors, especially those enhanced through nanotechnology, offer significant advantages, including improved diagnostic sensitivity, faster response times and reduced costs, and scalable, low-cost mass production suitable for both clinical and point-of-care applications[12,13]. Recent advances in bio-based materials with excellent flexibility and stretchability have further improved the comfort and usability of wearable biosensors, enabling continuous data collection over extended periods[14,15].

While these sensors excel at generating large volumes of physiological data, they often lack the capability to translate this information into clinically meaningful insights. Artificial intelligence (AI)-driven technologies, particularly machine learning (ML) and deep learning (DL), play a major role in addressing this challenge by enabling advanced data processing, pattern recognition, and predictive modeling[16,17]. These approaches can

[1]Department of Intelligent Semiconductor Engineering, Chung-Ang University, Seoul, Republic of Korea. [2]Department of Chemistry, University of Otago, PO Box 56 Dunedin, New Zealand. [3]Department of Chemistry and Chemical Engineering, Chalmers University of Technology, Gothenburg, Sweden. [4]Wallenberg Wood Science Center, Chalmers University of Technology, Gothenburg, Sweden. [5]School of Integrative Engineering, Chung-Ang University, Seoul, Republic of Korea.
✉e-mail: liyang.liu@chalmers.se; bihwang@cau.ac.kr

extract clinically relevant insights from complex datasets in real time, identify subtle physiological variations associated with early disease onset, provide personalized health recommendations, and deliver automated decision support for clinicians, thereby enhancing diagnostic accuracy and treatment efficiency. Thus, the integration of AI with smart wearable biosensors makes these devices more personalized, intelligent and adaptive to individual health needs[18,19].

Rapid progress in sensor materials, electronics, and signal processing has been achieved in recent years, yet comprehensive reviews addressing the mechanics of biosensors, especially in the context of continuous monitoring and implantable applications, remain scarce. This review focuses on the mechanics of wearable and implantable biosensors, followed by continuous health monitoring techniques, and the role of AI-driven approaches in transforming raw data into actionable clinical insights. By combining these perspectives, this review provides a comprehensive understanding of what makes smart biosensors not only technologically advanced but also practically viable for real-world healthcare applications. Figure 1 presents an overview of this review, emphasizing mechanical design principles and AI integration for continuous health monitoring.

Understanding mechanics in biosensors

Mechanical design considerations in biosensors

Mechanical design considerations are critical for wearable biosensors, particularly in skin-interfaced, implantable, and ingestible applications, as they enable devices to move naturally with the body, bending, stretching, and adapting to skin or tissue without loss of sensing accuracy. Adequate tensile strength and fatigue resistance help prevent cracking, delamination, or performance degradation under repeated deformation. Furthermore, optimizing mechanical robustness alongside sensitivity is essential to ensure stable signal output under real-world conditions, enabling reliable long-term health monitoring and continuous physiological data acquisition[20,21]. The key mechanical design parameters that influence the performance, durability, and comfort of flexible biosensors are outlined below.

Key mechanical design parameters for wearable and implantable biosensors

The mechanical performance of biosensors plays a critical role in determining their functionality, reliability, and long-term stability under real-world operating conditions. For clarity, the mechanical properties relevant to wearable and implantable biosensors can be broadly classified into two categories: (i) device-level deformation characteristics, which describe how a sensor accommodates external motion and conforms to biological surfaces and (ii) material-level strength and durability parameters, which govern the mechanical integrity of substrates and functional layers. Although conceptually distinct, both categories are essential for achieving mechanically robust and biologically compatible bioelectronic systems. Figure 2 provides an overview of representative wearable biosensors used during daily activities and the diverse mechanical environments they encounter. It highlights the mechanical mismatch between biological tissues and conventional electronic materials through a comparison of Young's modulus and illustrates typical bioelectrode configurations employed at biointerfaces. Based on these considerations, the key mechanical design parameters governing the deformation behavior and structural reliability of wearable and implantable biosensors are discussed below.

Flexibility. Flexibility describes the ability of a biosensor to bend and conform to curved or irregular surfaces, such as human skin or soft tissues, under low bending strain. This property is particularly important for wearable and epidermal biosensors, where intimate contact with the body is required without compromising structural or electrical integrity[22]. Flexible substrates such as conductive polymers, nanocomposites, metallic nanowires and hydrogels are commonly employed to reduce bending stiffness and enhance conformability[23,24]. The bending

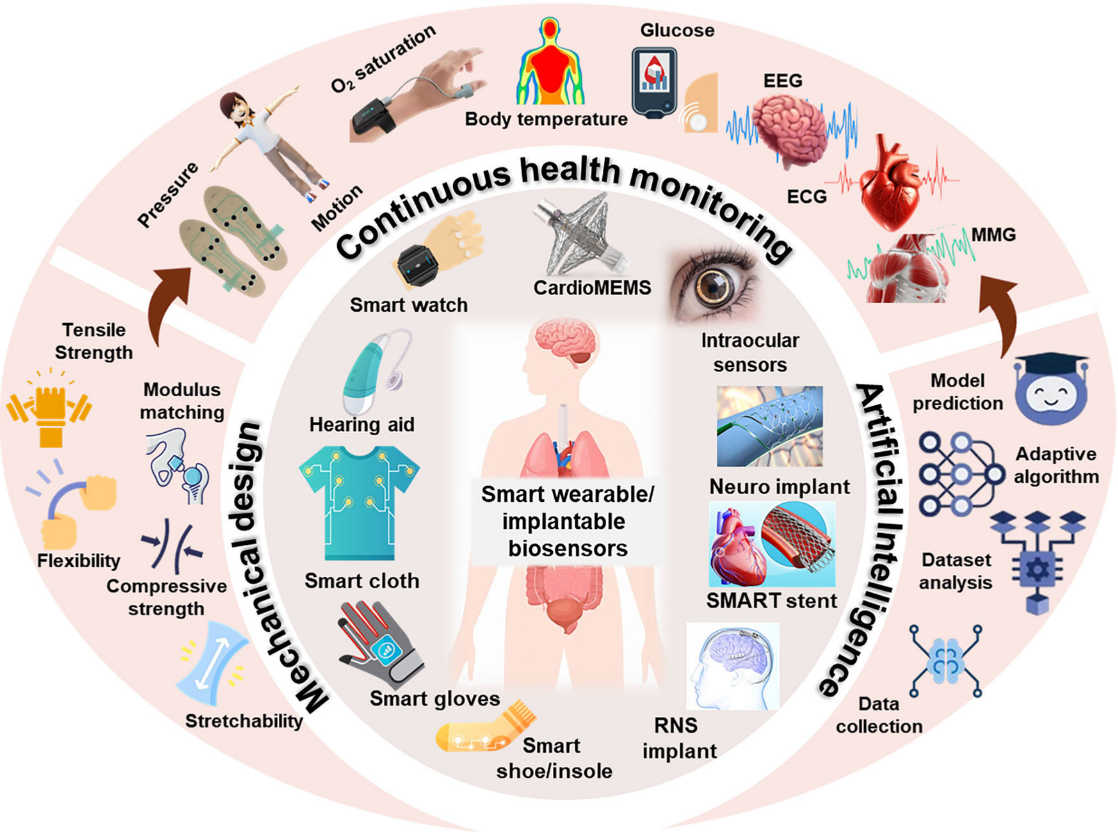

Fig. 1 | Schematic overview of mechanical design strategies and AI integration for continuous health monitoring.

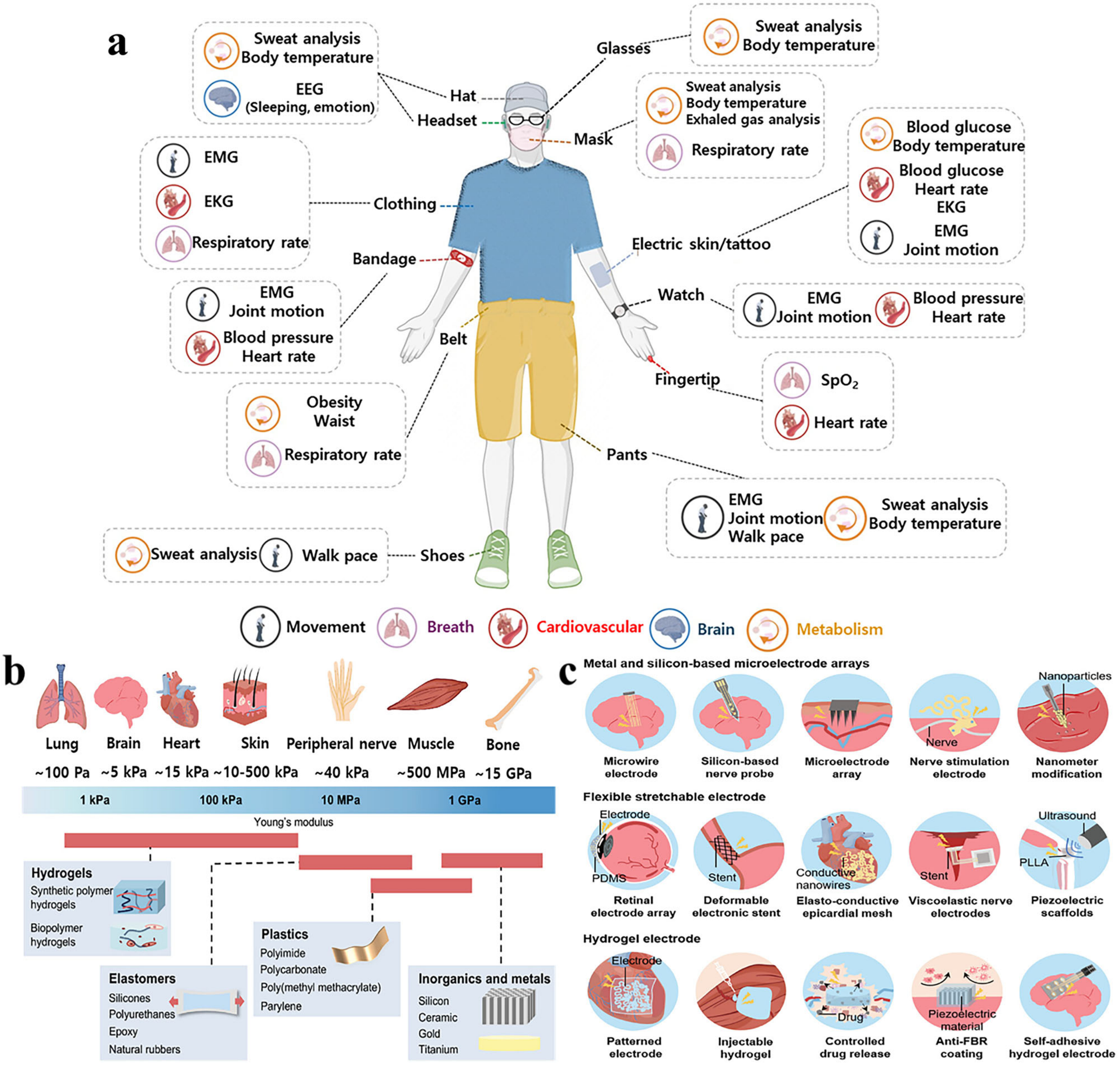

Fig. 2 | Overview of biosensor applications, material properties, and bioelectrode designs. a Wearable biosensors for real-time physiological monitoring across different body locations, detecting signals related to movement, cardiovascular activity, brain function, respiration, and metabolism[11], **b** Mechanical properties of biological tissues compared to commonly used biosensor materials, illustrating Young's modulus ranges for hydrogels, elastomers, plastics, and inorganic/metallic substrates, **c** Representative bioelectrode configurations, including metal and silicon-based microelectrode arrays, flexible stretchable electrodes, and hydrogel-based electrodes, designed for diverse biomedical applications[212].

radius and bending durability are key metrics used to evaluate the flexibility of a biosensor, which reflect a device's ability to maintain stable electrical performance under repeated bending associated with body movement[25,26].

Stretchability. Stretchability refers to the ability of a biosensor to sustain tensile deformation without mechanical failure. This property is especially critical for sensors deployed on highly dynamic regions of the body, such as joints and muscles, where large and repetitive strains are experienced. Wearable biosensors are often designed using highly stretchable materials or strain-accommodating architectures, such as elastomeric substrates and serpentine interconnects[27,28]. Depending on the sensing location, mode of deformation, and device architecture, reported stretchability values for wearable platforms range from several hundred percent to, in some cases, approaching or exceeding 1000%. In contrast, implantable biosensors generally operate in more mechanically constrained environments, where moderate stretchability, typically on the order of ~50–200% is sufficient to accommodate organ-specific motion while ensuring mechanical compatibility and long-term stability[29–34].

Elasticity and recoverability. Elasticity describes the reversible deformation behavior of a material within its elastic regime, whereas recoverability refers to the ability of a biosensor to return to its original geometry after repeated or large deformations, including those approaching the elastic-plastic transition[35]. High elasticity and recoverability are particularly essential for soft and stretchable biosensors that must endure cyclic loading without permanent deformation or signal drift. Materials such as hydrogels, shape-memory polymers, and rubber-like bio-elastomers such as poly(trimethylene carbonate), poly(glycerol sebacate) (PGS), poly(diol citrate) (PDC), and poly(ether carbonate) diol

(PECL), are commonly used to achieve these properties and ensure consistent sensing performance over extended operational cycles[36].

Tensile strength and fracture resistance. Tensile strength and fracture resistance are material-level properties that determine a biosensor's ability to withstand mechanical stress without cracking or failure. These parameters are particularly important for implantable biosensors, where mechanical integrity must be preserved under sustained loading and long-term physiological conditions[37]. Conventional implantable materials such as titanium alloys and SUS316L stainless steel exhibit high Young's moduli (~110 GPa), which are significantly greater than those of biological tissues such as bone (10–30 GPa). Consequently, balancing tensile strength with reduced stiffness and enhanced deformability is critical to minimizing mechanical mismatch, preventing fracture, and ensuring long-term device reliability[38,39].

Shear and compressive strength. Shear and compressive strength characterize a material's resistance to lateral and compressive forces, respectively. These properties are especially relevant for biosensors subjected to external pressure or contact forces, such as implantable pressure sensors, orthopedic monitoring devices, and tactile sensors integrated into prosthetics[40,41]. Adequate shear and compressive strength are required to maintain structural integrity and signal fidelity under complex loading conditions encountered in vivo.

Adhesion to biological tissues and substrates. Adhesion is a key requirement for biosensors that must maintain stable contact with biological tissues or supporting substrates over prolonged periods. Insufficient adhesion can lead to sensor delamination, motion-induced artifacts, and unreliable signal acquisition[42]. In epidermal biosensors, bioadhesive hydrogels and surface microstructures inspired by biological systems (e.g., gecko-inspired designs) are commonly used to enhance adhesion while minimizing skin irritation. For implantable biosensors, biocompatible coatings and surface modifications promote tissue integration and reduce inflammatory responses[43,44].

Biodegradability and mechanical degradation over time. For transient and resorbable biosensors, biodegradability introduces an additional mechanical design consideration. These devices must retain sufficient mechanical integrity throughout their functional lifetime before undergoing controlled degradation. The degradation rate must be carefully tuned to avoid premature mechanical failure or excessive rigidity prior to resorption, ensuring reliable sensing during the intended operational period[45].

Role of mechanics in bioelectronic devices' performance and longevity

Unlike conventional rigid electronics, bioelectronic devices must operate in soft, dynamic, and mechanically challenging environments, such as human skin, muscles, and internal organs. These devices are constantly exposed to mechanical deformations, repeated loading cycles, and environmental stresses, which can affect their signal accuracy, durability, biocompatibility, and overall performance[46]. A well-engineered mechanical design is essential to maintaining stable signal transduction, preventing structural failure, and ensuring user comfort and long-term integration with biological tissues. As the body's outermost interface, skin not only protects underlying tissues but also undergoes complex motions involving stretching, compression, and shear. Accordingly, wearable bioelectronic devices are typically positioned on the epidermis to enable continuous and noninvasive monitoring of biomechanical and physiological signals, including motion-induced strain and pressure, pulse waves, electrophysiological signals[47], and, in some cases, voice vibrations and movement patterns for activity recognition[48]. However, due to the inherent curvature, anisotropic deformation, and dynamic motion of different body regions, conventional rigid or planar sensors are prone to partial detachment and interfacial slippage, which can introduce motion artifacts and compromise sensing accuracy[49,50]. To overcome these limitations, researchers have focused on designing mechanically compliant biosensors by patterning, depositing, or integrating functional materials onto flexible substrates such as polyethylene terephthalate (PET), polydimethylsiloxane (PDMS), thermoplastic polyurethane (TPU), and elastomeric or hydrogel-based platforms[51]. In more advanced implementations, wireless communication modules integrated into flexible printed circuit boards (FPCBs) enable continuous biosignal acquisition under free movement conditions[52], eliminating rigid interconnects while preserving signal fidelity during daily activities.

In addition to flexibility, conformal contact and adhesion between the skin and bioelectronic devices, which enables intimate and uniform adhesion without creating interfacial gaps or discomfort, is crucial for obtaining accurate and stable biosignals. Poor adhesion can lead to device detachment, loss of electrical contact, and inaccurate readings, which severely impact the effectiveness of biosensors[53,54]. For instance, a biosensor that fails to adhere properly to the skin may generate inconsistent bioelectrical signals (e.g., electrocardiogram (ECG), electromyogram (EMG), electroencephalogram (EEG)), leading to unreliable diagnostics[55]. To achieve conformal contact with soft and irregular skin surfaces, several design strategies have been reported in the literature. Ultrathin device architectures reduce bending stiffness and allow sensors to be laminated onto skin via van der Waals forces, enabling stable contact without aggressive adhesives[56,57] (Fig. 3a–d). Soft adhesive hydrogels and elastomeric bioadhesives provide strong yet skin-friendly adhesion while accommodating natural skin deformation during daily activities[58] (Fig. 3e). In addition, microstructured and bioinspired adhesive interfaces, such as gecko- or octopus-inspired patterns, enhance conformability by increasing effective contact area and shear resistance under dynamic conditions[59,60]. Collectively, these adhesion and conformal-contact engineering strategies ensure continuous, reliable sensor-tissue interaction while maintaining user comfort and long-term operational stability[61,62].

Beyond flexibility and conformal contact, long-term epidermal operation of bioelectronic devices critically depends on their ability to accommodate large, repetitive deformations through sufficient stretchability and tissue-matched mechanical stiffness. Human skin exhibits low elastic moduli (typically on the order of ~0.1–2 MPa)[63] and undergoes complex stretching, compression, and shear during daily activities. When bioelectronic devices lack adequate stretchability or exhibit significant modulus mismatch with the skin, localized stress accumulation can occur at the device-tissue interface, leading to delamination, mechanical fatigue, and progressive signal degradation over time. Such mechanical incompatibility not only compromises signal stability but also accelerates material failure under cyclic loading, thereby limiting device lifespan. Consequently, achieving skin-like mechanical compliance and strain tolerance is essential for maintaining reliable electrical performance, minimizing motion-induced artifacts, and ensuring durable operation of wearable bioelectronic systems during continuous use[64]. As a result, skin-matched stretchability and mechanical compliance play a central role in preserving signal integrity and device durability during prolonged on-body use. However, when bioelectronic systems are implanted within the body, mechanical requirements become substantially more demanding due to continuous organ motion, confined anatomical spaces, and long-term tissue-device interactions[65].

