

Advanced engineered nanomaterials for next-generation flexible wearable bioelectronics interface: A comprehensive review

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Abstract: Nanomaterials have been found to possess tremendous potential as novel enabling elements in the highly dynamic field of flexible wearable bioelectronics. This is owing to their ability to allow for smooth interfacing between artificially designed devices and complex biological systems at both the molecular and cellular levels. Their highly desirable physicochemical properties, including elevated surface-area-to-volume ratios, quantum confinement, electronic conductivity, and mechanical flexibility, make nanomaterials promising candidates for novel wearable electronic devices that can find applications in continuous biosensing, bioactuation, neural interfacing, and real-time bioimaging. Most importantly, they can allow for the realization of basic elements of bioelectronics, such as bio-memory devices, biological logic gates, and biomolecule-integrated processors. These can potentially allow for overcoming the limitations of conventional rigid silicon-based electronic devices through intelligent integration with biomolecular recognition. This review article presents a systematic and comprehensive discussion on the most prominent classes of engineered nanomaterials utilized in the development of flexible wearable bioelectronics, including carbon-based nanostructured materials, intrinsically conducting polymers, metallic and bimetallic nanomaterials, as well as multifunctional nanocomposites. In addition, the review article places significant emphasis on the elucidation of the most significant structure-function relationships in the context of the most prominent application areas, including epidermal biosensing devices, soft neural interfaces, as well as biomimetic tissue engineering constructs. In addition, the most promising trends in the development of flexible, stretchable, as well as skin-conformable bioelectronic architectures are also critically discussed in the article. The current challenges in the development of flexible wearable bioelectronics, including the most prominent issues in the context of biocompatibility, long-term stability, and scalability, are also discussed in the article.

Keywords: nanomaterials; bioelectronics; biosensing; tissue engineering; neural interface

1. Introduction

The integration of materials science, nanotechnology, and biomedical engineering has ushered in a transformative era in which electronics may conform intimately to the soft, curved, and dynamically deforming surfaces of the human body, rather than rigid substrates [1]. This paradigm shift is largely driven by rapid progress in ultrathin electronic devices, bioresorbable encapsulation strategies, and advanced

soft sensing platforms, which collectively enable bioelectronic interfaces capable of seamlessly bridging the gap between the mechanical world of silicon-based electronics and the electrochemical world of living tissue [2]. At the heart of this transformation is the design and engineering of advanced nanomaterials, which provide an unrivaled mix of electrical, optical, mechanical, and biological capabilities that no single traditional bulk material can match [3]. These nanomaterials, which include zero-dimensional nanoparticles, one-dimensional nanowires and nanotubes, two-dimensional nanosheets, and three-dimensional nanostructured architectures, are critical functional building blocks for the next generation of wearable, implantable, and minimally invasive bioelectronic systems [4]. Traditional biomedical devices made from stiff and heavy materials have a basic mechanical mismatch with organic tissues. The human brain, heart, and skin demonstrate Young's moduli ranging from 0.1 to 100 kPa, whereas typical silicon- and metal-based electronics are orders of magnitude stiffer (100–200 GPa), resulting in chronic inflammatory reactions, signal deterioration, and device failure at the bioelectronic interface [5]. This mechanical incompatibility reduces device longevity while also compromising the quality and integrity of recorded electrophysiological and metabolic signals. To address this difficulty, material selection, device architecture, and fabrication methods must be fundamentally rethought [6]. A promising path forward is provided by nanomaterial-based methods, which allow for the simultaneous achievement of the mechanical compliance required for conformal tissue integration and the electrical conductivity required for high-fidelity signal transduction through nanoscale material engineering [7]. Next-generation bioelectronic interfaces that smoothly integrate with the dynamic, curved, and complex geometries of human tissues have been made possible by the rapid progress of ultrathin electronic devices, bioresorbable encapsulation technologies, and soft sensors [8]. Advanced nanomaterials are at the vanguard of this development, allowing bioelectronic interfaces that are not only biocompatible and mechanically adaptive but also have the ability to accurately record a variety of biological signals straight from the human body, such as biochemical and electrophysiological cues. The advancement of soft, stretchable bioelectronics relies on new material approaches, such as nanoscale engineering of conventional materials and the synthesis of new functional nanomaterials that preserve electrical and mechanical function during deformation [9]. Next-generation bioelectronic interfaces are made possible by advanced nanomaterials, which can be created using bottom-up methods or top-down nanoscale processing. These materials offer superior electrical, optical, and electrochemical properties, astonishing mechanical flexibility, and multifunctionality [10]. Bioelectronic technology is a revolutionary strategy in modern healthcare, providing unprecedented prospects for real-time monitoring, diagnosis, and therapy by directly interfacing electronic devices with biological systems. Rigid and bulky traditional biomedical devices have the inconvenience of poor mechanical compatibility with soft, curved, and dynamic tissues like the brain, heart, and skin [11]. Bioelectronic interface establishes close and high-fidelity contacts between the electronic device and the biological tissue to collect, transmit, and modulate physiological signals. In general, such interfaces are composed