Unlike skin, internal organs are continuously exposed to biofluids and cyclic mechanical loading, necessitating robust encapsulation strategies to prevent fluid ingress that can induce electrochemical corrosion, electrical short circuits, and drift in electrode impedance[66], ultimately leading to device failure. For implantable bioelectronic systems, mechanical design is therefore a decisive factor governing signal fidelity, chronic stability, and functional reliability under sustained physiological deformation[67]. When laminated onto soft, curved, and dynamically moving tissues such as the brain or heart, implantable biosensors must maintain intimate conformal contact while minimizing mechanical mismatch between the device (typically MPa–GPa modulus) and biological tissues (~1–40 kPa)[68,69]. Excessive modulus mismatch and insufficient strain accommodation result in localized stress concentrations, interfacial delamination, and progressive

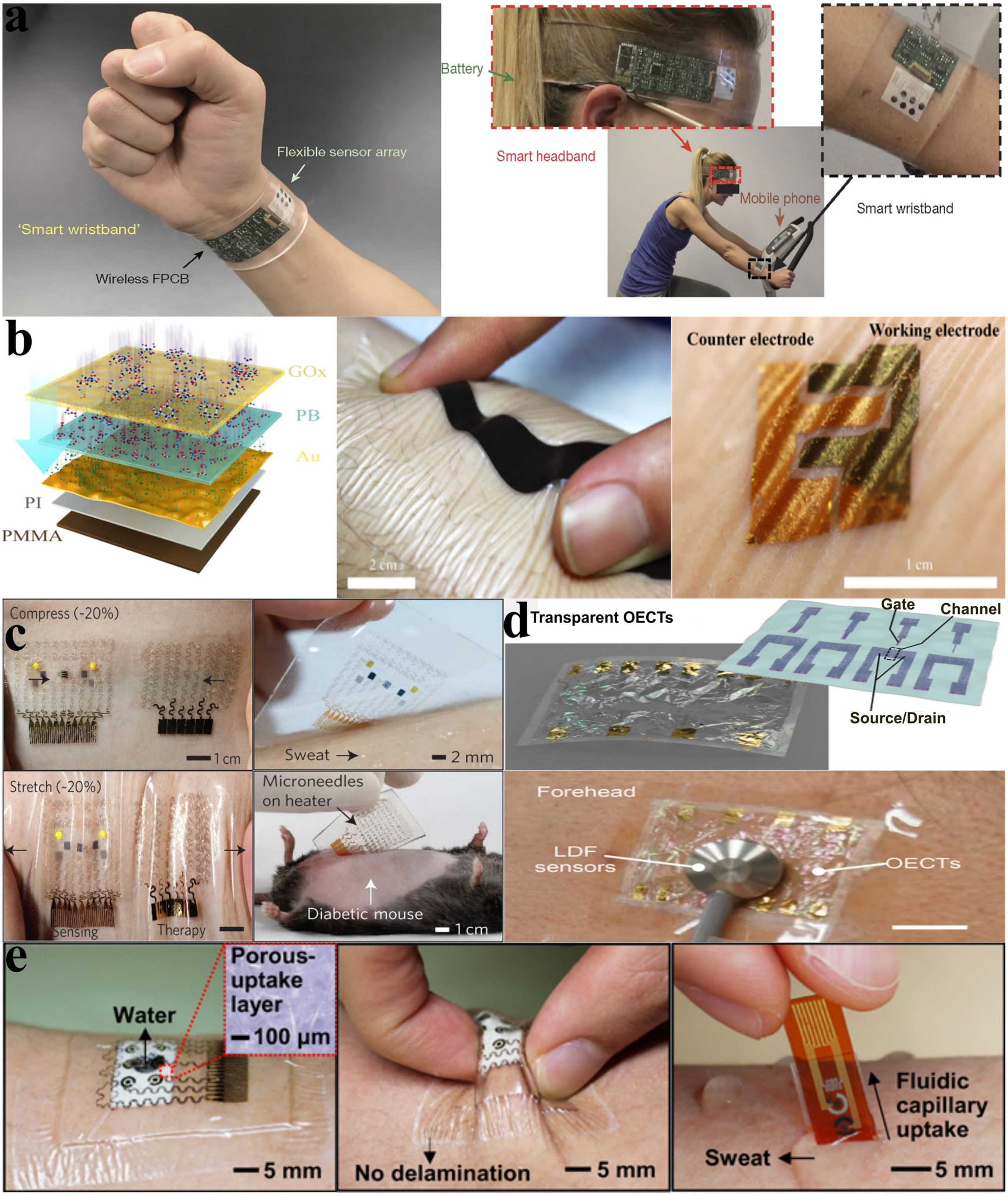

Fig. 3 | Mechanical compliance and conformal interfacing strategies in wearable bioelectronic devices. a Photograph of a wearable bioelectronic system integrating a wireless FPCB on a volunteer's wrist during daily activities[52], **b** Schematic illustration of a skin-like biosensor architecture designed to achieve intimate conformal contact with the epidermis[213], **c** Stretchable and deformable bioelectronic platforms exhibiting stable sensing and therapeutic functions under repeated mechanical deformation[214], **d** Ultrathin and transparent organic electrochemical transistor (OECT) based bioelectronic patch conformally laminated onto the skin (forehead), illustrating intimate epidermal contact[215], **e** Optical image of an epidermal sweat glucose sensor integrated with a soft, hydrogel-based adhesive interface that maintains intimate skin contact under dynamic conditions, enabling continuous, noninvasive electrochemical monitoring of sweat biomarkers[216].

degradation of electrode-tissue coupling during long-term implantation. To mitigate these effects, implantable platforms increasingly employ low-modulus or mechanically graded substrates, stretch-accommodating interconnect architectures, and soft conductive interlayers that redistribute applied strain and suppress strain transfer to active electronic components[70] (Fig. 4a–g). These design strategies reduce peak interfacial shear and tensile stresses, limit cyclic fatigue under repetitive tissue motion, and stabilize electrode impedance by preserving a consistent contact area at

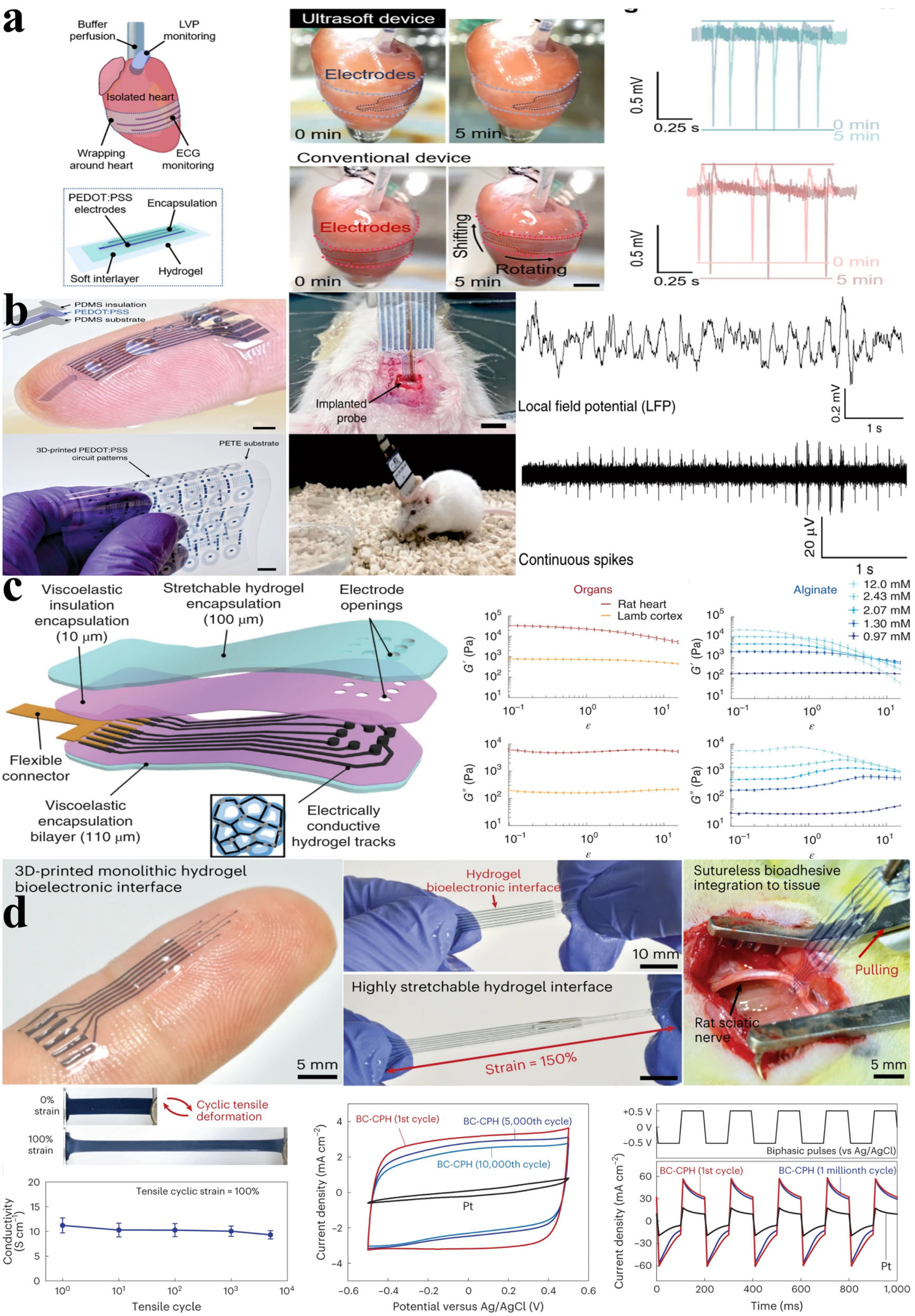

Fig. 4 | Mechanical compliance strategies in implantable bioelectronic devices. **a** Ultrasoft stretchable cardiac interface with a soft interlayer maintains conformal contact and stable ECG signals compared to a conventional device that undergoes shifting and rotation[217], **b** Soft, flexible neural probes and hydrogel-based electrodes demonstrating stable implantation and high-fidelity neural signal recording[218], **c** Multilayer hydrogel bioelectronic interface with viscoelastic encapsulation and electrically conductive tracks, exhibiting tissue-matched mechanical properties[219], **d** Monolithic, highly stretchable hydrogel bioelectronic interfaces showing sutureless tissue adhesion, large-strain tolerance, and stable electrochemical performance under cyclic deformation[220].

the tissue-device interface. In neural and cardiac environments, such mechanically compliant systems enable stable multichannel recording and stimulation under continuous deformation, supporting reliable closed-loop operation over extended implantation periods[22,71–73]. Taken together, these advances demonstrate that mechanical compliance, strain tolerance, and fatigue resistance are fundamental determinants of the long-term performance and durability of implantable bioelectronic devices.

Interaction of mechanics with biological systems

Living cells can sense mechanical forces and convert them into biological responses. Similarly, bioelectronic devices detect mechanical stimulus, such as pressure, strain, and deformation, and transform them into electronic signals for real-time monitoring and diagnostics[74]. To achieve this, numerous innovative strategies have emerged, integrating process and function in a continuous feedback loop, with mechanics serving as a fundamental driving force. This dynamic interaction between mechanics and biological systems is decisive for the design and functionality of bioelectronic devices, ensuring they perform efficiently in wearable, implantable, and biocompatible applications[75–77].

Structural mechanics strategies for flexible wearable bioelectronics

Wearable bioelectronics are transforming healthcare and personalized medicine by enabling continuous, real-time monitoring of physiological and biochemical signals. Unlike conventional rigid electronic devices, these systems must seamlessly conform to the human body, accommodating natural movements without compromising functionality[78]. Similar to their rigid counterparts, flexible biosensors typically consist of three key components: (i) a substrate that provides mechanical support and flexibility to the entire system, (ii) bioreceptors that selectively interact with target analytes, and (iii) active materials that transduce biochemical or physiological interactions into electrical signals[79,80]. These signals are then processed and converted into readable outputs, enabling real-time monitoring and diagnostics. In flexible bioelectronics, the selection of materials and structural design is critical to achieving mechanical durability, biocompatibility, and seamless integration with biological systems. Biointerfaces must be adaptable, conformable, and resilient to external forces to ensure long-term functionality. Therefore, an ideal biosensor design should incorporate key attributes such as mechanical flexibility, stretchability, thermal and chemical stability, resistance to non-target biological fluids, transparency, durability, and even self-healing capabilities[46,81].

Over the years, various flexible substrates have been explored, each exhibiting different combinations of these essential properties. The flexible substrate serves as the backbone of the biosensor, offering mechanical support, a smooth and uniform surface for functionalization, and a robust framework that binds all components together while preserving signal integrity[82]. Since bioreceptors and active materials are primarily integrated into these substrates, they must maintain their mechanical strength and stability even under continuous deformation, prolonged use, and exposure to dynamic biological environments.

There are two primary strategies commonly employed for designing flexible and stretchable biosensors: (1) developing materials that inherently possess both flexibility and stretchability while exhibiting conductive or semi-conductive properties, and (2) adapting rigid or semi-rigid materials by incorporating geometric engineering techniques (e.g., serpentine designs, kirigami structures, or porous frameworks) to enhance flexibility[83]. Thin metallic foils with a thickness of less than 200 µm, such as gold (Au), copper (Cu), silver (Ag), aluminum (Al), and platinum (Pt), serve as excellent flexible and conductive substrates, providing high electrical conductivity, superior thermal stability, mechanical robustness, and enhanced durability against external mechanical stresses[84]. These materials are widely used in bioelectronic applications such as wearable sensors, implantable devices, and flexible electrodes due to their ability to maintain stable electrical performance under repeated deformation[85]. Additionally, semi-metallic foils, such as indium tin oxide (ITO)[86] and doped graphene films, offer a balance between flexibility, transparency, and conductivity, making them ideal for applications requiring optical clarity, such as transparent biosensors, electronic skin, and stretchable displays[87]. However, these methods involve higher manufacturing costs, require high-temperature processing that can damage fragile bioreceptors, and lack biodegradability, thereby limiting their applicability in eco-friendly biosensing.

In contrast, paper stands out as an affordable, flexible, and widely available substrate, perfect for rapid point-of-care diagnostics, especially in resource-constrained environments. Paper-based substrates such as cellulose, cellulose nanocrystals (CNCs), nanofibrillated cellulose (NFCs), and bacterial nanocellulose (BNCs) can support various sensing modalities like optical, electrical, and electrochemical. Their versatility can be enhanced through conductive coatings, composites, or integration with soft metal foils. Though paper's mechanical fragility and low wet stability pose challenges, these issues can be addressed through material modifications, offering an eco-friendly alternative for biosensors[88]. Similar to paper-based substrates, textiles are also an inexpensive and versatile option for biosensor applications. Various types of textiles, such as knitted, woven, nonwoven, and crocheted fabrics, made from materials like nylon, polyester, cotton, spandex, and silk, are commonly used for applications including wearable sensors, healthcare monitoring, and implantable electronics. Conductive properties can be integrated into these textiles through various fabrication techniques, with conductive yarns being embedded by weaving, knitting, or electrospinning methods. Textiles offer multiple daily life advantages such as comfort, flexibility, breathability, and the ability to seamlessly integrate into clothing, making them ideal for long-term, continuous use in wearable bioelectronics[89]. Other than the above-mentioned substrates, polymers, both synthetic and natural, are widely used as flexible substrates due to their desirable properties such as optical transparency, high elasticity, low modulus, and biocompatibility. Synthetic polymers like PDMS, polyurethane (PU), polyvinyl alcohol (PVA), polycaprolactone (PCL), and PET, along with natural polymers like chitosan, collagen, gelatin, alginate, and hyaluronic acid, are commonly utilized. These polymers are nontoxic in nature, making them compatible for both in vitro and in vivo applications.

Another advantage of these materials is that they can be easily molded into desired shapes and structures, facilitating the fabrication of bioelectronic devices with intricate designs and conformable properties[10]. For example, polyimides (PI), such as Kapton®, are flexible, thermally stable materials that can be molded easily and modified for various functionalities. They are used as substrates in bioelectronics, including neural implants, due to their excellent dielectric properties, biocompatibility, and ability to enhance conductivity through metal deposition[90], and PDMS is a type of silicone-based elastomer known for its low cost, thermal stability, and flexibility. It is widely used in biomedical devices, such as catheters and implants, offering high elasticity, optical transparency, and biocompatibility, making it suitable for both in vitro and in vivo applications. Figure 5 highlights diverse flexible substrates demonstrating their use in wearable and epidermal biosensors.

To achieve flexibility and stretchability in bioelectronics, innovative geometric engineering techniques are employed to transform rigid, brittle materials into adaptable substrates capable of conforming to dynamic, soft biological tissues. Among the most effective methods are metallic buckling, serpentine configurations, and kirigami structures, each offering distinct advantages in terms of mechanical performance and integration with biological systems[91]. Metallic buckling, for instance, is a process where metal films are deposited on pre-strained elastomers. Once the strain is released, the metal forms a wrinkled, curved structure that can withstand repeated stretching without compromising electrical properties[92]. This technique has been successfully applied in stretchable semiconductor electronics, where GaAs nanoribbons on pre-stretched PDMS demonstrate stable performance under strain, providing a foundation for flexible and durable electronics[93].

Serpentine structures, featuring in-plane configurations, are widely utilized for bioelectronics requiring conformal attachment to soft tissues such as skin. These structures, designed with soft materials like Au for

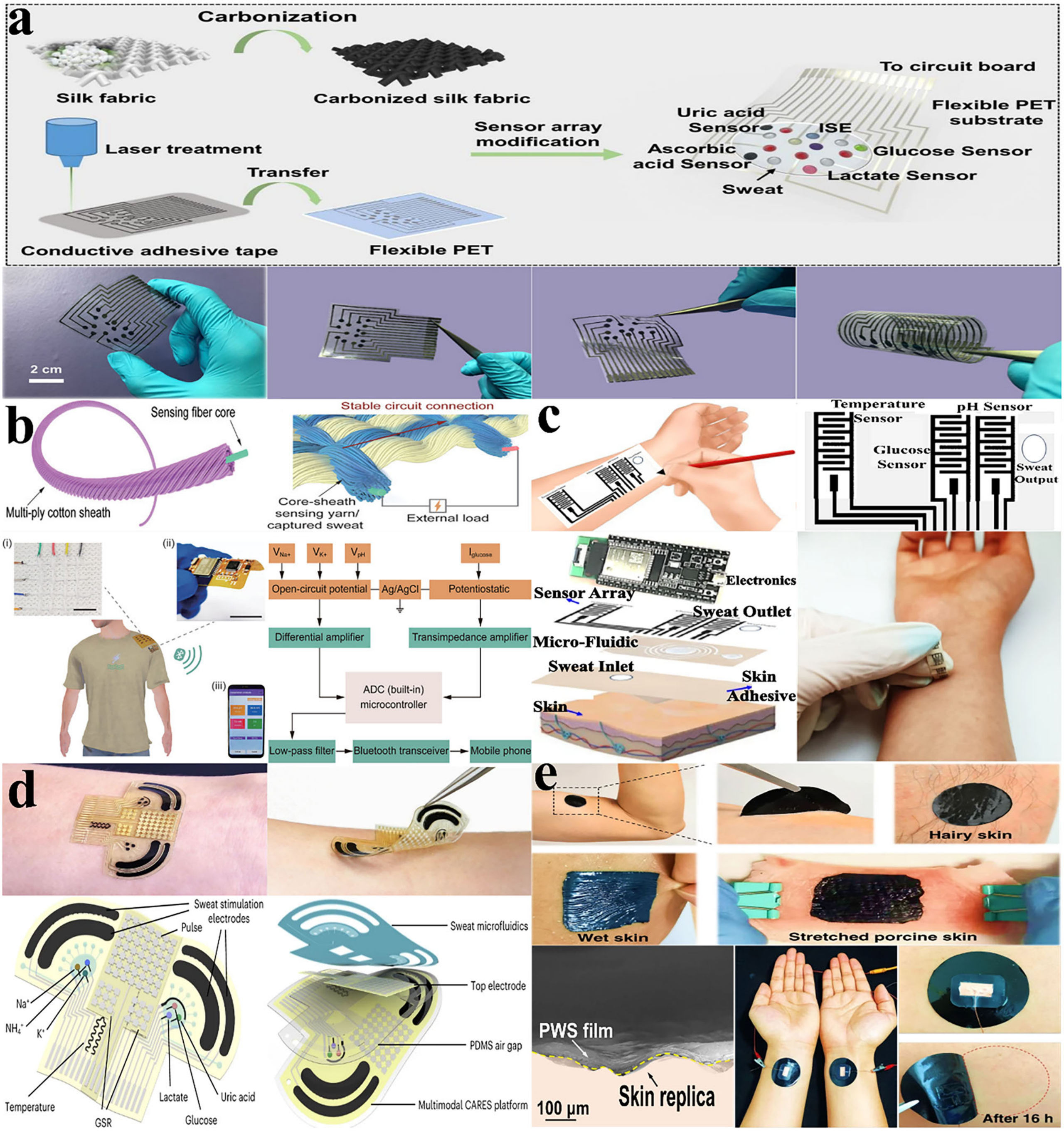

Fig. 5 | Representative examples of flexible and compliant substrates used in wearable bioelectronic sensors. a Silk fibroin- and PET-based substrates demonstrate breathable, lightweight platforms that enhance sweat permeability, flexibility, and wearer comfort in epidermal sensing systems[221]. **b** Cotton-based textile substrates enable soft, deformable, and skin-compatible architectures for continuous on-body sweat glucose monitoring[222]. **c** Paper-based substrates illustrate low-cost, disposable, and mechanically compliant platforms for bio-FET wearable e-skin devices[108]. **d** Flexible PI films provide a mechanically resilient substrate that balances flexibility and structural integrity, enabling reliable signal acquisition for long-term operation[223]. **e** Self-adhesive WPU substrates highlight conformal, adhesive-free integration with skin, enabling reliable epidermal biopotential recording across diverse skin conditions[224].

electrodes and Pt for sensors, provide an excellent balance between stretchability and electrical conductivity[91]. A prime example is the development of wearable bioelectronics composed of strain, temperature, and electrophysiological sensors that conform to the skin's surface, enabling seamless integration with the human body. This design allows for real-time monitoring of physiological signals with high mechanical compliance, ensuring stable function even during skin deformation. In addition to fully deformable architectures, rigid-island designs, where strain-sensitive electronic components are placed on mechanically stable islands interconnected by stretchable serpentine bridges have emerged as an effective strategy to protect active devices from excessive strain while preserving overall system flexibility[94,95]. Figure 6 showcases representative structural design strategies that enhance stretchability, conformability, and multifunctionality in wearable biosensors.

Kirigami-based configurations take flexibility a step further by incorporating cut patterns that enable both in-plane and out-of-plane deformation. This approach, inspired by the traditional paper-cutting art, allows bioelectronics to maintain stable performance even under

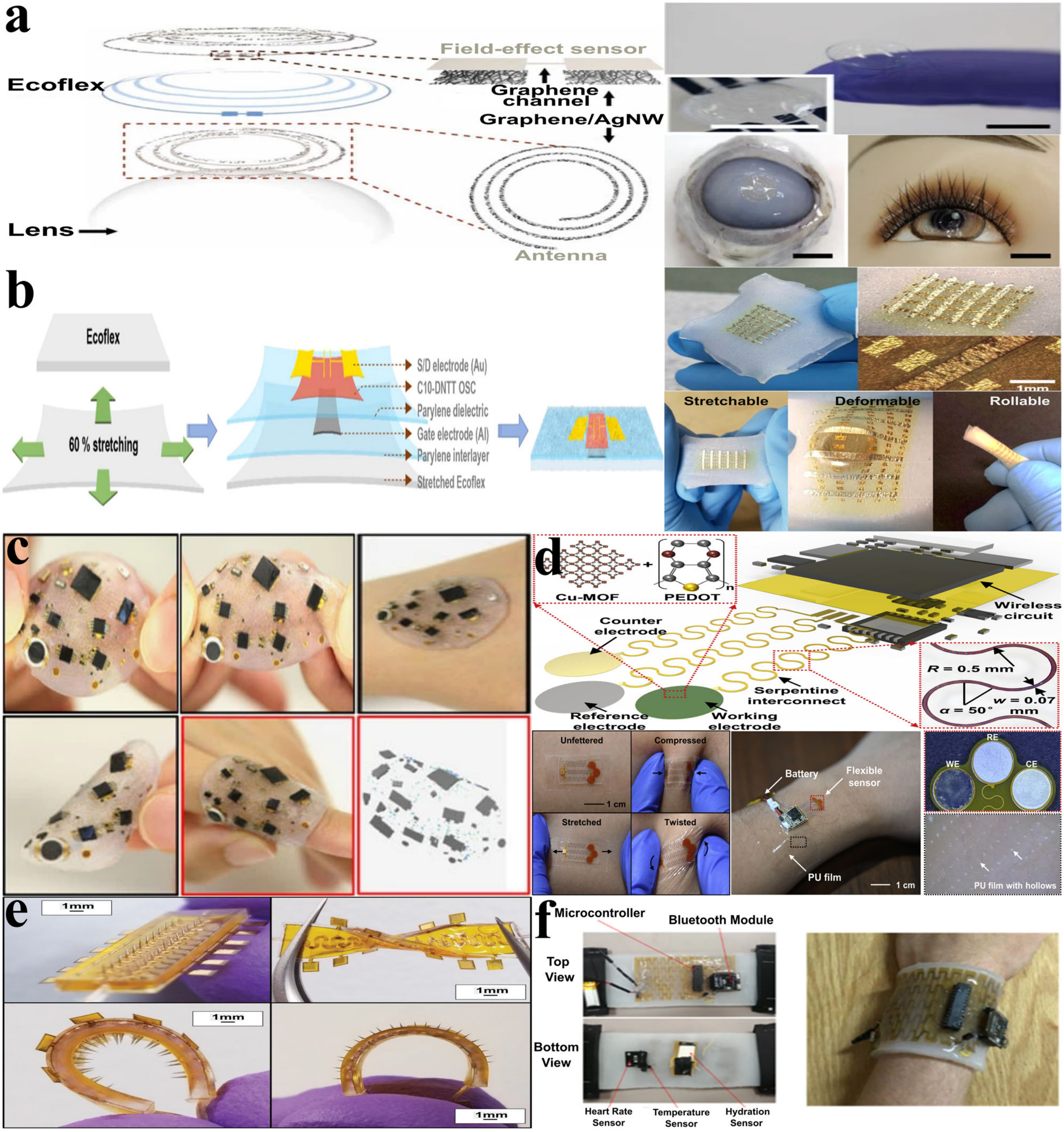

Fig. 6 | Representative structural and architectural design strategies enabling extreme stretchability, conformability, and functional stability in wearable bioelectronic devices. **a** Graphene/AgNW hybrid conductors integrated on Ecoflex substrates demonstrate ultrathin, soft, and wireless contact-lens sensors, highlighting mechanical transparency and intimate ocular interfacing for noninvasive diagnostics[206]. **b** Omnidirectionally stretchable organic transistors employing controlled wrinkling architectures illustrate strain-accommodating designs that preserve electrical performance under large biaxial deformation[225]. **c** Buckling-induced 3D helical coil networks enable soft electronic systems with enhanced stretchability and mechanical resilience for continuous physiological monitoring[226]. **d** Flexible electrochemical sensors incorporating serpentine interconnects demonstrate effective strain redistribution and conformal skin contact, enabling stable sweat ascorbic acid sensing during mechanical deformation[201], **e** 3D micro-serpentine structures illustrate geometry-driven mechanical compliance, allowing large reversible strain without compromising device integrity or signal fidelity[227]. **f** Kirigami-inspired wearable systems illustrate mechanically programmable deformation and scalability, enabling multifunctional health and crowd-monitoring applications on the wrist[228].

extreme stretching, mimicking the complex, irregular motion of human tissue[96]. For example, a kirigami-structured supercapacitor patch made from polyimide (PI) film demonstrated remarkable stretchability, with the electrochemical properties remaining stable even under elongation of up to 282.5%[97]. This highlights the potential of kirigami-based designs to enhance the mechanical flexibility of bioelectronics while retaining functionality, making them ideal for use in wearable sensors and other biointegrated devices.

Beyond these strategies, advanced design principles such as nanoscale engineering have been employed to make even high-modulus materials, like metals and semiconductors, more flexible. Techniques such as nano-patterning, serpentine layouts, and fractal designs can be used to enable bending, stretching, and conforming to various shapes while maintaining the intrinsic properties of conductive materials like Ag, Cu, and Au nanomaterials. For example, gold nanowires and silver nanoparticle-based circuits have been engineered to maintain excellent conductivity while exhibiting significant mechanical deformation capabilities[98,99]. These nanoscale structures are particularly valuable in the development of bioelectronics that require high performance and reliability under mechanical stress.

The application of these geometric engineering techniques in the field of biosensing has the potential to revolutionize the design of flexible, stretchable sensors capable of detecting a wide range of biological and chemical analytes. While much of the current research focuses on improving the mechanical properties and electrical performance of these materials, ongoing work is expanding into the immobilization of biorecognition molecules and their integration into flexible biosensor platforms. These advancements are poised to enable the development of highly sensitive, wearable biosensors capable of continuous, real-time monitoring of biomarkers, offering new possibilities in personalized medicine, health monitoring, and diagnostics.

Interplay between biocompatibility and mechanical compatibility in flexible and implantable bioelectronics

To accurately detect a wide range of biosignatures, including electrophysiological, physical, and biochemical signals, these devices must be able to maintain long-term integration with the human body for continuous daily use[100]. However, conventional electronic devices often lack mechanical adaptability, leading to discomfort and poor compatibility with biological tissues. This can result in skin irritation, inflammation, allergic reactions, and pressure sores. In implantable bioelectronics, prolonged mechanical mismatch may further induce tissue injury, fibrosis, and chronic inflammation, ultimately impairing device performance and long-term stability.

In addition to mechanical mismatch, exposure to biofluids such as sweat, saliva, mucus, and interstitial fluid can penetrate these devices, altering their original properties and compromising performance[101]. Ensuring stable adhesion remains one of the most significant challenges in developing reliable and long-lasting bioelectronic systems. Collectively, these factors highlight that the long-term functionality of bioelectronic devices largely depends on the biological and mechanical compatibility of the materials used in the devices with human tissues[102]. Thus, the primary challenge hindering the advancement of wearable and implantable bioelectronics lies in overcoming limitations related to biocompatibility and mechanical compatibility with body tissues. To develop highly functional and reliable bioelectronic devices, the materials replacing conventional rigid components must satisfy two closely interrelated requirements: (1) biocompatibility, to minimize immune responses and ensure safe tissue interaction[103] and (2) mechanical compatibility, since mismatched stiffness, flexibility or stretchability, can directly trigger inflammation, fibrosis, and device failure during long-term use[104]. Accordingly, this section discusses the key material and surface-engineering strategies that have been developed to improve biocompatibility in wearable and implantable bioelectronic devices, while simultaneously ensuring mechanical compatibility with biological tissues.

Over the past decades, extensive research has demonstrated the effectiveness of various biocompatible materials in bioelectronics, including natural biopolymers and synthetic polymers, which have been widely explored for their mechanical flexibility and biocompatibility. To enhance the electrical properties of bioelectronic devices, conductive polymers, including polypyrrole (PPY), polyaniline (PANI), and poly(3,4-ethylenedioxythiophene) (PEDOT), have been incorporated. These polymer-based biosensors have been successfully employed in detecting a wide range of analytes, including glucose, lactate, dopamine, and nucleic acids, making them essential for continuous health monitoring, disease diagnostics, and wearable sensing applications[10,105]. Among these, hydrogels have emerged as particularly advantageous for human tissue engineering, wound healing, and in vivo drug delivery, owing to their high-water content, tunable mechanical properties, and excellent biocompatibility. Their 3D porous network structure provides an ultrasensitive platform for detecting biomolecules such as proteins, enzymes, and DNA, making them highly effective in biosensing and regenerative medicine[106].

Next-generation bioelectronic devices incorporate various nanomaterials, including Ag and Au nanoparticles, carbon nanotubes (CNTs), graphene, transition metal dichalcogenides (TMDs), and MXenes, which significantly enhance device performance[107,108,109,110]. These nanomaterials offer numerous advantages, such as exceptional sensitivity towards biomolecular interactions, high thermal stability, rapid electron transport, and superior mechanical flexibility[111,107]. Furthermore, functionalized nanomaterials allow for effective conjugation with biological molecules, including enzymes, nucleic acids, and antibodies, thereby improving their biocompatibility and specificity for biomedical applications such as wearable health monitoring, neural interfaces, and point-of-care diagnostics[112]. Despite their advantages, nanomaterial-based bioelectronics face challenges such as cytotoxicity, as materials like CNTs and metal nanoparticles can induce oxidative stress and inflammation. High fabrication costs and complex synthesis methods hinder large-scale production, while long-term stability issues, including aggregation and oxidation, compromise device performance[113]. Biofouling and surface contamination compromise sensor performance and increase measurement variations, and toxic degradation byproducts raise safety concerns. Additionally, regulatory and environmental challenges limit clinical translation. Addressing these issues requires advances in biodegradable nanomaterials, improved surface functionalization, and cost-effective fabrication techniques to enhance safety, stability, and scalability[114]. Some of these disadvantages can be mitigated by applying various functional coatings over nanomaterials, such as non-immunogenic coatings, hydrophobic/hydrophilic antibiofouling coatings, and biocompatible polymer coatings. Existing coatings include polyethylene glycol (PEG) coatings to reduce biofouling, zwitterionic coatings for improved protein resistance, self-assembled monolayers to enhance surface functionality, and polydopamine coatings for strong adhesion and biocompatibility[115–117]. These strategies improve the stability, biocompatibility, and overall performance of nanomaterial-based bioelectronic devices.

For implantable bioelectronics, bioelectronic devices implanted in the human body, the body's immune system perceives those devices as foreign objects, triggering a foreign body reaction. This response leads to the formation of a dense fibrotic capsule around the implant, which significantly impairs overall device functionality[118]. To overcome this challenge, surface coatings have been developed to enhance biocompatibility and reduce immune responses. Self-mimicking coatings, such as zwitterionic or cell-membrane-coated surfaces, replicate natural cellular environments, minimizing immune activation and promoting seamless integration with tissues. Drug-releasing coatings, like dexamethasone-loaded hydrogels, provide localized anti-inflammatory effects, reducing fibrosis and enhancing long-term device performance. Immunoactive coatings, such as interleukin-10 (IL-10) or transforming growth factor-beta (TGF-β)-functionalized surfaces, actively modulate immune responses, suppressing chronic inflammation and facilitating stable bioelectronic operation[104]. These advanced coatings significantly improve the longevity and functionality of implantable bioelectronic devices.

Enhancing the assessment of bioelectronic biocompatibility requires a combination of in vivo, in vitro, and ex vivo methodologies to comprehensively evaluate their interactions with biological systems. In Vivo animal models provide critical insights into long-term tissue integration, immune responses, and device functionality under physiological conditions. In vitro tissue culture studies enable controlled investigations of cytotoxicity, cellular adhesion, and inflammatory markers, offering rapid and reproducible data on material-tissue interactions. Additionally, cell adhesion assays help determine how well bioelectronic surfaces support cellular attachment and proliferation, which is crucial for stability and integration[119]. Together, these complementary evaluation approaches provide a systematic framework for assessing material-tissue interactions and guiding the rational design of biocompatible bioelectronic devices.

In addition to biocompatibility, these materials exhibit excellent mechanical compatibility with biological tissues, which is essential for the effective performance and longevity of bioelectronic devices. Biological tissues and internal organs in the human body are extremely soft, with an elastic modulus of ~0.1–1 kPa for the central nervous system and 10–100 kPa for internal organs such as the heart, liver, and lungs, while their structural deformability allows for large mechanical strain without failure. In contrast, conventional rigid bioelectronic devices, such as silicon-based neural implants and metallic electrodes, possess an elastic modulus exceeding 100 GPa and a strain-at-break of less than 1%, making them significantly stiffer than biological tissues. This pronounced mechanical mismatch promotes localized stress concentration at the tissue-device interface, accelerating inflammatory responses, fibrotic encapsulation, and progressive degradation of signal quality during long-term implantation[120].

Overcoming this challenge requires the development of bioelectronic materials that not only exhibit mechanical compatibility closer to soft tissues but also maintain durability and functionality under dynamic physiological conditions. Three key mechanical properties are essential for ensuring mechanical compatibility with biological tissues: flexibility, stretchability, and conformability[74,121]. These properties collectively enhance the integration of bioelectronic devices with the body, reducing the risk of mechanical failure and adverse biological responses. Such mechanical matching improves overall comfort, stability, and long-term functionality of bioelectronic devices, allowing for their successful integration into biomedical applications. Building on mechanical and biological compatibility, reliable long-term operation of flexible biosensors requires stable electrical outputs under prolonged physiological exposure and repeated mechanical deformation[122]. Accordingly, several material and structural strategies have been developed to address signal drift, noise fluctuations, and performance degradation. Mechanically compliant substrates and stretchable device architectures reduce stress concentration at the tissue-device interface, preserving electrical continuity during bending and stretching[123]. Strong and durable adhesion layers minimize interfacial slippage and motion-induced artifacts, particularly in skin-interfaced and implantable systems[124]. Beyond their established role in improving biocompatibility, antifouling and anti-inflammatory surface coatings, such as PEG, zwitterionic, and hydrophilic coatings[125], limit biofluid infiltration, protein adsorption, and foreign body reactions, which are major causes of long-term signal instability[126]. To further elucidate how these modified surfaces interact with surrounding biological environments and device components, advanced surface energy characterization techniques capable of probing nanoscale interfacial properties should be integrated into biosensor development[127,128]. Collectively, these material, structural, and interfacial engineering strategies play a critical role in maintaining stable outputs and ensuring the long-term and dynamic stability of flexible bioelectronic devices under real-world operating conditions. Figures 7 and 8 present representative implantable biosensors from the literature, emphasizing their mechanical adaptability and tissue-compatible designs for on-organ monitoring and bioelectronic interfaces.

Biocompatible wearable and implantable biosensors for continuous health monitoring

Continuous health monitoring integrates wearable biosensors with digital health technologies to enable real-time acquisition of physiological signals, supporting proactive and data-driven healthcare. The effectiveness of continuous monitoring systems critically depends on their mechanical design, as long-term operation requires stable skin-sensor interfaces, suppression of motion-induced artifacts, and durability under repetitive deformation, as discussed in the previous section[53]. Recent advances in flexible and skin-conformal bioelectronics have enabled uninterrupted signal acquisition during daily activities, significantly improving data continuity and signal fidelity are key requirements for reliable continuous monitoring[129]. The rapid growth of this industry, driven by technological advancements and rising health awareness, is transforming traditional healthcare into a personalized, predictive, and preventive system[130]. Within this context, recent wearable biosensor platforms serve as representative case studies demonstrating how mechanically compliant designs enable robust, long-term physiological monitoring in real-world conditions.

Wearable biosensors for continuous health monitoring

Wearable biosensors have emerged as a key technological solution for continuous monitoring, enabling real-time tracking of diverse physiological and biochemical parameters through noninvasive and user-friendly platforms. These systems are now widely explored for applications ranging from cardiovascular and metabolic monitoring to stress assessment, hydration tracking, sleep analysis, and fatigue detection. A defining advantage of continuous wearable biosensing lies in its ability to capture subtle temporal variations and long-term biomarker trends that are often inaccessible through intermittent clinical measurements. Consequently, recent research has focused on developing highly sensitive, multimodal, and mechanically compliant wearable sensors that enhance measurement accuracy while maintaining user comfort and operational stability during prolonged use[131,132].

Sheng et al. have developed a flexible wearable biosensor for pressure monitoring. Recent advancements have led to capacitor sensors using 3 M VHB 4905 tape and GaInSn, integrated with the CAV444 chip, which exhibited a highly linear response to stretching, rotation, and pressure. The prepared sensors have promising applications in motion tracking, electronic skin, accident alerts, and remote monitoring. With high stretchability (250%), excellent repeatability (>500 cycles), and a fast response time (<10 ms), they offer new possibilities for biomedical sensor design and healthcare applications[133]. Carreiro et al. reported a wearable biosensor to monitor physiological changes during opioid use. Tested on 30 ED patients, the wristband tracked electrodermal activity, skin temperature, and locomotion before and after opioid administration. The results exhibited decreased locomotion and increased skin temperature, while electrodermal activity changes were inconsistent. The heavy opioid users exhibited greater reductions in fidgeting movements without any significant differences based on gender or opioid type[134]. That work highlights the potential of wearable biosensors for real-time opioid use monitoring and relapse detection.

Kweon et al. designed a polymer-based pressure biosensor using conductive core/shell nanofibers composed of PVDF-HFP/PEDOT. Fabricated through 3D electrospinning and vapor deposition polymerization, the sponge-like 3D membranes exhibited high porosity and a hierarchical conductive surface, enhancing pressure sensitivity. The sensors demonstrated a sensitivity of 13.5 kPa^{-1}, over twice that of conventional electrospun mats, with a detection limit of 1 Pa and durability over 10,000 cycles. That study revealed the potential of scalable, low-cost polymer-based pressure sensors for biomedical diagnostics, environmental monitoring, and wearable electronics[135]. Hallfors et al. developed a novel self-powered wearable IoT ECG sensor using Nylon® coated with reduced graphene oxide (rGOx). The conductive fabric functioned as ECG electrodes, capturing reliable signals from the wrist and neck. That study highlights the potential of rGOx-based ECG sensors for continuous cardiovascular monitoring and emergency response[136]. Sekine et al. prepared a wearable fluorometric microfluidic platform for sweat analysis, integrating a smartphone-based imaging module for real-time biomarker detection. The system features microchannels and reservoirs pre-filled with fluorescent probes that selectively react with chloride, sodium and zinc in sweat with high selectivity. Field studies demonstrated accurate measurements of chloride, sodium, and zinc levels, matching conventional lab techniques. This offered a low-cost, user-friendly solution for point-of-care diagnostics and wearable health monitoring[137].