of biochemical sensors, actuators, electrophysiological sensors, and auxiliary parts such as a signal display system, data storage, and power modules [12]. The characteristics of the materials, such as Young's modulus, electrical conductivity, and ion permeability, as well as the design techniques, such as the island-bridge method and the use of curved shapes, control their performance. Furthermore, the development of intrinsically stretchable nanocomposites, which contain conductive fillers scattered throughout soft matrices such as hydrogels and elastomers, has produced biocompatible, multipurpose devices that can replicate the mechanical characteristics of biological tissues. Bioelectronic devices with integrated solutions for real-time disease diagnosis and treatment are now available in epidermal, implantable, and injectable versions [13]. In recent years, advanced engineered nanomaterials have been found to hold considerable promise for the development of flexible wearable bioelectronic interfaces. This is because of their exceptional physiochemical properties, which allow for the design of wearable bioelectronic interfaces with superior performance. A wide variety of nanomaterials have been explored for this purpose [14]. These include carbon-based nanostructures such as carbon nanotubes and graphene. Additionally, metallic nanostructures such as gold and silver nanoparticles have been explored. Moreover, conductive polymers such as polyaniline and PEDOT: PSS have been used. In addition to this, hybrid nanocomposites have also been explored to enhance signal transduction, sensitivity, and device durability [15]. Among the most extensively investigated nanomaterials for flexible bioelectronics are carbon-based nanostructures. Carbon-based nanostructures, such as graphene and its derivatives (graphene oxide, reduced graphene oxide, and functionalized graphene), single- and multi-walled carbon nanotubes (SWCNTs and MWCNTs), carbon nanofibers, and carbon dots, are among the most researched nanomaterials for flexible bioelectronics. Graphene's remarkable intrinsic carrier mobility ($\sim 200,000 \text{ cm}^2 \text{ V}^{-1} \text{ s}^{-1}$), huge specific surface area ($\sim 2,630 \text{ m}^2 \text{ g}^{-1}$), and optical transparency make it a perfect option for flexible, transparent electrodes in epidermal electronic systems. In a recent study, by conformally integrating PEDOT: PSS with nanowire-templated 3D fuzzy graphene (NT-3DFG), Garg et al. [16] created a hybrid nanostructured electrode to get around the drawbacks of traditional planar electrodes. Because of its large surface area and volumetric charge storage, the resultant material showed markedly decreased resistance and dramatically increased charge injection capacity. The electrodes' potential for sophisticated miniaturized bioelectronic interfaces was further highlighted by their enhanced functional stability. In order to overcome this trade-off between mechanical strength and conductivity, Wang et al. [17] synthesized a multiscale hierarchical hydrogel based on PVA/CNT@CNF using a freeze-casting/hot-pressing method. The hydrogel exhibited anisotropic fracture, improved conductivity, tensile strength, and enhanced crystallinity, which enabled it to function effectively in different applications, including touch-sensitive human-machine interaction and human motion tracking. Metallic nanostructures are another important material class in flexible bioelectronics, known for their excellent electrical conductivity, adjustable plasmonic characteristics, and ease of chemical functionalization. In wearable sensor arrays, gold nanoparticles (AuNPs), silver nanowires (AgNWs), and copper nano mesh