Anuradha et al. reported a paper strip-based optical biosensor for noninvasive salivary glucose analysis. The sensor is glucose oxidase and a pH indicator on a filter paper strip, which is able to detect glucose by color change, which is scanned and analyzed with RGB profiling software. The sensor showed a strong correlation between salivary glucose (SGL) and

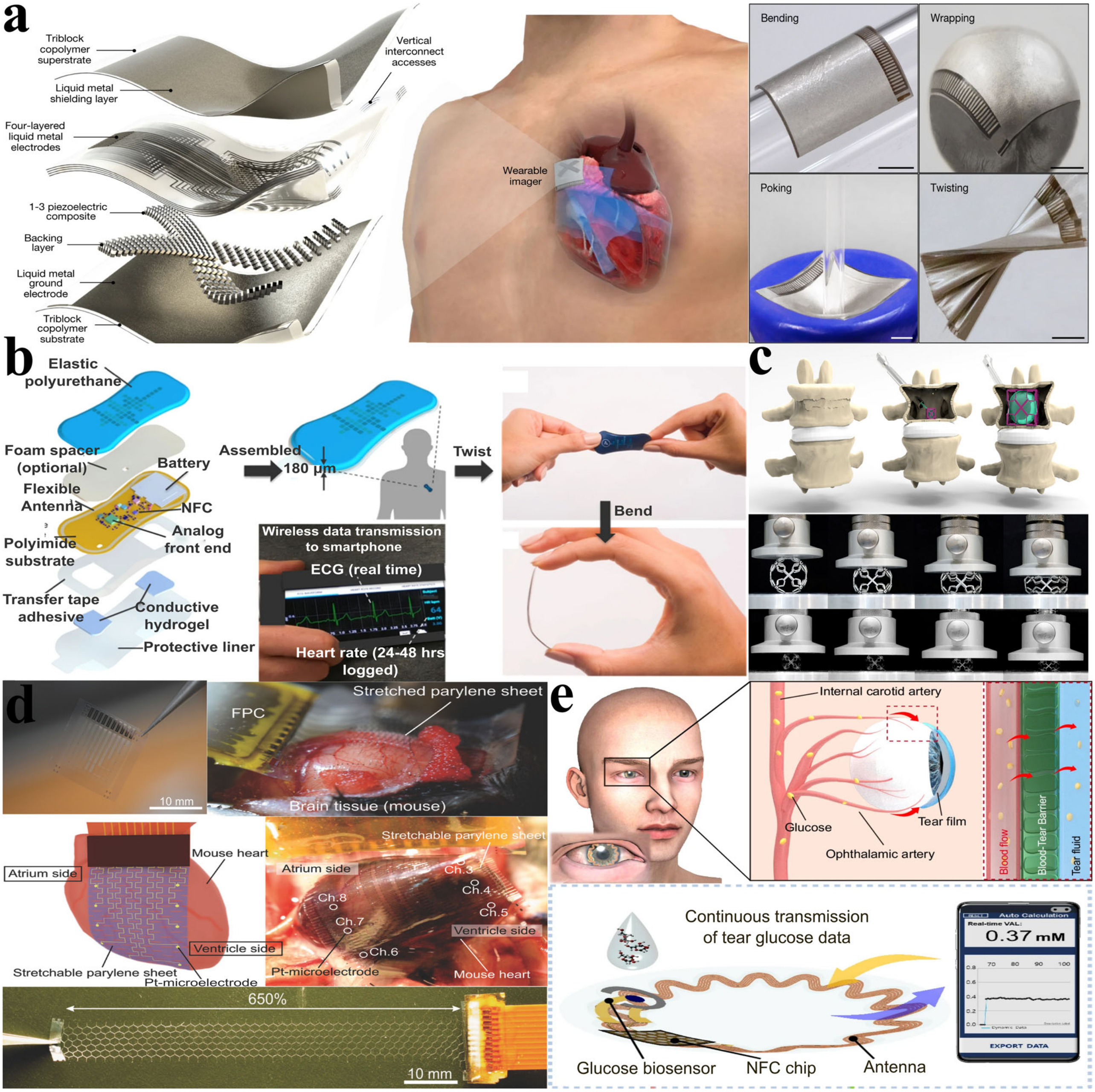

Fig. 7 | Mechanical and biocompatibility of biosensors in implantable devices. a A wearable cardiac ultrasound imager illustrates multilayer soft architectures that maintain conformal contact and functional integrity under bending, wrapping, poking, and twisting, highlighting mechanical compatibility with dynamic cardiac motion[229]. **b** An ultrathin, flexible cardiac biosensor demonstrates bendability and twist tolerance while enabling continuous, wireless physiological data acquisition, emphasizing the importance of device miniaturization and substrate softness for implantable monitoring[230], **c** An origami-inspired deployable implant for vertebral fracture repair exemplifies geometry-driven mechanical adaptability, combining compact insertion with high compressive strength after deployment[231]. **d** Kirigami-engineered parylene films provide highly transparent, stretchable, and tissue-conformal interfaces for brain and cardiac electrophysiology, enabling large-strain deformation without mechanical mismatch or tissue damage[232]. **e** serpentine, ring-shaped polyimide platform integrating metallic interconnects and antennas demonstrates strain-tolerant implantable biosensing, enabling continuous tear-glucose monitoring through mechanically compliant ocular interfaces[233].

blood glucose levels, with a detection range of 9–1350 mg/dL and a response time of 45 s. Moreover, the prepared biosensor is a low-cost, rapid method for diabetes screening, but is influenced by interferents like lactic and ascorbic acid. Further studies are planned for improvement and standardization[138]. Table 1 provides an overview of recent wearable biosensors designed for monitoring diverse physiological signals. These studies represent just a glimpse into the recent advancements in continuous monitoring technologies, showcasing their transformative potential in healthcare and personal wellness. While these wearable platforms demonstrate the effectiveness of mechanically compliant, skin-mounted biosensors for continuous and noninvasive monitoring, implantable sensing platforms have emerged as a highly effective approach for achieving uninterrupted, long-term physiological surveillance. While wearable systems enable convenient surface-level measurements, implantable biosensors provide direct access to internal organs and deep tissues, allowing more stable and physiologically relevant signal acquisition over extended periods. By interfacing directly with the biological environment, implantable devices enable continuous monitoring of critical internal parameters that are difficult to assess reliably through epidermal interfaces, albeit with additional material, mechanical, and biological design considerations.

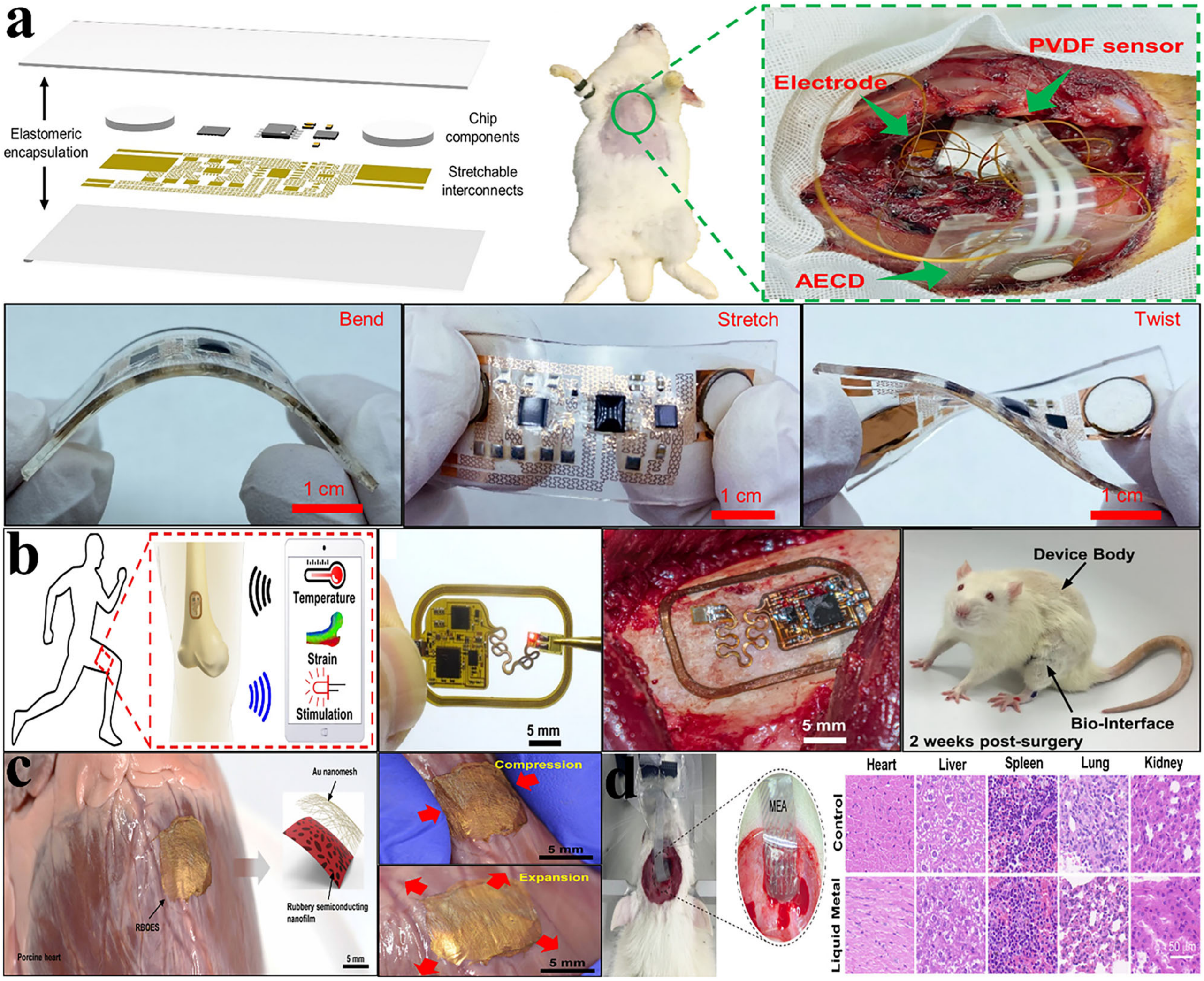

Fig. 8 | Mechanical compliance and biocompatibility of biosensors in implantable devices. a Ultrathin PI-based implantable electronics illustrate how mechanically compliant substrates and stretchable interconnects preserve device functionality under bending, stretching, and twisting, which is critical for long-term cardiac monitoring under continuous organ motion[234]. **b** PI/copper osseosurface electronics demonstrate multimodal sensing and stimulation at the musculoskeletal interface, highlighting how conformal mechanics improve signal fidelity and stable biointegration at load-bearing tissues[235]. **c** Regioregular P3HT/SEBS rubbery bio-optoelectronic devices with Au nanomesh electrodes exemplify soft, tissue-matched electronics capable of maintaining intimate contact with dynamic cardiac tissue for reliable stimulation and sensing[236]. **d** Liquid metal–based stretchable electrode arrays showcase an alternative strategy for achieving extreme deformability and biocompatibility in neural interfaces, with histological analysis confirming minimal tissue response across major organs[237].

Implantable biosensors for long-term continuous health monitoring

Extending continuous health monitoring beyond wearable systems, implantable devices have revolutionized modern medicine by enabling continuous monitoring and treatment of various health conditions. In the year of 1950s, when Clark and Lyons pioneered the first implantable devices, advancements in sensor technology have significantly expanded their applications[139]. Nowadays, the devices incorporate electrochemical, mechanical, optical, and thermal sensors to monitor cardiac health, neurological conditions, and glucose levels, improving patient care and outcomes. The performance of implantable devices depends on the materials based on the construction, with biocompatibility, corrosion resistance, flexibility, and conductivity being critical factors. Each material plays a vital role, from signal conduction to energy storage and device protection, ensuring both safety and functionality. Additionally, the advanced manufacturing techniques such as microfabrication, 3D printing, and nanofabrication have enabled the development of highly intricate and efficient implantable devices. As technology continues to evolve, innovations in materials and fabrication methods will further enhance the capabilities of implantable devices, paving the way for improved diagnostics, personalized treatments, and long-term health monitoring solutions[140,141]. Kim et al. developed a flexible, implantable temperature sensor for dental applications that can provide early warning signals in real time before implant failure. The sensor was fabricated on a flexible polyimide film using a microfabrication process and exhibited high accuracy, durability, and stability, with a temperature coefficient of resistance (TCR) of 3.33×10^{-3} °C^{-1}. The mechanical stability tests confirmed its suitability for long-term implantation, underscoring its potential for advanced dental health monitoring and personalized diagnostics[142]. Seongmun et al. reported an implantable electromagnetic-based glucose sensor as a novel alternative to enzyme- and optical-based continuous glucose monitoring (CGM) systems. Instead of directly detecting glucose molecules, the sensor tracks blood glucose trends by measuring changes in dielectric permittivity. Proof-of-concept in vivo studies on swine and beagles demonstrated a strong correlation between sensor frequency and blood glucose levels during glucose tolerance tests. The dedicated sensor interface module and mobile application enable real-time, continuous monitoring. While still in the early stages, the technology shows promise for long-term glucose tracking with ongoing developments

Table 1 | Summary of representative wearable biosensors highlighting physiological targets, materials, and real-time performance features

Physiological target	Sensing material	Flexible substrate	Mechanical properties	Real-time monitoring performance	Ref
Body Motion/joint angle	GaInSn alloy	3 M VHB 4905 elastomer	stretchability (up to 250%)	stable electrical properties (0.077–0.23 pF/mm^2), and a fast response time (<10 ms)	133
Pressure/tactile mapping	Electrospun PVDF-HFP / PEDOT nanofibers	Sponge-like 3D NF mat	High compression stability	enhanced sensitivity (13.5 kPa^{-1})	135
Cardiac electrical activity	Reduced graphene oxide	Nylon textile	Good strength and smoothness	ECG acquisition, wireless transmission, and visualization on a mobile/IoT interface in real time	136
Sweat Analysis (sodium, chloride, Zinc)	Fluorescent dyes in PDMS microfluidics	Skin-adhered PDMS patch	low elastic modulus (~1 MPa) and high elasticity (up to ~200%)	chloride (28–31 mM), zinc (~2.5 μM), and sodium (35–50 mM) concentrations after workout routine	137
Salivary glucose concentration	glucose oxidase (GOD) and methyl red dye	Filter paper	-	able to detect glucose concentrations in the range of 9–1350 mg/dL in 45 seconds	138
Dermal interstitial fluid (ISF)	arrays of metallic MNs	stainless steel sheets	Mechanically strong enough to penetrate the skin surface without causing pain or damage	Allows continuous and minimally invasive monitoring of biochemical changes in real time	199
Glucose sensing from sweat	Ni–Co metal–organic framework (MOF) nanosheets	Stretchable fiber (Ag/rGO/PU composite) mounted on stretchable PDMS substrate	maintains stable conductivity and sensing response under repeated stretching, bending, and twisting.	good electrochemical performance with a high sensitivity of 425.9 μA·mM^{-1}·cm^{-2} and a wide linear range of 10 μM–0.66 mM.	200
Sweat ascorbic acid (AA) levels	Cu-MOF/PEDOT composites	polyimide (PI) film	Serpentine interconnects and Ecoflex encapsulation ensure flexibility and waterproof stability; maintains <3% signal change after 1000 stretch-bend cycles.	enabled a high sensitivity of 725.7 μA/(mM·cm^2) towards AA with a low detection limit of 0.76 μM, and the sensor showed a rapid response time of less than 10 s.	201
Occlusal force	Au nanowires	Ecoflex elastomer	Highly stretchable (tested at 40% strain), multibranch vein structure improves stress distribution and durability (≥1000 cycles)	Gauge factor ~2.17 × 10^2; sensing range ~60 kPa; response time ~210 ms, recovery ~190 ms	202
Interstitial ketone and glucose monitoring	Vertical graphene nanowalls coated on microneedles, functionalized with chitosan/enzyme composite	ceramic substrate	Microneedle tip stress <112.9 MPa, exceeding skin elastic modulus (stratum corneum 0.752 MPa, epidermis 0.489 MPa)	High sensitivity (~234.18 μA·mM^{-1}·cm^{-2}), low limit of detection (~1.21 μM)	203

in biocompatible packaging and system optimization[143]. Li et al. developed a wireless implantable bio-microsystem for real-time bladder pressure monitoring. Initially, tested in rabbits, the device featured a flexible, biocompatible sensor with a <1% error rate and a temperature rise of <2 °C. It wirelessly transmitted data with high accuracy (correlation 0.885) to an external unit. Long-term tests confirmed durability, stability, and superior sensitivity over conventional methods. The future improvements focus on miniaturization, wireless charging, and optimized buoyancy, making this system a promising solution for long-term physiological monitoring and clinical applications[144].

Ma et al. developed a self-powered, multifunctional implantable triboelectric active sensor (iTEAS) capable of real-time biomedical monitoring without the need for external power sources. The device harvests biomechanical energy from organ motion via the triboelectric effect, enabling continuous monitoring of multiple physiological parameters such as heart rate, respiration, blood flow, and blood pressure with high accuracy (~99%). The core-shell packaging ensured device durability and biocompatibility, maintaining functionality for 72 h post-implantation and proving safe after two weeks in vivo. The flexibility and minimally invasive implantation, iTEAS represents a promising advancement in next-generation biomedical sensors for long-term healthcare monitoring[145]. De la Paz et al. reported a battery-free, self-powered ingestible biosensing capsule for real-time glucose monitoring in the small intestine. The device integrates a glucose biofuel cell that harvests energy, enabling wireless telemetry via magnetic human body communication. Validated in porcine models, the sensor demonstrated high specificity, stable performance, and minimal cross-reactivity with interfering compounds. In situ tests confirmed accurate glucose detection, correlating well with blood glucose levels[146]. Table 2 summarizes furthermore research works focused on implantable biosensors designed for monitoring diverse physiological and biochemical signals within the body.

Beyond the representative systems summarized in Table 2, the long-term functionality of implantable bioelectronic devices is often constrained by chronic foreign body responses at the tissue-device interface. Following implantation, nonspecific protein adsorption and acute inflammatory signaling trigger macrophage recruitment and activation, which subsequently drives fibroblast proliferation and collagen deposition over timescales ranging from weeks to months. This progressive fibrotic encapsulation mechanically isolates the device from surrounding tissue, increases interfacial stiffness, and elevates electrical impedance, collectively leading to signal attenuation, reduced signal-to-noise ratio, and long-term recording instability. In addition to biochemical fouling, the mechanical mismatch between rigid electronic components and soft tissues exacerbates micromotion-induced stress, further accelerating inflammatory responses and fatigue-driven electrical failure. Recent studies highlight that mitigating these chronic degradation pathways requires intrinsically soft, tissue-matched materials, antifouling or bioactive interfacial coatings, and mechanically compliant encapsulation strategies that suppress immune activation while preserving stable performance. Addressing these immune-mechanical interactions is therefore critical for extending device lifetime and ensuring reliable long-term performance of implantable bioelectronic systems[147]. To mitigate these chronic failure mechanisms, several studies have reported antifouling and anti-fibrotic surface-engineering strategies, including zwitterionic coatings, hydrogel-based interlayers, ultrasoft elastomeric encapsulation, and bioinspired slippery or hydrated interfaces. Wai et al. developed a zwitterionic hydrogel-conducting polymer system to mitigate foreign body responses in implantable bioelectronics. The zwitterionic PEDOT: PSS hydrogel reduced fibrotic encapsulation by approximately 64% compared with unmodified PEDOT: PSS and exhibited a significantly lower collagen density at the tissue-device interface. Simultaneously, the modified hydrogel enhanced electrical conductivity by more than an order of magnitude. Chronic in vivo electrocardiographic recordings in murine models demonstrated that electrodes incorporating this zwitterionic hydrogel interface maintained more stable signal quality over extended implantation periods, highlighting its potential for improving long-term biocompatibility and electrical reliability in implantable electrophysiological devices[148].

Tan et al. reported a bioactivated encapsulation membrane strategy to mitigate fibrotic encapsulation and enhance cell survival in long-term implantable systems. In this work, semiporous poly(ether sulfone) (PES) hollow-fiber membranes were functionalized internally with fibronectin to promote therapeutic cell attachment and externally with the anti-inflammatory cytokine interleukin-4 (IL-4) to polarize macrophages toward an M2 phenotype and attenuate local foreign body responses. In a murine subcutaneous model, dual-coated fibers showed markedly reduced immune cell accumulation, elevated M2 macrophage presence, and suppressed fibrotic encapsulation compared with unmodified membranes, which was accompanied by enhanced survival and functional integration of encapsulated islet cells with host vasculature. This study highlights how immunomodulatory surface coatings on implantable devices can reshape host responses and decrease fibrotic tissue formation to improve chronic implant performance and therapeutic cell viability[149]. Wang et al. developed an antifouling, super-water-absorbent supramolecular polymer hydrogel (N-acryloyl glycinamide (NAGA) and carboxybetaine acrylamide (CBAA)) designed as an artificial vitreous body for long-term implantation. The hydrogel combines high-water content (98.4 wt%) and supramolecular network architecture with strong antifouling characteristics imparted by zwitterionic polymer segments, which significantly reduce nonspecific protein adsorption and cell adhesion compared to conventional hydrogels. In vivo studies demonstrated that this hydrogel maintained stable volume and mechanical properties in the vitreous cavity over extended periods (after 16 weeks post operation), while minimizing inflammatory responses and foreign body reactions. Its structural and optical properties closely mimic those of the natural vitreous humor, suggesting its promise as a long-lasting, biocompatible substitute that resists biofouling and maintains functional integration with ocular tissues[150]. Overall, recent implantable biosensor designs demonstrate impressive progress in flexible electronics, wireless operation, and multifunctional physiological monitoring. However, chronic implantation introduces additional challenges beyond initial device performance, particularly immune-mediated encapsulation, long-term impedance drift, and mechanically induced signal degradation. Addressing these issues requires a shift toward tissue-matched mechanical properties and interface-engineered materials that actively regulate the biological response. Such approaches are expected to play a central role in enabling stable, long-term implantable bioelectronic systems for clinical translation.

Importance of modern biosensing methods in continuous monitoring

While wearable and implantable platforms provide the physical interface for continuous health monitoring, the reliability and clinical value of long-term operation are ultimately governed by the underlying biosensing methodologies. Biosensors have transformed various industries, with the most profound impact in medical, clinical, and healthcare applications[151]. They play a pivotal role in disease detection, retinal prostheses, MRI contrast imaging, heart diagnostics, medical mycology, and continuous health monitoring. Beyond diagnostics, biosensors drive advancements in wearable and portable healthcare technologies, contributing to disease surveillance, treatment, fitness tracking, and overall well-being while lowering healthcare costs. Their growing adoption across different age groups has accelerated global healthcare market expansion.

Unlike traditional periodic checkups and manual biomarker measurements, modern continuous health monitoring systems provide real-time, accurate, and automated physiological data tracking. These innovations empower individuals to take a proactive approach to health management while enabling remote monitoring by healthcare providers. Modern biosensing methods integrate wearable, electrochemical, and optical sensors to monitor vital parameters such as heart rate, glucose levels, oxygen saturation, and molecular biomarkers. Technologies like ECG sensors, molecular biosensors, and lab-on-a-chip systems enable rapid,

Table 2 | Summary of representative implantable biosensors highlighting physiological targets, materials, and real-time performance features

Physiological target	Functional material	Flexible/ biodegradable substrate	Mechanical & electrical properties	Biocompatibility/ stability	Real-time monitoring	Ref
Dental implant (Peri-implant inflammation)	Platinum resistor with gold interconnects	Polyimide film	TCR = 3.33×10^{-3}/°C; maintains conductivity and elasticity under bending and humidity; substrate is durable for long-term implantation	No cytotoxicity to oral epithelial cells; stable in artificial saliva for 2 months	Continuous local temperature monitoring around the dental implant for early infection detection	142
Blood glucose level (BGL) in the subcutaneous region	Implantable EM resonator	-	Resonance frequency shift ~32 MHz for BGL change (61–376 mg/dL) in swine; sensitivity ~0.104 MHz/mg/dL	Tested in swine and beagle models; stable operation over ~52 h OGTT; packaging minimized foreign body reaction	Continuous glucose monitoring; frequency data transmitted via interface board and mobile app; high correlation (R^2 ~0.93) with reference glucose measurements	143
Intracranial pressure, temperature, strain, motion (for post-traumatic monitoring)	CVD-grown monolayer MoS_2	nanoporous silicon substrate + Poly(lactic-co-glycolic acid) PLGA (~30 µm)	pressure sensitivity ~65 kΩ per mmHg; temperature sensitivity ~51 kΩ/°C	Demonstrated long-term cell viability, in vivo implantation in mice for 4 weeks without adverse immune response; slow hydrolysis of MoS_2 in PBS.	Implanted in a rat for continuous monitoring of temperature and pressure via a bioabsorbable sensor and compared with a commercial device.	204
Cardiac monitoring after heart surgery	Mg electrodes, Zn NPs, PEDOT:PSS, PANI/PVA composites for sensing layers	biodegradable poly(lactic acid) (PLA)	sensor responds at 5.6 kPa and 12.2 kPa; biosensors show sensitivity 38.85 mV/pH and 1.11 µA/decade (lactate)	In vitro with cardiac cells (H9c2), no cytotoxicity; Mg dissolves in ~24 h, Zn NPs <2 months, PLA ~1 year in simulated body fluid	Ex vivo tests on a 3D printed heart model; sensors transmit data via IoT + AI data fusion for health assessment	205
Tear fluid and intraocular pressure	Graphene– AgNW hybrid transparent electrode	Cu foil	transparency (>91%) and Stretchable up to ~25% tensile strain, ΔR < 6% under 25% strain, ΔR ~20% after 10,000 cycles	In vivo test on rabbit eye; no adverse behavior; transparency and good oxygen/ water permeability	Wireless detection of glucose in tears (1 µM–10 mM) and IOP (5–50 mmHg) via antenna coupling, real-time on rabbit/bovine eye	206
Deep-brain chemical activity (glutamate) and chemical delivery	Gallium (Ga) liquid metal wires and Pt electrodes	PDMS thin film	Tunable stiffness over ~5 orders of magnitude; Glutamate sensing: sensitivity ≈8.2 pA/µM, detection limit ≈0.39 µM, response time ~1 s	Reduced astrocytic encapsulation vs rigid silicon probes at 4 weeks	Demonstrated repeated glutamate injections into the rat striatum with sensor read-out and microfluidic agent release	207
Wound closure and tissue recovery	Mg filament core + triboelectric layers (PLGA nanofibers + PCL sheath)	PLGA nanofibers	Tensile strength ~265 MPa; Voltage output in vivo ~2.3 V under normal muscle activity	Biocompatible (cell viability >90%); materials degrade in vivo (~14 d for Mg core, full absorption by ~24 weeks)	Continuous electrical stimulation during healing; accelerated wound closure (~50% faster), and lower infection rate in the animal model	208
Cell-free DNA	Clustered regularly interspaced short palindromic repeats (CRISPR)-dCas9 and dRNP immobilized graphene layer as working electrode	Commercial indwelling needle	The indwelling needle substrate exhibits excellent mechanical properties, including high tensile strength (can withstand at least 3 N of force) and flexibility (bending stress of 0.12–0.15 MPa at 10% strain)	Graphene coating showed low cytotoxicity; minimal inflammation and platelet aggregation in rats; CRP and IL-6 were stable; maintained cfDNA sensing stability for 3 days in 60% serum.	Continuous monitoring and adjustment of therapy in response to cfDNA dynamics in real time	209
Early detection of kidney transplant rejection	Ultrathin patterned gold disk (~100 nm) as a thermal sensor on the kidney surface	polyimide (10 µm) and silicone (100 µm)	Detects anomalous kidney temperature rises (~0.5–0.6 °C increase) and rhythm changes	Tested in rat transplant models; no major adverse effects reported; detected rejection ~2–3 weeks earlier than blood biomarkers in immunosuppressed animals, and ~3 days earlier when therapy stopped.	Continuous, wireless, real-time monitoring of graft health; data streamed to an external device/ tracking system for early intervention.	210
Deep-brain dopamine release	Fluorescent Eu-MOF	Graphene/polyimide film	Detection limit ~79.9 nM; integrated wireless circuit ~0.85 g for seamless animal implantation	Cytotoxicity tests show low cell toxicity; immunofluorescence indicates good in vivo biocompatibility	Continuous monitoring of dopamine during deep-brain stimulation in freely moving rats	211

point-of-care diagnostics. Nanotechnology-integrated biosensors further enhance detection sensitivity, facilitating early disease identification. Innovations such as smart contact lenses for glucose monitoring and flexible sensors for hydration tracking make healthcare more personalized, accessible, and proactive. One of the most critical applications of biosensors is in cardiovascular disease diagnosis, as heart disease remains the leading global cause of mortality, claiming over 17 million lives annually. By utilizing highly sensitive biomarkers such as C-reactive protein (CRP), myoglobin, myeloperoxidase (MPO), interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor alpha (TNF-α), biosensors enable early detection and precise monitoring of heart conditions[152,153]. Advanced biosensor technologies, integrating innovative surface chemistries and nanomaterials, are crucial for enhancing diagnostic accuracy and improving clinical outcomes.

Similarly, biosensors play a transformative role in diabetes management, addressing the rising prevalence of diabetes worldwide. The demand for rapid and preventive glucose monitoring continues to grow, driving innovations that enhance sensitivity, specificity, and real-time monitoring accuracy. Biosensors are transforming diabetes care by enabling continuous, real-time glucose monitoring and proactive disease management. By integrating biomarker analysis, these technologies facilitate personalized treatment, minimizing the risks of hypoglycemia and hyperglycemia. Noninvasive biomarkers like glycated HbA1c and C-peptide aid in early diabetes detection, allowing timely intervention and potential disease prevention. Beyond glucose tracking, biosensors can detect early signs of diabetic complications such as nephropathy and neuropathy, ensuring prompt treatment[154,155]. These advancements ensure minimally invasive, reliable, and continuous monitoring, making biosensors indispensable in personalized diabetes management.

Additionally, biosensors play a crucial role in remote healthcare, improving patient accessibility and reducing the burden on healthcare facilities. Wearable and implantable biosensors facilitate real-time health tracking, ensuring continuous monitoring outside clinical settings[156]. This is particularly beneficial for elderly patients, individuals in remote areas, and those with limited access to medical care. Energy-harvesting biosensors and self-powered systems also contribute to long-term monitoring solutions without the need for frequent replacements or external power sources. As biosensing technology continues to evolve, its impact on digital health, precision medicine, and preventive care will expand. By integrating biosensors with smart wearables, telemedicine platforms, and AI-driven analytics, modern healthcare is shifting towards a more proactive, patient-centric approach. These advancements ensure continuous, accurate, and efficient monitoring, significantly improving health outcomes and redefining the future of medical diagnostics[157,158].

Comparison with traditional measurement methods

Despite the widespread utility of conventional monitoring, traditional measurement approaches are largely episodic and lack the temporal resolution required for truly continuous health assessment. Traditional continuous monitoring methods rely on manual, automated, or hybrid approaches. Manual systems require human oversight, such as log reviews and physical inspections, whereas automated systems use software tools to track performance, health, or security in real time, triggering alerts when anomalies occur. Hybrid systems combine automation with human decision-making, yet they still cannot fully capture dynamic physiological changes or subtle trends occurring between measurement intervals[159].

Despite their utility, traditional monitoring approaches have significant drawbacks. Manual systems are slow, often dependent on human response, leading to delays in issue resolution. They are also prone to human error, increasing the risk of missed alerts and inaccurate data interpretation. Additionally, these methods are labor-intensive and costly, making them difficult to scale for modern, complex environments. Intermittent reviews fail to capture issues occurring between monitoring intervals, and surveillance systems may overlook real-time threats. Even hybrid models, despite integrating automation, still rely on human decision-making, reducing efficiency[160].

In contrast, modern continuous monitoring systems, particularly those enabled by biosensor technology, offer automated high-fidelity data acquisition that mitigates many of these limitations. By continuously recording physiological signals, these platforms reduce gaps in information, minimize human error, and improve predictive accuracy. Furthermore, the integration of AI and data analytics enhances the utility of continuous monitoring by enabling adaptive anomaly detection, predictive analytics, trend forecasting, and automated decision-making. AI is revolutionizing clinical practice by enhancing disease diagnosis, optimizing treatment recommendations, and improving patient engagement. AI-powered algorithms analyze vast medical data, including imaging scans and lab results, to detect patterns and abnormalities with high accuracy, aiding in the early detection of conditions like cancer and cardiovascular diseases. In treatment, AI-driven decision support tools integrate insights from clinical trials and patient histories to suggest personalized therapies, improving drug selection and minimizing adverse effects. Additionally, AI enhances patient engagement through wearable health trackers, real-time monitoring, and virtual assistants that provide medical guidance and support remote care. Despite its benefits, AI adoption in healthcare faces challenges such as ethical concerns, data privacy issues, algorithmic bias, and the need for regulatory frameworks to ensure fairness and transparency. Human expertise remains crucial in interpreting AI-generated insights and making final medical decisions, reinforcing the collaborative role of AI in modern healthcare. By addressing these challenges, AI-driven innovations can significantly improve diagnostic accuracy, treatment outcomes, and overall patient care[161]. Unlike traditional methods that rely on static rules and manual analysis, AI-driven approaches enhance accuracy, adaptability, and efficiency. With their ability to predict and mitigate risks before they escalate, AI-based monitoring has become indispensable in dynamic and complex environments.

Real-time AI-enabled analytics

Alongside advances in wearable and implantable biosensing platforms, real-time AI-enabled analytical frameworks have become essential for transforming continuously acquired physiological and biochemical signals into clinically actionable information. The integration of AI with wearable and implantable biosensing technologies represents a transformative evolution in continuous health monitoring, enabling the conversion of raw physiological and biochemical data into clinically actionable insights[162]. However, conventional analytical techniques, while effective in detecting and quantifying specific biological analytes, often suffer from inherent limitations such as delayed processing, susceptibility to noise interference, poor real-time adaptability, and reliance on extensive sample preparation and laboratory infrastructure. Recent advancements in AI-driven acquisition techniques, particularly those leveraging ML and DL, have revolutionized biosensing by enabling adaptive signal enhancement, predictive analytics, and autonomous real-time decision-making. These AI-powered approaches not only enhance both the quantitative and qualitative accuracy of biosensing data but also enable simultaneous multi-analyte detection with superior efficiency[163,164].

In addition to data analysis, AI plays a pivotal role in system robustness and error mitigation. While AI does not directly repair hardware, ML and DL models can compensate for variability in sensor readings caused by motion, environmental fluctuations, and gradual sensor drift, improving the reliability and interpretability of real-time outputs[165] and even enabling learned compensation for hardware non-idealities in flexible electronics[166]. Edge AI architectures, which process data locally on the devices rather than relying on cloud connectivity, reduce latency, preserve user privacy, enhance real-time decision-making and allow continuous monitoring even in resource-constrained or network-limited environments[167], and support adaptive, real-time model correction strategies for wearable systems[168]. These developments echo the need for AI-driven modeling frameworks that adapt to device variability in challenging contexts[169], and motivate materials-AI co-design strategies that integrate algorithmic error mitigation with hardware physics for enhanced reliability[170]. Furthermore, AI integration supports clinical impact and personalized healthcare by enabling early detection of anomalies, predictive trend analysis, and individualized monitoring. Multimodal AI models can fuse data from multiple sensor types to improve accuracy and provide actionable feedback, extending the utility of biosensors beyond conventional laboratory settings into real-world, continuous healthcare applications[171,172]. Overall, AI-enabled analytics are transforming wearable and implantable biosensors into intelligent, adaptive platforms capable of continuous, precise, and personalized health monitoring, paving the way for next-generation point-of-care diagnostics and proactive medical interventions.

Overview of data processing and interpretation

Although the fundamental stages of signal conditioning and feature extraction are shared with conventional signal processing, their implementation in AI-integrated wearable and implantable biosensors is increasingly optimized for real-time learning, adaptive inference, and resource-constrained deployment. Advances in wearable and implantable biosensors generate vast streams of complex physiological and biochemical data that require sophisticated processing to extract meaningful information. Raw signals collected from these platforms are often noisy, irregular, and influenced by environmental factors, motion artifacts, or device limitations, which can compromise diagnostic accuracy if left uncorrected. To address these challenges, artificial intelligence, particularly ML and DL, has emerged as a critical tool for real-time signal preprocessing, feature extraction, and interpretation, enabling high-fidelity monitoring and rapid decision-making[173,174].

Raw biosensor outputs generally require systematic signal conditioning to suppress noise and improve data fidelity. This process follows a structured analytical pipeline comprising signal acquisition, preprocessing, feature extraction, pattern recognition, and final interpretation[175]. Signal preprocessing plays a critical role in ensuring reliable downstream analysis by attenuating noise and artifacts while preserving physiologically meaningful information. A wide range of established filtering strategies have been reported for biosensor signal conditioning, including high-pass filtering for baseline drift removal, Savitzky-Golay smoothing, moving-average filtering, Kalman filtering, and wavelet-based approaches such as the stationary wavelet transform. These methods aim to balance effective noise suppression with the retention of essential signal morphology, which is critical for accurate feature extraction and physiological interpretation. In complex or non-stationary signals, typical in wearable sensors monitoring ECG, EEG, or biochemical markers hybrid filtering strategies often provide superior performance by combining multiple approaches to preserve essential information while minimizing noise[176–178].

Once preprocessed, signals are transformed into meaningful representations through feature extraction, reducing dimensionality while capturing critical temporal, spectral, or spatial characteristics. Time-domain analyses, frequency-domain transformations, and advanced methods such as principal component analysis (PCA) or independent component analysis (ICA) are routinely employed[179]. These extracted features form the basis for predictive modeling, enabling real-time detection of physiological changes, disease markers, or environmental perturbations. Advanced architectures, including convolutional neural networks (CNNs), recurrent neural networks (RNNs), and transformer-based models, further enhance feature representation by learning hierarchical and temporal patterns directly from raw data, obviating the need for manual feature selection[180–184].

A particularly promising development is the integration of multi-omics approaches into AI-enabled biosensors. By concurrently monitoring multiple molecular layers, such as metabolites, proteins, and nucleic acids, these platforms can capture the dynamic interplay of physiological processes in real time[185]. Unlike traditional multi-omics studies that rely on batch processing and centralized laboratories, biosensor-based multi-omics allows continuous observation at the individual level. This capability facilitates early detection of pathological changes, personalized intervention strategies, and real-time trend analysis, bridging the gap between high-throughput molecular profiling and everyday health monitoring. ML algorithms, as they can integrate multi-layered datasets, identify complex interdependencies among biomarkers, and generate clinically actionable predictions with higher sensitivity and specificity[186]. Through these AI-enabled processing pipelines, biosensors can deliver not only accurate and continuous health assessment but also predictive insights that enable proactive interventions. Importantly, the robustness of these systems depends on the quality and diversity of training datasets, careful calibration, and the selection of appropriate ML/DL architectures, which together ensure generalizability across heterogeneous populations and environmental conditions. Unlike conventional digital signals, biosensor-acquired data are often affected by sensor-specific noise sources, including motion artifacts, electrode-skin impedance variation, and irregular sampling caused by power and bandwidth constraints. These characteristics impose strict requirements on AI models deployed in wearable and implantable platforms, favoring lightweight, low-latency edge AI architectures capable of real-time inference under limited computational and energy resources[167]. Moreover, physiological prediction models face interpretability challenges, as black-box decisions may obscure clinically relevant signal features[187], motivating the integration of explainable AI techniques for reliable health monitoring. Personalization further remains essential, as inter-subject variability and longitudinal physiological drift limit the generalizability of population-trained models.

Integration of machine learning and data analytics for continuous monitoring

While the preceding subsection emphasized AI-enabled analytical frameworks and real-time inference architectures for biosensing systems, their practical utility ultimately depends on how effectively learning algorithms are trained, validated, and deployed under continuous monitoring conditions. In this context, machine learning-driven data analytics form the operational backbone that transforms raw, high-frequency biosensor outputs into reliable physiological insights, enabling sustained, adaptive, and personalized health monitoring.

Continuous monitoring in healthcare and biomedical research refers to the real-time tracking and analysis of patients' physiological and biological signals using wearable and implantable sensors, medical devices, and advanced data analytics. To ensure high-quality healthcare, continuous monitoring of vital parameters, the ability to detect complex diseases at an early stage, and the provision of timely medical interventions are essential. However, several challenges remain, such as data accuracy and reliability, real-time data processing limitations, and ensuring patient privacy and security in remote monitoring systems. Overcoming these challenges requires advancements in sensor technology, efficient signal processing techniques, and robust machine learning models for improved real-time decision-making[172,188]. Thus, in recent years, the integration of ML and data science has been pivotal for early detection, accurate diagnosis, and personalized treatment of various diseases. Beyond inference, ML plays a critical role in model training and continuous recalibration, particularly for wearable and implantable sensors where signal drift, inter-subject variability and environmental interference are unavoidable[189]. Effective training strategies enable models to generalize across users while maintaining sensitivity to subtle physiological changes during long-term monitoring.

Recent global health crises, such as the COVID-19 outbreak, have further highlighted the critical role of AI and data analytics in the assessment of life-threatening conditions, predicting disease progression, and optimizing healthcare resources[190]. Given the immense volume and diversity of data produced through continuous health monitoring, ML algorithms are essential for identifying meaningful patterns, improving predictive accuracy, and facilitating automated decision-making to ensure timely medical interventions. Deep learning, a subset of ML, leverages neural networks with multiple layers to automatically extract intricate features from raw data[191]. It excels in analyzing complex biomedical signals, enabling precise disease prediction, anomaly detection, and personalized treatment recommendations in real-time conditions of patients, including future conditions, and critical diseases such as diabetes, cardiovascular diseases, cancer, neurological disorders, respiratory diseases, kidney failure, and so on[192].

AI plays a pivotal role in advancing continuous health monitoring systems, leveraging ML-generated data. Unlike conventional software, ML models adapt and improve by utilizing large datasets, enabling them to learn and perform tasks through a range of algorithms such as Support Vector Machines (SVM), Decision Trees, Random Forests, K-Nearest Neighbors (KNN), Naive Bayes, Neural Networks, and advanced DL frameworks like CNN and RNN[193]. However, training robust ML and DL models for self-developed wearable biosensors remains challenging due to limited labeled datasets, subject-dependent signal variability, and the difficulty of collecting long-term clinical data[194]. To address these constraints, recent studies increasingly adopt data-efficient strategies such as transfer learning, semi-supervised learning, self-supervised representation learning, and synthetic data augmentation[195]. These approaches allow models to leverage knowledge from related datasets or unlabeled signals while reducing dependence on large annotated cohorts.