structures are frequently used as electrode materials, conductive interconnects, and transduction elements. The ability of silver nanowire networks to create highly conductive, optically transparent percolation networks in elastomeric matrices is especially remarkable [18]. This allows stretchable conductors to maintain low sheet resistance even at tensile strains greater than 100%. Conversely, gold nanoparticles are highly valued for their biocompatibility, oxidation resistance, and easy surface chemistry through thiol-gold interactions, which enable accurate conjugation of bioreceptors for electrochemical biosensing [19]. In order to take advantage of the synergistic catalytic and electrochemical properties of multiple metals within a single nanoscale entity, bimetallic and core-shell nanostructures, such as Au@Ag and Pt-decorated AuNPs, have been synthesized [20]. This has improved the sensitivity and selectivity of bioelectronic sensing platforms beyond what is possible with single-component metallic nanomaterials. Conducting polymers, such as polyaniline (PANI) [21], Polypyrrole (PPy) [22], poly(3,4-ethylenedioxythiophene): poly(styrene sulfonate) (PEDOT: PSS), and poly(3-hexylthiophene) (P3HT), are the only materials that are electrically conductive, ionically permeable, and mechanically soft in the hydrated state. These combined ionic-electronic conductors bridge the transduction modality gap between biological systems' ionic current and conventional devices' electronic current, allowing for bioelectronic interfaces with low resistance and large charge injection capacity [23]. Bioelectronic devices can now be used in three main ways, each specifically designed for different clinical and research settings, thanks to developments in nanomaterial science and microfabrication. Electrocardiograms (ECG), electromyograms (EMG), electroencephalograms (EEG), skin temperature, hydration, and sweat biochemistry are just a few of the physiological parameters that can be continuously and non-invasively monitored by epidermal bioelectronic devices that are laminated on the skin's surface using adhesive or van der Waals forces. Compared to surface-based modalities, implantable bioelectronic devices offer access to physiological signals with significantly higher spatial resolution and signal-to-noise ratios when surgically positioned in proximity to internal organs, nerves, or the brain.

The review article focuses on the design, engineering, and application of the latest nanomaterials used in the development of the next generation of bioelectronic interfaces. To address the main issue of the mechanical and chemical imbalance between rigid electronic devices and biological tissues, it explores the incorporation of nanomaterials, such as carbon nanostructures, metallic nanowires, conductive polymers, and nanocomposites, into flexible substrates. The scope includes a thorough explanation of material selection, top-down and bottom-up synthesis processes, and design methods that provide bioelectronic devices with their stretchability, biocompatibility, and multifunctionality, as shown in **Figure 1**. Further, looks into how these materials enable the development of device components, including sensors, actuators, power sources, and data storage modules designed for implantable, wearable, and minimally invasive medical applications. The goal is to establish a scientific basis for the development of next-generation bioelectronic platforms that, in addition to seamless tissue integration, will not only deliver improved electrical function, long-term stability, and therapeutic responsiveness but also pave the way for future

clinical translation.