As illustrated in Fig. 9, AI-enabled continuous monitoring systems generally operate through an end-to-end real-time pipeline in which multimodal biosignals are first acquired and preprocessed on-device, followed by feature extraction, model inference, and application-level decision outputs. Figure 9a highlights representative preprocessing workflows for electrophysiological and biomechanical signals, emphasizing filtering and normalization steps that suppress noise and standardize inputs prior to learning. The corresponding inference stage, summarized in Fig. 9b, relies on a range of neural network architectures, including convolutional and recurrent models selected to balance predictive accuracy with low-latency requirements in wearable systems. Model training and validation are integral to this pipeline, as illustrated in Fig. 9c, where epoch-wise learning behavior and confusion-matrix-based evaluation are used to assess convergence, generalization, and classification reliability under continuous monitoring conditions. For self-developed wearable and implantable biosensors, collecting large, well-labeled datasets remains a major bottleneck due to limited subject pools, short deployment durations, and device-specific signal characteristics. This constraint necessitates data-efficient training strategies, such as transfer learning from public physiological datasets, subject-adaptive fine-tuning, and self-supervised pretraining on unlabeled biosensor data, to achieve robust performance under real-world monitoring conditions. Beyond classification tasks, Fig. 9d, e emphasizes the importance of temporal and hybrid modeling strategies for physiological parameter estimation. In particular, LSTM-based and LSTM-ANN hybrid architectures enable robust learning of long-range temporal dependencies in biosignals, improving the stability and accuracy of vital sign prediction in real-world continuous health monitoring.

While real-time pipelines operate at the individual sensor and patient level, their continuous deployment over extended monitoring periods inevitably generates large-scale, heterogeneous datasets. As wearable and implantable biosensors transition from isolated systems to networked healthcare infrastructures, advanced big data analytics become essential for aggregating, managing, and interpreting these longitudinal data streams. In healthcare, continuous health monitoring relies on effective data utilization for accurate diagnostics and informed decision-making. Both structured and unstructured data are integrated: structured data follows a predefined schema, while unstructured data, or Big Data, lacks a fixed format, complicating storage and analysis. Big Data Analytics (BDA) overcomes these challenges by using advanced tools to extract meaningful insights, enabling predictions and trend analysis. A significant challenge is managing the vast, continuously growing streams of data from electronic medical records, wearable sensors, and social media. Additionally, the medical industry generates extensive clinical records, imaging data, genomic sequences, and health behavior data, all of which require sophisticated processing. Proper use of Big Data enhances clinical decision-making, supports disease surveillance, and strengthens public health management, transforming healthcare monitoring[196].

BDA in healthcare is categorized into four main areas: descriptive, predictive, prescriptive, and discovery analytics. Descriptive analytics converts historical and real-time data into insights for performance evaluation, patient trends, and resource optimization. Predictive analytics uses past data to identify patterns, forecast health outcomes, and model epidemics. Prescriptive analytics combines medical knowledge with data-driven insights to optimize decision-making for treatments and drug prescriptions. Discovery analytics uncovers new medical discoveries, such as drug innovations or previously unknown diseases. These analytics methods work synergistically, driving more efficient healthcare interventions[197]. The effectiveness of BDA is grounded in the Four V's of Big Data: Volume, Variety, Velocity, and Veracity. Volume refers to the massive data from EHRs, imaging, wearables, and genomics. Variety encompasses structured data (like lab results) and unstructured data (like clinical notes and social media). Velocity describes the rapid generation and processing of real-time data for continuous health monitoring. Veracity ensures data accuracy and reliability, making insights actionable. Integrating these Four V's enhances BDA's ability to support precision medicine, early disease detection, and overall healthcare efficiency[198]. In conclusion, data analytics has revolutionized healthcare by improving diagnostic accuracy, optimizing treatments, and enabling early interventions, particularly in preventive medicine. The integration of data analytics into healthcare systems enhances patient outcomes and fosters proactive, personalized care, shaping the future of healthcare delivery.

Challenges and future directions of smart wearable and implantable biosensors

Smart wearable biosensors are rapidly transforming health monitoring by combining flexible, stretchable materials, miniaturized electronics, and advanced signal processing to capture real-time physiological and biochemical information. Despite these advances, several challenges limit their long-term use. Mechanically, devices must remain highly flexible and fatigue-resistant while conforming to complex skin or organ surfaces, yet repeated movement or deformation can cause delamination or microfractures that compromise performance. Biocompatibility is equally crucial, especially for implantable sensors, as chronic immune responses or tissue irritation can affect reliability. Maintaining accurate and stable signals is also difficult due to motion artifacts, environmental changes, and interference from sweat or other biological fluids, and integrating multiple sensing modalities often involves trade-offs between sensitivity, specificity, and flexibility. Table 3 provides a comparative overview of wearable and implantable biosensors, highlighting their key characteristics, performance requirements, and emerging research directions.

Power is another key concern; wearable sensors require energy-efficient solutions or integrated harvesting systems, such as thermoelectric, piezoelectric, or biofuel-based converters, to function continuously without frequent recharging. AI-assisted biosensors hold enormous promise for predictive health insights, personalized monitoring, and early disease detection, but challenges remain, including limited high-quality datasets, algorithmic bias, overfitting, high computational demand, and lack of interpretability, all of which can hinder clinical adoption. Addressing these challenges will require explainable AI models, edge computing for real-time analysis, adaptive learning algorithms, and robust data privacy measures to build trust.

Looking forward, the next generation of wearable biosensors will likely combine self-healing, biodegradable, and highly responsive materials with micro-/nano-structured electrodes and integrated energy-harvesting platforms to enhance comfort, durability, and sensitivity. AI will play a critical role not only in analyzing data but also in guiding the design of materials and devices, optimizing their performance and sustainability. Innovations in multiplexed sensing, quantum-computing-assisted data processing, and secure data management will further enable real-time, personalized, and predictive healthcare, environmental monitoring, and food safety applications. Together, these advances are paving the way for intelligent, adaptive, and clinically reliable biosensors that can truly transform healthcare delivery and empower individuals with actionable health insights.

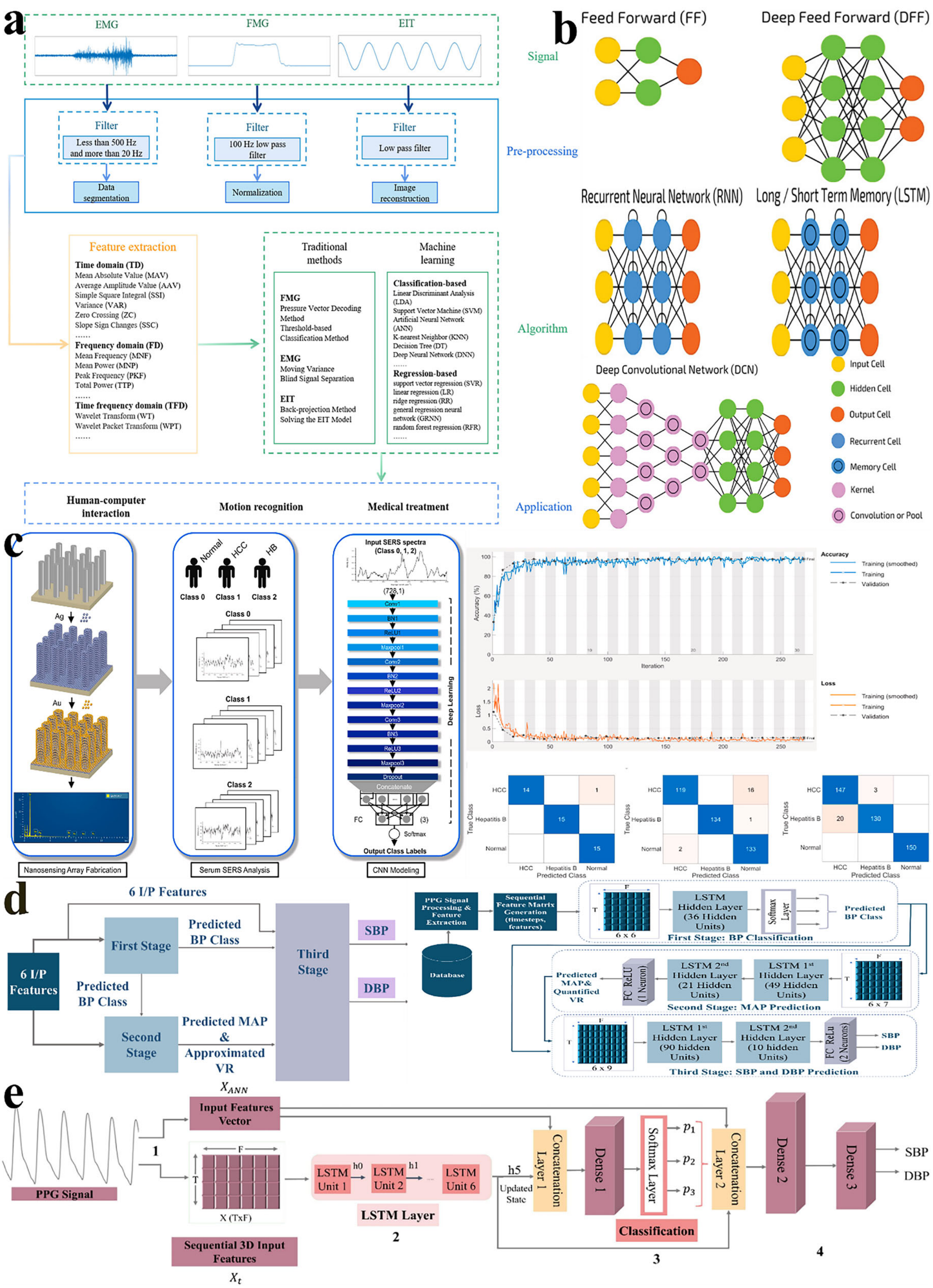

Fig. 9 | AI-enabled signal processing and learning architectures for continuous biosensor-based health monitoring. **a** Representative end-to-end data flow in AI-driven IoT biosensor networks, illustrating how raw physiological signals are acquired, preprocessed, transmitted, and analyzed to enable real-time clinical inference and remote decision-making[238]. **b** Conceptual overview of neural network architectures commonly employed in biosensing, highlighting their role in automated feature extraction, noise suppression, and pattern recognition across heterogeneous biological signals[239]. **c** Example of a CNN-based biosensing workflow, demonstrating training convergence, cross-validation, and independent testing as key elements for ensuring model robustness and generalization in disease classification tasks[240]. **d** LSTM-based multistage modeling strategy for blood pressure estimation, emphasizing the importance of temporal dependency learning in continuous cardiovascular monitoring[241]. **e** Hybrid LSTM-ANN architecture integrating sequential feature learning with nonlinear regression, illustrating how model fusion enhances predictive accuracy and stability in real-time photoplethysmography-based blood pressure monitoring[242].

Table 3 | Comparative overview of wearable and implantable biosensors outlining their key characteristics, performance requirements, and emerging research directions

Parameters	Wearable biosensors	Implantable biosensors	Emerging research needs for both wearable and implantable biosensors
Operational environment	Functions at the skin-device interface, constantly exposed to variations in humidity, temperature, and mechanical strain during motion.	Functions within complex biological environments, such as interstitial fluids, tissues, or organ surfaces with fluctuating ionic and enzymatic activities.	For wearables, ensuring stable performance under sweat, friction, temperature shifts, and repetitive deformation. For implantables, maintaining stable operation in enzyme-active and corrosive bodily fluid environments over long periods is crucial.
Interaction with Body	Noninvasive attachment on the epidermis to monitor signals such as sweat electrolytes, temperature, pulse or even more physiological signals.	Embedded beneath skin or within tissue for continuous measurement of neural, cardiac, or other metabolic signals.	Realizing long-term biointerfaces that minimize irritation or inflammation. Hybrid coatings that mimic the extracellular matrix could promote biointegration and tissue harmony.
Miniaturization and less invasive implantation	Compact and flexible designs for unobtrusive daily wear.	Requires micro- to nanoscale architectures to enable minimally invasive implantation that can be implemented without major surgery via injection or bioresorbable microneedles.	Advancing ultrathin, soft, and self-deploying architectures that reduce surgical trauma and enhance implant safety.
User / clinical comfort	Lightweight, breathable, and skin-compatible for prolonged wear.	Must minimize immune rejection, fibrosis, and inflammation.	Designing tissue-conformal, minimally invasive systems that balance comfort, function, and safety during chronic use.
Material requirement	Use of soft, breathable, and stretchable materials (PDMS, TPU, conductive textiles) enabling conformal skin adhesion and comfort.	Employ biocompatible and often biodegradable materials (PLGA, silk fibroin, collagen) for safe tissue integration.	Developing bioadaptive and self-healing materials that combine mechanical softness with stability under physiological stress.
Mechanical compliance	Must sustain repeated bending, stretching, and torsion without loss of function.	Elastic modulus should closely match soft tissues (10–100 kPa) to avoid mechanical mismatch.	Engineering materials with tunable viscoelasticity and fatigue resistance for prolonged bio-conformability.
Material degradation/ stability	Chemically stable and skin-friendly, though typically non-biodegradable.	Often designed for controlled biodegradation or long-term biostability.	Achieving programmable degradation kinetics and nontoxic byproducts to ensure safe device clearance or longevity.
Multimodal sensing	Integration of motion, temperature, and biochemical sensing on flexible platforms.	Integration of chemical, electrophysiological, and metabolic sensing at organ/tissue interfaces.	Advancing multi-analyte, spatially resolved sensors with real-time data fusion to improve diagnostic precision.
Signal type and sensitivity	Detects surface-level physiological or biochemical parameters (e.g., sweat ions, temperature, strain).	Captures deep-tissue biochemical, electrophysiological, or electrochemical signals (e.g., glucose, neural activity).	Improving multimodal sensing and cross-signal calibration to maintain accuracy under dynamic biological noise.
Signal stability	Affected by motion artifacts, sweat, pH variation, and temperature fluctuations.	Limited by biofouling, enzymatic degradation, and immune encapsulation.	Developing antifouling, self-healing, and thermally stable coatings to ensure long-term operational stability.
Proactive disease detection and intervention	Continuous tracking of external biomarkers for early symptom detection (stress, dehydration, wound infection).	Real-time monitoring of internal biochemical markers for early intervention in metabolic or neural disorders.	Integrating AI-driven predictive analytics for early disease diagnosis and adaptive therapy delivery.
Power source and data communication	Powered by rechargeable micro-batteries or energy-harvesting modules; Bluetooth or NFC for data transfer.	Wireless power transfer, inductive coupling, or biofuel-based systems for energy and communication through tissues.	Designing self-powered, miniaturized telemetry systems with low power consumption, secure, interference-free wireless communication, and bidirectional data exchange.
Durability and lifetime	Short- to mid-term use (weeks to months); easily replaceable.	Long-term (months to years) or transient operation, depending on biodegradation.	Enhancing electrochemical, mechanical, and biological stability for prolonged, maintenance-free function.
Data security and regulatory standards	Relies on wireless and cloud-based data sharing, which can risk data leakage or unauthorized access.	Handles continuous physiological data streams that directly reflect patient health and identity.	Establishing robust data encryption, privacy protocols, edge computing for on-site analysis, and transparent regulatory frameworks to ensure both privacy and clinical reliability.
Applications	Fitness tracking, wound monitoring, thermal mapping, sweat analysis, ECG/ EEG recording.	Neural sensing, cardiac and metabolic monitoring, drug delivery, and organ diagnostics.	Translating laboratory prototypes into clinically reliable systems through real-time analytics, data fusion, and AI-assisted interpretation.

Conclusion

Looking ahead, the field of smart wearable and implantable biosensors is growing rapidly, driven by multiple breakthroughs in materials, sensing technologies, and the integration of artificial intelligence. Its inherently interdisciplinary nature demands synergistic collaborations across engineering, materials science, and medicine to address the challenges discussed in previous sections. Continuous innovation in flexible and functional substrates, advanced sensing methods, sensor architectures, and AI-assisted analytics will be critical to push the boundaries of personalized and real-time healthcare monitoring.

Smart wearable and implantable biosensors are redefining healthcare by enabling continuous, personalized, and predictive monitoring of human physiology. Advances in flexible materials, self-healing substrates, and biocompatible designs have enhanced comfort and durability, yet challenges remain in achieving long-term reliability, accurate multi-analyte sensing, energy autonomy, and secure data management. AI-assisted biosensors offer powerful capabilities for data interpretation, pattern recognition, and individualized healthcare, yet overcoming limitations in datasets, algorithmic bias, computational demands, and model transparency is essential for clinical translation. Future developments will leverage the synergy of advanced materials, multiplexed sensing, edge AI, and quantum-assisted computing to develop next-generation devices that are highly adaptive, precise, and clinically robust. By integrating these innovations, smart biosensors have the potential to improve patient engagement, enable early disease detection, and expand applications beyond healthcare to include environmental monitoring, food safety, and precision medicine. This review highlights the pivotal role of combining materials science, biocompatibility, and AI technologies in shaping the future of smart biosensing and outlines a strategic roadmap for translating these advances into practical, real-world solutions.

Data availability

No datasets were generated or analysed during the current study.

Received: 17 November 2025; Accepted: 26 February 2026;

References

1. Shankar, S. et al. Nanodot zirconium trisulfide modified conducting thread: a smart substrate for fabrication of next generation biosensor. *Biosens. Bioelectron.* **242**, 115722 (2023).
2. Heikenfeld, J. et al. Wearable sensors: modalities, challenges, and prospects. *Lab Chip* **18**, 217–248 (2018).
3. Soleymani, L. & Li, F. Mechanistic challenges and advantages of biosensor miniaturization into the nanoscale. *ACS Sens.* **2**, 458–467 (2017).
4. Vo, T. S. et al. Recent trends of bioanalytical sensors with smart health monitoring systems: from materials to applications. *Adv. Healthc. Mater.* **13**, e2303923 (2024).
5. Wang, L., Lou, Z., Jiang, K. & Shen, G. Bio-multifunctional smart wearable sensors for medical devices. *Adv. Intell. Syst.* **1**, 1900040 (2019).
6. Ha, M., Lim, S. & Ko, H. Wearable and flexible sensors for user-interactive health-monitoring devices. *J. Mater. Chem. B* **6**, 4043–4064 (2018).
7. Song, Y., Mukasa, D., Zhang, H. & Gao, W. Self-powered wearable biosensors. *Acc. Mater. Res.* **2**, 184–197 (2021).
8. Hassan, M. et al. Significance of flexible substrates for wearable and implantable devices: recent advances and perspectives. *Adv. Mater. Technol.* **7**, 2100773 (2021).
9. Shan, G., Li, X. & Huang, W. AI-enabled wearable and flexible electronics for assessing full personal exposures. *Innovation* **1**, 100031 (2020).
10. Gideon, O., Samuel, H. S. & Okino, I. A. Biocompatible materials for next-generation biosensors. *Discov. Chem.* **1**, 34 (2024).
11. Lu, T. et al. Biocompatible and long-term monitoring strategies of wearable, ingestible and implantable biosensors: reform the next generation healthcare. *Sensors* **23**, 2991 (2023).
12. Zhang, H. et al. Graphene-enabled wearable sensors for healthcare monitoring. *Biosens. Bioelectron.* **197**, 113777 (2022).
13. Zhu, P., Peng, H. & Rwei, A. Y. Flexible, wearable biosensors for digital health. *Med. Nov. Technol. Devices* **14**, 100118 (2022).
14. Yin, Z., Clark, K. M. & Ray, T. R. Emerging additive manufacturing methods for wearable sensors: opportunities to expand access to personalized health monitoring. *Adv. Sens. Res.* **3**, 2300137 (2023).
15. Wang, Y. et al. Skin bioelectronics towards long-term, continuous health monitoring. *Chem. Soc. Rev.* **51**, 3759–3793 (2022).
16. Vo, D. K. & Trinh, K. T. L. Advances in wearable biosensors for healthcare: current trends, applications, and future perspectives. *Biosensors* **14**, 560 (2024).
17. Ren, M. et al. Highly strain-sensitive and stretchable multilayer conductive composite based on aligned thermoplastic polyurethane fibrous mat for human motion monitoring. *Compos. Commun.* **46**, 101840 (2024).
18. Chen, S. et al. Transforming healthcare: intelligent wearable sensors empowered by smart materials and artificial intelligence. *Adv. Mater.* **37**, e2500412 (2025).
19. Shajari, S., Kuruvinashetti, K., Komeili, A. & Sundararaj, U. The emergence of AI-based wearable sensors for digital health technology: a review. *Sensors* **23**, 9498 (2023).
20. Gao, W., Ota, H., Kiriya, D., Takei, K. & Javey, A. Flexible electronics toward wearable sensing. *Acc. Chem. Res.* **52**, 523–533 (2019).
21. Wei, Y. et al. A biosensor material with robust mechanical properties, fatigue-resistance, biocompatibility, biodegradability, and anti-freezing capabilities. *J. Mater. Chem. A* **10**, 8491–8500 (2022).
22. Chitrakar, C., Hedrick, E., Adegoke, L. & Ecker, M. Flexible and stretchable bioelectronics. *Materials* **15**, 1664 (2022).
23. Wang, S., Chinnasamy, T., Lifson, M. A., Inci, F. & Demirci, U. Flexible substrate-based devices for point-of-care diagnostics. *Trends Biotechnol.* **34**, 909–921 (2016).
24. Kenry, Yeo, J. C. & Lim, C. T. Emerging flexible and wearable physical sensing platforms for healthcare and biomedical applications. *Microsyst. Nanoeng.* **2**, 16043 (2016).
25. Bocchetta, P. et al. Soft materials for wearable/flexible electrochemical energy conversion, storage, and biosensor devices. *Materials* **13**, 2733 (2020).
26. Yang, Y. et al. Ultrafine graphene nanomesh with large on/off ratio for high-performance flexible biosensors. *Adv. Funct. Mater.* **27**, 1604096 (2016).
27. Shetti, N. P. et al. Skin-patchable electrodes for biosensor applications: a review. *ACS Biomater. Sci. Eng.* **6**, 1823–1835 (2020).
28. Saeidi, M. et al. Electrochemical wearable biosensors and bioelectronic devices based on hydrogels: mechanical properties and electrochemical behavior. *Biosensors* **13**, 823 (2023).
29. Kim, S. et al. An intrinsically stretchable multi-biochemical sensor for sweat analysis using photo-patternable ecoflex. *npj Flex Electron.* **7**, 33 (2023).
30. Maiya, D., Patel, T. & Pandya, A. In *Progress in Molecular Biology and Translational Science* (eds K. Mahato & A. Pandya) Ch. 5 (Academic Press, 2025).
31. Oh, B. et al. Ultra-soft and highly stretchable tissue-adhesive hydrogel based multifunctional implantable sensor for monitoring of overactive bladder. *Biosens. Bioelectron.* **225**, 115060 (2023).
32. Lee, S. H. et al. Intrinsically soft implantable electronics for long-term biosensing applications. *Adv. Sens. Res.* **4**, 2500002 (2025).
33. Souri, H. et al. Wearable and stretchable strain sensors: materials, sensing mechanisms, and applications. *Adv. Intell. Syst.* **2**, 2000039 (2020).
34. Salim, A. & Lim, S. Recent advances in noninvasive flexible and wearable wireless biosensors. *Biosens. Bioelectron.* **141**, 111422 (2019).
35. Vedadghavami, A. et al. Manufacturing of hydrogel biomaterials with controlled mechanical properties for tissue engineering applications. *Acta Biomater.* **62**, 42–63 (2017).
36. Liu, Q. et al. Bio-based elastomers: design, properties, and biomedical applications.*Adv. Mater.* **37**, e2417193 (2025).
37. Prasadh, S. & Wong, R. C. W. Unraveling the mechanical strength of biomaterials used as a bone scaffold in oral and maxillofacial defects. *Oral Sci. Int.* **15**, 48–55 (2018).
38. Niinomi, M. & Nakai, M. Titanium-based biomaterials for preventing stress shielding between implant devices and bone. *Int. J. Biomater.* **2011**, 836587 (2011).
39. Ge, Z., Yang, F., Goh, J. C., Ramakrishna, S. & Lee, E. H. Biomaterials and scaffolds for ligament tissue engineering. *J. Biomed. Mater. Res. A* **77**, 639–652 (2006).

40. Tan, E. L. et al. Implantable biosensors for real-time strain and pressure monitoring. *Sensors* **8**, 6396–6406 (2008).
41. Wang, L. & Beebe, D. J. Characterization of a silicon-based shear-force sensor on human subjects. *IEEE Trans. Biomed. Eng.* **49**, 1340–1347 (2002).
42. Wu, S. J. & Zhao, X. Bioadhesive technology platforms. *Chem. Rev.* **123**, 14084–14118 (2023).
43. Wong, S. H. D. et al. Smart skin-adhesive patches: from design to biomedical applications. *Adv. Funct. Mater.* **33**, 2213560 (2023).
44. Liu, X. et al. Bioinspired, microstructured silk fibroin adhesives for flexible skin sensors. *ACS Appl. Mater. Interfaces* **12**, 5601–5609 (2020).
45. Liu, H. et al. Application of biodegradable and biocompatible nanocomposites in electronics: current status and future directions. *Nanomaterials* **9**, 950 (2019).
46. Xu, M., Obodo, D. & Yadavalli, V. K. The design, fabrication, and applications of flexible biosensing devices. *Biosens. Bioelectron.* **124-125**, 96–114 (2019).
47. Kim, J. et al. Ultrathin soft wearable sensor materials and structures: a review of current trends and prospectives. *ACS Appl. Mater. Interfaces* **17**, 59994–60027 (2025).
48. Lee, S. et al. An ultrathin conformable vibration-responsive electronic skin for quantitative vocal recognition. *Nat. Commun.* **10**, 2468 (2019).
49. Kwon, S. et al. Skin-conformal, soft material-enabled bioelectronic system with minimized motion artifacts for reliable health and performance monitoring of athletes. *Biosens. Bioelectron.* **151**, 111981 (2020).
50. Reis Carneiro, M., Tavakoli, M. & Majidi, C. Soft skin-interfacing electrodes for wearable bioelectronics. *Matter* **8**, 102409 (2025).
51. Wang, R. et al. Wet chemically produced nanomaterials for soft wearable biosensors. *Nanoscale Horiz.* **10**, 1517–1541 (2025).
52. Gao, W. et al. Fully integrated wearable sensor arrays for multiplexed in situ perspiration analysis. *Nature* **529**, 509–514 (2016).
53. Ershad, F. et al. Ultra-conformal drawn-on-skin electronics for multifunctional motion artifact-free sensing and point-of-care treatment. *Nat. Commun.* **11**, 3823 (2020).
54. Jung, H. et al. Hydrogel-elastomer-based conductive nanomembranes for soft bioelectronics. *Nat. Nanotechnol.* **20**, 1822–1830 (2025).
55. Park, J. et al. Conformal fixation strategies and bioadhesives for soft bioelectronics. *Adv. Funct. Mater.* **34**, 2313728 (2024).
56. Yan, Z. et al. Highly stretchable van der Waals thin films for adaptable and breathable electronic membranes. *Science* **375**, 852–859 (2022).
57. Jang, J. et al. Reconfigurable assembly of self-healing stretchable transistors and circuits for integrated systems. *Nat. Electron.* **8**, 474–484 (2025).
58. Yang, X. et al. Role of chemistry in nature-inspired skin adhesives. *Chem. Sci.* **16**, 10665–10690 (2025).
59. Liu, S., Rao, Y., Jang, H., Tan, P. & Lu, N. Strategies for body-conformable electronics. *Matter* **5**, 1104–1136 (2022).
60. Seong, D. et al. Sticky and strain-gradient artificial epineurium for sutureless nerve repair in rodents and nonhuman primates. *Adv. Mater.* **36**, e2307810 (2024).
61. Gong, S., Lu, Y., Yin, J., Levin, A. & Cheng, W. Materials-driven soft wearable bioelectronics for connected healthcare. *Chem. Rev.* **124**, 455–553 (2024).
62. Lee, S. et al. A shape-morphing cortex-adhesive sensor for closed-loop transcranial ultrasound neurostimulation. *Nat. Electron.* **7**, 800–814 (2024).
63. Wang, L., Wang, J., Fan, C., Xu, T. & Zhang, X. Skin-like hydrogel-elastomer based electrochemical device for comfortable wearable biofluid monitoring. *Chem. Eng. J.* **455**, 140609 (2023).
64. Lin, Y., Qiu, W. & Kong, D. Stretchable and body-conformable physical sensors for emerging wearable technology. *Sens. Diagn.* **3**, 1442–1455 (2024).
65. Kim, S., Shin, Y., Han, J., Kim, H. J. & Sunwoo, S. H. Introductory review of soft implantable bioelectronics using conductive and functional hydrogels and hydrogel nanocomposites. *Gels* **10**, 614 (2024).
66. Yuk, H., Lu, B. & Zhao, X. Hydrogel bioelectronics. *Chem. Soc. Rev.* **48**, 1642–1667 (2019).
67. Li, Y., Li, N., De Oliveira, N. & Wang, S. Implantable bioelectronics toward long-term stability and sustainability. *Matter* **4**, 1125–1141 (2021).
68. Jang, J., Jin, S., Yoon, S., Shin, M. & Son, D. Materials strategy and device fabrication for stable closed-loop bioelectronics. *npj Biosensing* **2**, 27 (2025).
69. Koo, J. H., Song, J.-K., Kim, D.-H. & Son, D. Soft implantable bioelectronics. *ACS Mater. Lett.* **3**, 1528–1540 (2021).
70. Choi, H. et al. Adhesive bioelectronics for sutureless epicardial interfacing. *Nat. Electron.* **6**, 779–789 (2023).
71. Chen, B. et al. Long-term implantable flexible neural interfaces for electrophysiological monitoring. *J. Mater. Chem. C* **13**, 5951–5980 (2025).
72. Sun, C., Cheng, Z., Abu-Halimah, J. & Tian, B. Perspectives on tissue-like bioelectronics for neural modulation. *iScience* **26**, 106715 (2023).
73. Niemiec, M. & Kim, K. Lifetime engineering of bioelectronic implants with mechanically reliable thin film encapsulations. *Prog. Biomed. Eng.* **6**, 012001 (2023).
74. Trung, T. Q. & Lee, N. E. Flexible and stretchable physical sensor integrated platforms for wearable human-activity monitoring and personal healthcare. *Adv. Mater.* **28**, 4338–4372 (2016).
75. Bao, G. & Suresh, S. Cell and molecular mechanics of biological materials. *Nat. Mater.* **2**, 715–725 (2003).
76. Egan, P., Sinko, R., LeDuc, P. R. & Keten, S. The role of mechanics in biological and bio-inspired systems. *Nat. Commun.* **6**, 7418 (2015).
77. Bruck, H., Evans, J. & Peterson, M. The role of mechanics in biological and biologically inspired materials. *Exp. Mech.* **42**, 361–371 (2002).
78. Zhai, Q. & Cheng, W. Soft and stretchable electrochemical biosensors. *Mater. Today Nano* **7**, 100041 (2019).
79. Wang, X., Liu, Z. & Zhang, T. Flexible sensing electronics for wearable/attachable health monitoring. *Small* **13**, 1602790 (2017).
80. Qiao, L., Benzigar, M. R., Subramony, J. A., Lovell, N. H. & Liu, G. Advances in sweat wearables: sample extraction, real-time biosensing, and flexible platforms. *ACS Appl. Mater. Interfaces* **12**, 34337–34361 (2020).
81. Deo, K. A. et al. Nanoengineered ink for designing 3D printable flexible bioelectronics. *ACS Nano* **16**, 8798–8811 (2022).
82. Su, X. et al. Integrated wearable sensors with bending/stretching selectivity and extremely enhanced sensitivity derived from agarose-based ionic conductor and its 3D-shaping. *Chem. Eng. J.* **389**, 124503 (2020).
83. Wang, C., Yokota, T. & Someya, T. Natural biopolymer-based biocompatible conductors for stretchable bioelectronics. *Chem. Rev.* **121**, 2109–2146 (2021).
84. Choi, S., Lee, H., Ghaffari, R., Hyeon, T. & Kim, D. H. Recent advances in flexible and stretchable bio-electronic devices integrated with nanomaterials. *Adv. Mater.* **28**, 4203–4218 (2016).
85. Ling, H., Liu, S., Zheng, Z. & Yan, F. Organic flexible electronics. *Small Methods* **2**, 1800070 (2018).
86. Choi, C. K., English, A. E., Jun, S.-I., Kihm, K. D. & Rack, P. D. An endothelial cell compatible biosensor fabricated using optically thin indium tin oxide silicon nitride electrodes. *Biosens. Bioelectron.* **22**, 2585–2590 (2007).

87. Miao, J. & Fan, T. Flexible and stretchable transparent conductive graphene-based electrodes for emerging wearable electronics. *Carbon* **202**, 495–527 (2023).
88. Brennan, D. & Galvin, P. Flexible substrate sensors for multiplex biomarker monitoring. *MRS Commun.* **8**, 627–641 (2018).
89. Windmiller, J. R. & Wang, J. Wearable electrochemical sensors and biosensors: a review. *Electroanalysis* **25**, 29–46 (2012).
90. Ashok, A. et al. Flexible nanoarchitectonics for biosensing and physiological monitoring applications. *Small* **19**, 2204946 (2023).
91. Li, Y., Veronica, A., Ma, J. & Nyein, H. Y. Y. Materials, structure, and interface of stretchable interconnects for wearable bioelectronics. *Adv. Mater* **37**, e2408456 (2024).
92. Park, B., Jeong, C., Ok, J. & Kim, T. -i. Materials and structural designs toward motion artifact-free bioelectronics. *Chem. Rev.* **124**, 6148–6197 (2024).
93. Wu, H., Huang, Y., Xu, F., Duan, Y. & Yin, Z. Energy harvesters for wearable and stretchable electronics: from flexibility to stretchability. *Adv. Mater.* **28**, 9881–9919 (2016).
94. Yang, J. C. et al. Geometrically engineered rigid island array for stretchable electronics capable of withstanding various deformation modes. *Sci. Adv.* **8**, eabn3863 (2022).
95. Wang, W. et al. Strain-insensitive intrinsically stretchable transistors and circuits. *Nat. Electron.* **4**, 143–150 (2021).
96. Brooks, A. K., Chakravarty, S., Ali, M. & Yadavalli, V. K. Kirigami-inspired biodesign for applications in healthcare. *Adv. Mater.* **34**, 2109550 (2022).
97. Xu, R. et al. Kirigami-inspired, highly stretchable micro-supercapacitor patches fabricated by laser conversion and cutting. *Microsyst. Nanoeng.* **4**, 36 (2018).
98. Xiao, Y. et al. High-adhesive flexible electrodes and their manufacture: a review. *Micromachines* **12**, 1505 (2021).
99. Zhang, Y. In *Stretchable Bioelectronics for Medical Devices and Systems* (eds Kim, D. -H., Rogers, J. A. & Ghaffari, R.) Ch. 3 (Springer International Publishing, 2016).
100. Chen, Y. et al. Flexible inorganic bioelectronics. *npj Flex Electron.* **4**, 2 (2020).
101. Jiao, Y. et al. A multifunctional bioelectronic device with switchable rigidity and reconfigurable shapes for comprehensive diagnosis. *Adv. Electron. Mater.* **9**, 2201343 (2023).
102. Jin, S., Choi, H., Son, D. & Shin, M. An injectable conductive hydrogel for closed-loop and robot-assisted rehabilitation via stretchable patch-type electrodes. *Nat. Protoc.* **21**, 238–262 (2026).
103. Choi, C., Lee, Y., Cho, K. W., Koo, J. H. & Kim, D. H. Wearable and implantable soft bioelectronics using two-dimensional materials. *Acc. Chem. Res.* **52**, 73–81 (2019).
104. Park, J., Lee, Y., Kim, T. Y., Hwang, S. & Seo, J. Functional bioelectronic materials for long-term biocompatibility and functionality. *ACS Appl. Electron. Mater.* **4**, 1449–1468 (2022).
105. Liu, G. et al. Biocompatible material-based flexible biosensors: from materials design to wearable/implantable devices and integrated sensing systems. *Small* **19**, 2207879 (2023).
106. Li, S., Cong, Y. & Fu, J. Tissue adhesive hydrogel bioelectronics. *J. Mater. Chem. B* **9**, 4423–4443 (2021).
107. Xiao, F. et al. Growth of metal–metal oxide nanostructures on freestanding graphene paper for flexible biosensors. *Adv. Funct. Mater.* **22**, 2487–2494 (2012).
108. Farahmandpour, M. & Kordrostami, Z. Wearable MXene-enhanced organic bio-FET paper patch for glucose detection in sweat with pH and temperature calibration. *Sci. Rep.* **15**, 16219 (2025).
109. Choi, C., Qaiser, N. & Hwang, B. Mechanically pressed polymer-matrix composites with 3d structured filler networks for electromagnetic interference shielding application. Facta Universitatis, Series. *Mech. Eng* **22**, 601–14 (2024).
110. Ilgamov, M.A., Aitbaeva, A.A., Pavlov, I.S. and Dmitriev, S.V. Carbon nanotube under pulsed pressure. Facta Universitatis, Series: *Mech. Eng.* **22**, 275-92 (2024).
111. Mathew, M., Radhakrishnan, S., Vaidyanathan, A., Chakraborty, B. & Rout, C. S. Flexible and wearable electrochemical biosensors based on two-dimensional materials: Recent developments. *Anal. Bioanal. Chem.* **413**, 727–762 (2021).
112. Eivazzadeh-Keihan, R. et al. Applications of carbon-based conductive nanomaterials in biosensors. *Chem. Eng. J.* **442**, 136183 (2022).
113. Shvedova, A. A., Pietroiusti, A., Fadeel, B. & Kagan, V. E. Mechanisms of carbon nanotube-induced toxicity: focus on oxidative stress. *Toxicol. Appl. Pharmacol.* **261**, 121–133 (2012).
114. Arsiwala, A. M., Raval, A. J. & Patravale, V. B. Nanocoatings on implantable medical devices. *Pharm. Pat. Anal.* **2**, 499–512 (2013).
115. Coronel-Meneses, D., Sanchez-Trasvina, C., Ratera, I. & Mayolo-Deloisa, K. Strategies for surface coatings of implantable cardiac medical devices. *Front. Bioeng. Biotechnol.* **11**, 1173260 (2023).
116. Barfidokht, A. & Gooding, J. J. Approaches toward allowing electroanalytical devices to be used in biological fluids. *Electroanalysis* **26**, 1182–1196 (2014).
117. Jiang, C. et al. Aryldiazonium salt derived mixed organic layers: from surface chemistry to their applications. *J. Electroanal. Chem.* **785**, 265–278 (2017).
118. Woo, J. et al. Functional ferrocene polymer multilayer coatings for implantable medical devices: Biocompatible, antifouling, and ROS-sensitive controlled release of therapeutic drugs. *Acta Biomater.* **125**, 242–252 (2021).
119. Park, G. et al. Immunologic and tissue biocompatibility of flexible/stretchable electronics and optoelectronics. *Adv. Healthcare Mater.* **3**, 515–525 (2014).
120. Oh, S. et al. Softening implantable bioelectronics: Material designs, applications, and future directions. *Biosens. Bioelectron.* **258**, 116328 (2024).
121. Luo, Y. et al. Technology roadmap for flexible sensors. *ACS Nano* **17**, 5211–5295 (2023).
122. Kim, H. et al. Advances and perspectives in fiber-based electronic devices for next-generation soft systems. *npj Flex Electron.* **9**, 84 (2025).
123. Lim, M. S. & Jeong, E. G. Developments and future directions in stretchable display technology: materials, architectures, and applications. *Micromachines* **16**, 772 (2025).
124. Ji, S. & Chen, X. Enhancing the interfacial binding strength between modular stretchable electronic components. *Natl. Sci. Rev.* **10**, nwac172 (2023).
125. Lin, P., Lin, C. W., Mansour, R. & Gu, F. Improving biocompatibility by surface modification techniques on implantable bioelectronics. *Biosens. Bioelectron.* **47**, 451–460 (2013).
126. Rao, L. T., Mandal, C. K. & Patolsky, F. Body biofluids for minimally-invasive diagnostics: insights, challenges, emerging technologies, and clinical potential.*Adv. Healthc. Mater* **15**, e03096 (2025).
127. Ha, H., Müller, S., Baumann, R.P. & Hwang, B. Peakforce quantitative nanomechanical mapping for surface energy characterization on the nanoscale: A mini-review. Facta Universitatis, Series: *Mech. Eng.* **2**, 001-12 (2024).
128. Ha, H., Mueller, S., Guriyanova, S. & Hwang, B. Surface energy characterization of a single microsphere particle using peakforce quantitative nanomechanical mapping mode of atomic force microscope. Facta Universitatis, Series: *Mech. Eng.* **23**, 171-81 (2025).
129. Xu, Y. et al. Porous liquid metal–elastomer composites with high leakage resistance and antimicrobial property for skin-interfaced bioelectronics. *Sci. Adv.* **9**, eadf0575 (2023).
130. Ming, D. K. et al. Continuous physiological monitoring using wearable technology to inform individual management of infectious