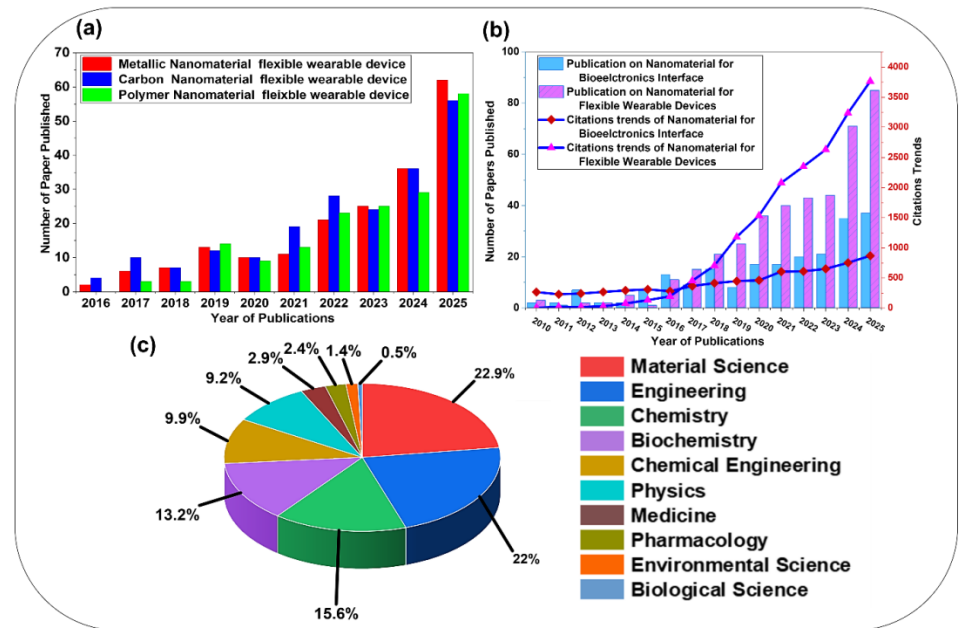


Figure 1. Publication trend in (a) Number of papers published on various nanomaterials (Metallic, Carbon, polymer) for flexible wearable devices from 2016–2025; (b) Publication and citation trends on advanced nanomaterials for the bioelectronics interface and flexible wearable devices; (c) Number of papers published in different subject areas with keywords Advanced nanomaterial for bioelectronics interface from 2007 to 2025.

Source: Data were collected from the Web of Science and Scopus.

2. Fundamentals of bioelectronic interfaces

The bioelectronic interface that integrates both nanotechnology and biology constitutes a new frontier with great relevance in areas such as brain prostheses, biomedical diagnosis, and sensors. Such interfaces facilitate effective communication between biological processes and electric machines in order to achieve enhanced functionality in terms of monitoring, treatment, and diagnosis [24]. The strategic use of nanotechnology is crucial in this context due to its unprecedented potential for tissue integration and sub-cellular spatial resolution. This encompasses an analysis of recent advancements in materials that enable the fabrication of such multimodal bioelectronic devices, spanning from sophisticated three-dimensional structures to two-dimensional materials. To achieve efficient devices with optimal safety features, the design process must involve a comprehensive examination of the electrochemical properties of conductive materials, particularly with respect to their use in nerve signal stimulation and recording [25]. Through the process of translating biochemical and ionic signals into measurable electrical outputs, bioelectronic interfaces represent the essential connection between biological systems and electronic components. While electronics rely on the transportation of electrons to function, the majority of biological environments make use of ions and oxidation reactions for the purpose of conveying messages. Effective interfaces that facilitate efficient signal conduction while maintaining biocompatibility are required as a consequence of the aforementioned dichotomy [26]. As a result of their unique physicochemical properties, including high surface area, electrical conductivity, and programmable surface chemistry, modern

nanomaterials play an indispensable role in this context. In a new study, attention is being paid to neuromodulation mediated by the photothermal effect based on graphene diyne (GDY) for precise neuron stimulation, which was proposed by Shao et al. [27] GDY functionalization by attaching specific antibodies to TRPV1 through PEGylation made it possible to target neurons with high selectivity. The developed photothermal nano agent towards TRPV1 receptors and its ability to generate heat energy under near-infrared irradiation were shown in experiments. Local heat generation led to neurotransmitter release upon TRPV1 activation, causing neuromodulation in living samples. The detailed workflow for study inclusion and exclusion (PRISMA) is presented in **Figure 2**.