diseases, public health and outbreak responses. *Int. J. Infect. Dis.* **96**, 648–654 (2020).
131. Mohankumar, P., Ajayan, J., Mohanraj, T. & Yasodharan, R. Recent developments in biosensors for healthcare and biomedical applications: a review. *Measurement* **167**, 108293 (2021).
132. Kim, J., Campbell, A. S., de Ávila, B. E.-F. & Wang, J. Wearable biosensors for healthcare monitoring. *Nat. Biotechnol.* **37**, 389–406 (2019).
133. Sheng, L., Teo, S. & Liu, J. Liquid-metal-painted stretchable capacitor sensors for wearable healthcare electronics. *J. Med. Biol. Eng.* **36**, 265–272 (2016).
134. Carreiro, S. et al. Wearable biosensors to detect physiologic change during opioid use. *J. Med. Toxicol.* **12**, 255–262 (2016).
135. Kweon, O. Y., Lee, S. J. & Oh, J. H. Wearable high-performance pressure sensors based on three-dimensional electrospun conductive nanofibers. *NPG Asia Mater* **10**, 540–551 (2018).
136. Hallfors, N. et al. Graphene oxide: nylon ECG sensors for wearable IoT healthcare-nanomaterial and SoC interface. *Analog Integr. Circ. Signal Process* **96**, 253–260 (2018).
137. Sekine, Y. et al. A fluorometric skin-interfaced microfluidic device and smartphone imaging module for in situ quantitative analysis of sweat chemistry. *Lab Chip* **18**, 2178–2186 (2018).
138. Soni, A. & Jha, S. K. A paper strip based non-invasive glucose biosensor for salivary analysis. *Biosens. Bioelectron.* **67**, 763–768 (2015).
139. Khan, A. A. & Kim, J.-H. Recent advances in materials and manufacturing of implantable devices for continuous health monitoring. *Biosens. Bioelectron.* **261**, 116461 (2024).
140. Verma, D. et al. Internet of things (IoT) in nano-integrated wearable biosensor devices for healthcare applications. *Biosens. Bioelectron. X* **11**, 100153 (2022).
141. Zhang, J. et al. Wearable biosensors for human fatigue diagnosis: a review. *Bioeng. Transl. Med.* **8**, e10318 (2023).
142. Kim, J. J., Stafford, G. R., Beauchamp, C. & Kim, S. A. Development of a dental implantable temperature sensor for real-time diagnosis of infectious disease. *Sensors* **20**, 3953 (2020).
143. Kim, S., Malik, J., Seo, J. M., Cho, Y. M. & Bien, F. Subcutaneously implantable electromagnetic biosensor system for continuous glucose monitoring. *Sci. Rep.* **12**, 17395 (2022).
144. Li, Y.-T., Yang, L.-Y., Hsu, W.-T. & Peng, C.-W. Designing and implementing an implantable wireless micromanometer system for real-time bladder pressure monitoring: a preliminary study. *Sensors* **20**, 4610 (2020).
145. Ma, Y. et al. Self-powered, one-stop, and multifunctional implantable triboelectric active sensor for real-time biomedical monitoring. *Nano Lett.* **16**, 6042–6051 (2016).
146. De la Paz, E. et al. A self-powered ingestible wireless biosensing system for real-time in situ monitoring of gastrointestinal tract metabolites. *Nat. Commun.* **13**, 7405 (2022).
147. Kalashnikov, N., Barralet, J. & Vorstenbosch, J. Implantable medical devices, biomaterials, and the foreign body response: a surgical perspective. *J. Biomed. Mater. Res. A* **113**, e37983 (2025).
148. Wai, S. et al. Zwitterionic hydrogel designs for conducting polymers enable bioelectronics with suppressed foreign body responses. bioRxiv, 2025.2010.2031.683260 (2025).
149. Tan, R. P. et al. Bioactivation of encapsulation membranes reduces fibrosis and enhances cell survival. *ACS Appl. Mater. Interfaces* **12**, 56908–56923 (2020).
150. Wang, H., Wu, Y., Cui, C., Yang, J. & Liu, W. Antifouling super water absorbent supramolecular polymer hydrogel as an artificial vitreous body. *Adv. Sci.* **5**, 1800711 (2018).
151. Wu, Y., Tilley, R. D. & Gooding, J. J. Challenges and solutions in developing ultrasensitive biosensors. *J. Am. Chem. Soc.* **141**, 1162–1170 (2019).
152. Qureshi, A., Gurbuz, Y. & Niazi, J. H. Biosensors for cardiac biomarkers detection: a review. *Sens. Actuator B Chem.* **171-172**, 62–76 (2012).
153. Tang, L., Yang, J., Wang, Y. & Deng, R. Recent advances in cardiovascular disease biosensors and monitoring technologies. *ACS Sens.* **8**, 956–973 (2023).
154. Balkrishna, A. et al. Impact of biosensors and biomarkers in diabetes care: a review. *Biomed. Mater. Devices* https://doi.org/10.1007/s44174-024-00230-z (2024).
155. Purohit, B., Kumar, A., Mahato, K. & Chandra, P. In *Miniaturized Biosensing Devices: Fabrication and Applications* (Springer, 2022).
156. Song, L., Chen, J., Xu, B. B. & Huang, Y. Flexible plasmonic biosensors for healthcare monitoring: progress and prospects. *ACS Nano* **15**, 18822–18847 (2021).
157. Talal, M. et al. Smart home-based IoT for real-time and secure remote health monitoring of triage and priority system using body sensors: multi-driven systematic review. *J. Med. Syst.* **43**, 42 (2019).
158. Soh, P. J., Vandenbosch, G. A., Mercuri, M. & Schreurs, D. M.-P. Wearable wireless health monitoring: current developments, challenges, and future trends. *IEEE Microw. Mag.* **16**, 55–70 (2015).
159. Baig, M. M. & Gholamhosseini, H. Smart health monitoring systems: an overview of design and modeling. *J. Med. Syst.* **37**, 9898 (2013).
160. Comito, C., Falcone, D. & Forestiero, A. In *2020 IEEE International Conference on Bioinformatics and Biomedicine* 2577–2584 (2020).
161. Alowais, S. A. et al. Revolutionizing healthcare: the role of artificial intelligence in clinical practice. *BMC Med. Educ.* **23**, 689 (2023).
162. Subburaj, S., Liu, C. & Xu, T. Emerging trends in AI-integrated optical biosensors for point-of-care diagnostics: current status and future prospects. *Chem. Commun.* **61**, 18464–18489 (2025).
163. Zhou, Z., Xu, T. & Zhang, X. Empowerment of AI algorithms in biochemical sensors.*Trends Anal. Chem.* **173**, 117613 (2024).
164. Ding, Z., Fang, W., Zhang, J., Fang, C. & Sun, Y. in *Progress in Molecular Biology and Translational Sci* Vol. 216 (eds K. Mahato & A. Pandya) (Academic Press, 2025).
165. Chamon, C.. Sarkar, A. & Abbott, L., Noise-Driven AI Sensors: Secure Healthcare Monitoring with PUFs, 2025 IEEE 68thInternational Midwest Symposium on Circuits and Systems (MWSCAS)135-139 (Lansing/E. Lansing, MI, USA, 2025).
166. Song, J.-K. et al. Stretchable colour-sensitive quantum dot nanocomposites for shape-tunable multiplexed phototransistor arrays. *Nat. Nanotechnol.* **17**, 849–856 (2022).
167. Huang, G., Chen, X. & Liao, C. AI-driven wearable bioelectronics in digital healthcare. *Biosensors* **15**, 410 (2025).
168. Kim, Y. et al. Performance-recoverable closed-loop neuroprosthetic system. *Adv. Mater.* **37**, e2503413 (2025).
169. Zhang, W., Zhang, L., Liao, Y. & Cheng, H. Conformal manufacturing of soft deformable sensors on the curved surface. *Int. J. Extreme Manuf* **3**, 042001 (2021).
170. Yoon, J. et al. Intrinsically stretchable sensory-neuromorphic system for sign language translation.*Curr. Opin. Solid State Mater. Sci* **29**, 101142 (2024).
171. Hagos, D. H., Aryal, S. K., Ymele-Leki, P. & Burge, L. L. AI-driven multimodal colorimetric analytics for biomedical and behavioral health diagnostics. *Comput. Struct. Biotechnol. J.* **27**, 2219–2232 (2025).
172. Kovur, P., Kovur, K. M., Rayat, D. Y. & Wishart, D. S. POC sensor systems and artificial intelligence-Where we are now and where we are going?. *Biosensors* **15**, 589 (2025).
173. Paganelli, A. I. et al. Real-time data analysis in health monitoring systems: a comprehensive systematic literature review. *J. Biomed. Inform.* **127**, 104009 (2022).
174. Jamali, S. S., Wu, Y., Homborg, A. M., Lemay, S. G. & Gooding, J. J. Interpretation of stochastic electrochemical data. *Curr. Opin. Electrochem.* **46**, 101505 (2024).
175. Wen, C., Dematties, D. & Zhang, S. L. A guide to signal processing algorithms for nanopore sensors. *ACS Sens.* **6**, 3536–3555 (2021).

176. Adam, N., Val'ko, D., Balogh, Z., Mados, B. & Hurtuk, J. Comparative evaluation of filtration techniques for ECG signal denoising with emphasis on stationary wavelet transform. *Sci. Rep.* **15**, 42514 (2025).
177. Chatterjee, S., Thakur, R. S., Yadav, R. N., Gupta, L. & Raghuvanshi, D. K. Review of noise removal techniques in ECG signals. *IET Signal. Process.* **14**, 569–590 (2020).
178. Jayaraman Rajendiran, D. K., Ganesh Babu, C., Priyadharsini, K. & Karthi, S. P. Certain investigation on hybrid neural network method for classification of ECG signal with the suitable a FIR filter. *Sci. Rep.* **14**, 15087 (2024).
179. Setyorini, S., Zaeni, I. A. E. & Elmunsyah, H. A hybrid machine learning approach utilizing PCA and ICA features for stress classification. *JOIV Int. J. Inform. Visualization* **9**, 1226–1234 (2025).
180. Gupta, V., Mittal, M., Mittal, V. & Saxena, N. K. A critical review of feature extraction techniques for ECG signal analysis. *J. Inst. Eng. India Ser. B* **102**, 1049–1060 (2021).
181. Zhang, C. et al. Vibration feature extraction using signal processing techniques for structural health monitoring: a review. *Mech. Syst. Signal Process.* **177**, 109175 (2022).
182. Al-Fahoum, A. S. & Al-Fraihat, A. A. Methods of EEG signal features extraction using linear analysis in frequency and time-frequency domains. *ISRN Neurosci.* **2014**, 730218 (2014).
183. Behbahani, S., Ahmadieh, H. & Rajan, S. Feature extraction methods for electroretinogram signal analysis: a review. *IEEE Access* **9**, 116879–116897 (2021).
184. Zhang, Y., Hu, Y., Jiang, N. & Yetisen, A. K. Wearable artificial intelligence biosensor networks. *Biosens. Bioelectron.* **219**, 114825 (2023).
185. Han, S. et al. Multi-omics analytics and biosensors to enable digital twin platforms for P4 medicine. *Device* **0**, 101017 (2025).
186. Theodorakis, N. et al. Integrating machine learning with multi-omics technologies in geroscience: Towards personalized medicine. *J. Pers. Med.* **14**, 931 (2024).
187. Moss, L., Corsar, D., Shaw, M., Piper, I. & Hawthorne, C. Demystifying the black box: the importance of interpretability of predictive models in neurocritical care. *Neurocrit. Care* **37**, 185–191 (2022).
188. Nosonovsky, M. & Aglikov, AS. Triboinformatics: Machine learning methods for frictional instabilities. Facta Universitatis, Series: *Mech. Eng* **22**, 423–33 (2024).
189. Jeong, I. et al. Machine learning in biosignal analysis from wearable devices. *Mater. Horiz.* **12**, 6587–6621 (2025).
190. Javaid, M., Haleem, A., Pratap Singh, R., Suman, R. & Rab, S. Significance of machine learning in healthcare: features, pillars and applications. *Int. J. Intell. Netw.* **3**, 58–73 (2022).
191. Wu, W. et al. Chemometrics-based signal processing methods for biosensors in health and environment: a review. *Electroanalysis* **36**, e202300207 (2023).
192. Akkas, T., Reshadsedghi, M., Sen, M., Kilic, V. & Horzum, N. The role of artificial intelligence in advancing biosensor technology: past, present, and future perspectives. *Adv. Mater.* **34**, e2504796 (2025).
193. Zhang, G., Atasoy, H. & Vasarhelyi, M. A. Continuous monitoring with machine learning and interactive data visualization: an application to a healthcare payroll process. *Int. J. Account. Infor. Syst.* **46**, 100570 (2022).
194. Zhai, B., Elder, G. J. & Godfrey, A. Challenges and opportunities of deep learning for wearable-based objective sleep assessment. *NPJ Digit. Med.* **7**, 85 (2024).
195. Zhao, Z., Alzubaidi, L., Zhang, J., Duan, Y. & Gu, Y. A comparison review of transfer learning and self-supervised learning: definitions, applications, advantages and limitations. *Expert Syst. Appl.* **242**, 122807 (2024).
196. Guo, C. & Chen, J. Big data analytics in healthcare: data-driven methods for typical treatment pattern mining. *J. Syst. Sci. Syst. Eng.* **28**, 694–714 (2019).
197. Qureshi, R. et al. Artificial intelligence and biosensors in healthcare and its clinical relevance: a review. *IEEE Access* **11**, 61600–61620 (2023).
198. Raghupathi, W. & Raghupathi, V. Big data analytics in healthcare: promise and potential. *Health Inf. Sci. Syst.* **2**, 3 (2014).
199. Kolluru, C., Williams, M., Chae, J. & Prausnitz, M. R. Recruitment and collection of dermal interstitial fluid using a microneedle patch. *Adv. Healthc. Mater.* **8**, e1801262 (2019).
200. Shu, Y. et al. Highly stretchable wearable electrochemical sensor based on Ni-Co MOF nanosheet-decorated Ag/rGO/PU fiber for continuous sweat glucose detection. *Anal. Chem.* **93**, 16222–16230 (2021).
201. Ling, W., Shang, X., Liu, J. & Tang, T. A skin-mountable flexible biosensor based on Cu-MOF/PEDOT composites for sweat ascorbic acid monitoring. *Biosens. Bioelectron.* **267**, 116852 (2025).
202. Zhang, W. et al. Bioinspired leaf vein-architected gold nanowire ecoflexible biosensors for ultrasensitive occlusal force monitoring. *Mater. Horiz.* **12**, 6229–6240 (2025).
203. Wang, Q., Liu, Q., Zhong, G., Xu, T. & Zhang, X. Wearable vertical graphene-based microneedle biosensor for real-time ketogenic diet management. *Anal. Chem.* **96**, 8713–8720 (2024).
204. Chen, X. et al. CVD-grown monolayer MoS2 in bioabsorbable electronics and biosensors. *Nat. Commun.* **9**, 1690 (2018).
205. Omar, R. et al. Biodegradable, biocompatible, and implantable multifunctional sensing platform for cardiac monitoring. *ACS Sens.* **9**, 126–138 (2024).
206. Kim, J. et al. Wearable smart sensor systems integrated on soft contact lenses for wireless ocular diagnostics. *Nat. Commun.* **8**, 14997 (2017).
207. Wen, X. et al. Flexible, multifunctional neural probe with liquid metal enabled, ultra-large tunable stiffness for deep-brain chemical sensing and agent delivery. *Biosens. Bioelectron.* **131**, 37–45 (2019).
208. Sun, Z. et al. A bioabsorbable mechanoelectric fiber as electrical stimulation suture. *Nat. Commun.* **15**, 8462 (2024).
209. Wang, H., Yang, B., Li, D., Kong, J. & Fang, X. Dynamic monitoring cell-free DNA using integrated diagnosis and therapy semi-implantable bioelectronics. *Chem. Eng. J.* **512**, 162291 (2025).
210. Madhvapathy, S. R. et al. Implantable bioelectronic systems for early detection of kidney transplant rejection. *Science* **381**, 1105–1112 (2023).
211. Ling, W. et al. Miniaturized implantable fluorescence probes integrated with metal–organic frameworks for deep brain dopamine sensing. *ACS Nano* **18**, 10596–10608 (2024).
212. Cui, X., Wu, L., Zhang, C. & Li, Z. Implantable self-powered systems for electrical stimulation medical devices.*Adv. Sci* **12**, e2412044 (2024).
213. Chen, Y. et al. Skin-like biosensor system via electrochemical channels for noninvasive blood glucose monitoring. *Sci. Adv.* **3**, e1701629 (2017).
214. Lee, H. et al. A graphene-based electrochemical device with thermoresponsive microneedles for diabetes monitoring and therapy. *Nat. Nanotechnol.* **11**, 566–572 (2016).
215. Takemoto, A. et al. Fully transparent, ultrathin flexible organic electrochemical transistors with additive integration for bioelectronic applications. *Adv. Sci.* **10**, e2204746 (2023).
216. Lee, H. et al. Wearable/disposable sweat-based glucose monitoring device with multistage transdermal drug delivery module. *Sci. Adv.* **3**, e1601314 (2017).
217. Li, Y. et al. Achieving tissue-level softness on stretchable electronics through a generalizable soft interlayer design. *Nat. Commun.* **14**, 4488 (2023).
218. Yuk, H. et al. 3D printing of conducting polymers. *Nat. Commun.* **11**, 1604 (2020).
219. Tringides, C. M. et al. Viscoelastic surface electrode arrays to interface with viscoelastic tissues. *Nat. Nanotechnol.* **16**, 1019–1029 (2021).

220. Zhou, T. et al. 3D printable high-performance conducting polymer hydrogel for all-hydrogel bioelectronic interfaces. *Nat. Mater.* **22**, 895–902 (2023).
221. He, W. et al. Integrated textile sensor patch for real-time and multiplex sweat analysis. *Sci. Adv.* **5**, eaax0649 (2019).
222. Wang, L. et al. A core–sheath sensing yarn-based electrochemical fabric system for powerful sweat capture and stable sensing. *Adv. Funct. Mater.* **32**, 2200922 (2022).
223. Xu, C. et al. A physicochemical-sensing electronic skin for stress response monitoring. *Nat. Electron.* **7**, 168–179 (2024).
224. Zhang, L. et al. Fully organic compliant dry electrodes self-adhesive to skin for long-term motion-robust epidermal biopotential monitoring. *Nat. Commun.* **11**, 4683 (2020).
225. Choi, G. et al. Omnidirectionally stretchable organic transistors for use in wearable electronics: ensuring overall stretchability by applying nonstretchable wrinkled components. *ACS Appl. Mater. Interfaces* **12**, 32979–32986 (2020).
226. Jang, K. I. et al. Self-assembled three dimensional network designs for soft electronics. *Nat. Commun.* **8**, 15894 (2017).
227. Didier, C., Kundu, A. & Rajaraman, S. Capabilities and limitations of 3D printed microserpentines and integrated 3D electrodes for stretchable and conformable biosensor applications. *Microsyst. Nanoeng.* **6**, 15 (2020).
228. Rojas, J. P. et al. Kirigami-enabled wearable health and crowd monitoring system. *Arab J. Sci. Eng.* **47**, 3583–3595 (2022).
229. Hu, H. et al. A wearable cardiac ultrasound imager. *Nature* **613**, 667–675 (2023).
230. Lee, S. P. et al. Highly flexible, wearable, and disposable cardiac biosensors for remote and ambulatory monitoring. *NPJ Digit. Med.* **1**, 2 (2018).
231. Bobbert, F. S. L., Janbaz, S., van Manen, T., Li, Y. & Zadpoor, A. A. Russian doll deployable meta-implants: fusion of kirigami, origami, and multi-stability. *Mater. Des.* **191**, 108624 (2020).
232. Morikawa, Y. et al. Ultrastretchable kirigami bioprobes. *Adv. Healthc. Mater.* **7**, 1701100 (2018).
233. Park, W. et al. In-depth correlation analysis between tear glucose and blood glucose using a wireless smart contact lens. *Nat. Commun.* **15**, 2828 (2024).
234. Jin, P. et al. A flexible, stretchable system for simultaneous acoustic energy transfer and communication. *Sci. Adv.* **7**, eabg2507 (2021).
235. Cai, L. et al. Osseosurface electronics-thin, wireless, battery-free and multimodal musculoskeletal biointerfaces. *Nat. Commun.* **12**, 6707 (2021).
236. Rao, Z. et al. Ultrathin rubbery bio-optoelectronic stimulators for untethered cardiac stimulation. *Sci. Adv.* **10**, eadq5061 (2024).
237. Dong, R. et al. Stretchable, self-rolled, microfluidic electronics enable conformable neural interfaces of brain and vagus neuromodulation. *ACS Nano* **18**, 1702–1713 (2024).
238. Zheng, Z. et al. A review of EMG-, FMG-, and EIT-based biosensors and relevant human-machine interactivities and biomedical applications. *Biosensors* **12**, 516 (2022).
239. Zhang, K. et al. Machine learning-reinforced noninvasive biosensors for healthcare. *Adv. Healthc. Mater.* **10**, e2100734 (2021).
240. Cheng, N., Chen, D., Lou, B., Fu, J. & Wang, H. A biosensing method for the direct serological detection of liver diseases by integrating a SERS-based sensor and a CNN classifier. *Biosens. Bioelectron.* **186**, 113246 (2021).
241. Ali, N. F. & Atef, M. LSTM multi-stage transfer learning for blood pressure estimation using photoplethysmography. *Electronics* **11**, 3749 (2022).
242. Faris Ali, N. & Atef, M. An efficient hybrid LSTM-ANN joint classification-regression model for PPG based blood pressure monitoring. *Biomed. Signal Process. Control* **84**, 104782 (2023).

Acknowledgements

This research was supported by the Global Research Development Center (GRDC) Cooperative Hub Program through the National Research Foundation of Korea (NRF), funded by the Ministry of Science and ICT (MSIT) (RS-2023-00257595).

Author contributions

Thirumalaisamy Suryaprabha: Writing—review and editing, writing—original draft, and conceptualization. Chunghyeon Choi: Writing—review and editing. Yanfang Wu: Review and editing. Liyang Liu: Editing and review. Byungil Hwang: Review and editing, supervision, and funding acquisition. All authors have read and approved the manuscript.

Funding

Open access funding provided by Chalmers University of Technology.

Competing interests

The authors declare no competing interests.

Additional information

Correspondence and requests for materials should be addressed to Liyang Liu or Byungil Hwang.