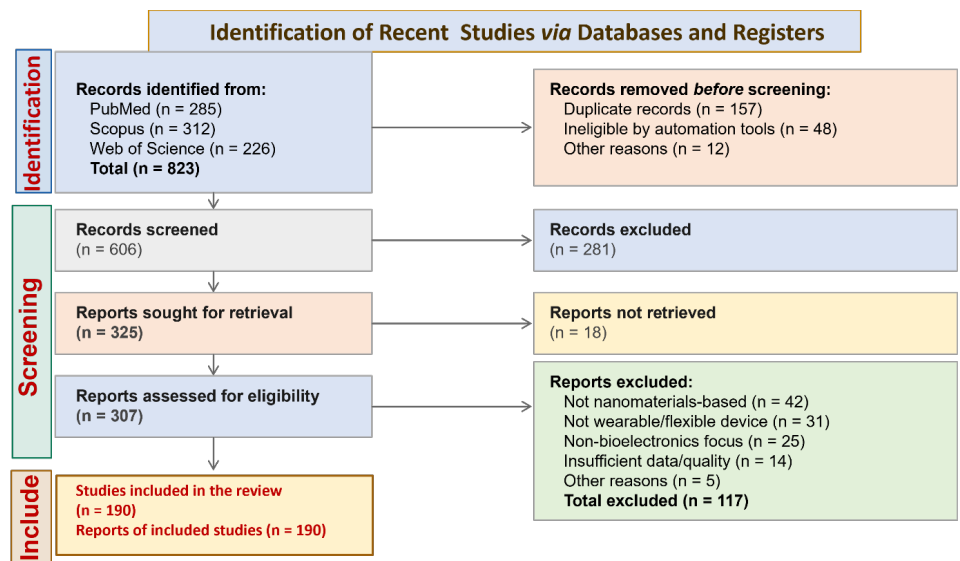


Figure 2. PRISMA flow diagram.

Note: The diagram illustrates the identification, screening, eligibility assessment, and final inclusion of studies related to advanced engineered nanomaterials for next-generation flexible wearable bioelectronics interfaces, and summarizes the database search process, removal of duplicate and irrelevant records, full-text evaluation, and selection of studies included in this comprehensive review.

2.1. Principles of bioelectronic signal transduction

Bioelectronic signal transduction means the process of converting biological signals into electronic signals that can be detected, measured, or processed by electronic devices or vice versa [28]. This process is essential for building communication between the human body and machines, such as in wearable sensors, neural interfaces, and implantable medical devices. Within our body, cells, particularly neurons and muscle cells, exchange information by the transport of ions such as sodium (Na^+), potassium (K^+), and calcium (Ca^{2+}) across their membranes [29]. These ion transports create small voltage changes referred to as action potentials [30]. But in electronic circuits, signals are transported by electrons, not ions. To translate between ions and electrons, a unique interface is required since they are distinct forms of charge carriers. The point of contact between the electronic equipment and the biological tissue is known as the biointerface [31]. Various transduction processes can be employed at the biointerface, depending on the signal type and the material. Capacitive transduction is a commonly used method for bioelectronic signal transduction, wherein an electrical double layer forms at the interface between the electrode and the surrounding ionic

environment. By using this technique, the biological signal can be detected without direct chemical interaction because no actual ions enter the device; instead, the electrical field produced by the adjacent ions brings about a detectable change in voltage on the electrode [32]. Another method of bioelectronic signal transduction is faradaic transduction, wherein real electrochemical reactions occur at the interface. Ions in the surrounding biological fluid experience oxidation or reduction reactions when a voltage is provided, which causes electrons to move from the device to the ions. This electron transfer produces a measurable faradaic current, which allows ionic biological signals to be converted to electrical signals. Advanced sensing platforms also make use of field-effect transistors (FETs), in which the electric field produced by adjacent charged biological species governs the current passing through a semiconductor channel [33]. This method provides high sensitivity for detecting minute biological signals in the absence of direct ion exchange [34]. Furthermore, in the photoelectrochemical transduction method, when light interacts with a semiconductor material, it excites electrons and forms electron-hole pairs. These charge carriers produce photocurrents, which can either stimulate neighbouring cells or detect cellular activity [35]. Last but not least, photothermal transduction involves the absorption of light by materials such as gold nanoparticles or silicon structures and its conversion into heat. This localized heating might affect biological processes, such as activating heat-sensitive ion channels, or it can improve signal delivery and response by increasing the coupling between the device and the biological tissue [36]. In a recent study, Ramasamy et al. [37] designed electrospun PLLA nanofiber scaffolds containing nanofillers functionalized with Pluronic F-127 (PL-cMWCNTs, PL-EBN). The use of conductive 1D nanotubes together with piezoelectric 2D nanosheets improved the mechanical properties, hydrophilicity, and piezoelectricity of the nanofiber scaffolds. Results from in vitro tests indicated a boost in cell proliferation, as shown in **Figure 3a**. Soft nano bioelectronics leverage both nanomaterial integration and nanoscale structural design to achieve multimodal sensing and stimulation, facilitating bidirectional communication across brain regions and peripheral nerves [38] as shown in **Figure 3b**.

2.2. Interface requirements: Electrical, mechanical, and biocompatibility

To integrate smoothly with biological tissues, effective bioelectronic interfaces must meet fundamental mechanical, electrical, and biocompatibility requirements [39]. Mechanically, the interface must be soft, flexible, and elastic, preferably matching the modulus of soft tissues (1–100 kPa), to maintain conformal contact and reduce injury during motion [40]. Electrically, materials should have low impedance, good conductivity, and stable charge injection to ensure correct signal transduction [41]. Biocompatibility necessitates non-toxic, non-immunogenic, and cell-friendly surfaces that enable long-term interaction without causing inflammation [42]. Conductive polymers [43], hydrogels [44], and bio-inspired coatings [45] are commonly used to deliver these multifunctional features.

fabrication methods further limit design flexibility, making it not feasible to achieve the stretchability, self-healing, and multifunctionality needed for next-generation wearables and implantable devices [48]. The above-mentioned challenges highlight the need for the development of soft, bioactive, and adaptable materials that can better mimic the mechanical and biochemical environments of living tissues.

3. Material design at the bio-nano interface

The design of materials at the bio-nano interface plays an important role in the development of future flexible wearable bioelectronics. The bio-nano interface serves as a medium to establish interactions between biological systems skin, tissue, and biofluids and nanomaterials, which will significantly affect the quality of signals and stability of the bioelectronic device. An effective bio-nano interface should be able to overcome the inherent gap between the biological environment and the rigid/electronically flexible bioelectronic device [49]. The bio-nano interface is the point at which engineered nanomaterials (ENMs) interact with the biological system. Here, the ENMs either have the ability to perform their desired biological function or, if they are in the wrong place, such as the natural environment, they have the ability to induce an undesired effect on the cell or the organism's system [50]. In a recent study, an A PPy–MXene/PDA composite was prepared using electropolymerization of MXene nanosheets and the codeposition of polypyrrole and polydopamine by Zeng et al. [51]. High photoelectrochemical sensitivity, superior charge injection/storage capability, remarkable stability, and extremely low interface resistance were among the features exhibited by the fabricated bioelectrode. Furthermore, it showed improved sensitivity to ascorbic acid, as shown in **Figure 4a**. The combination of PANI/SnO₂ coating on an integrated passive device was used by Tang et al. [52] to design a microwave resonator-based ammonia gas sensor, which showed efficient detection of ammonia gas with a significant shift in frequency in the range of 10–120 ppm, along with good sensitivity and recovery at room temperature, as shown in **Figure 4b**. For instance, with the incorporation of catechols, Lao et al. [53] designed a naturally conducting and adhering PEDOT-containing hydrogel to enable the recording of electrical signals with high conductivity, flexibility, and adhesion. The ability of the hydrogel to support the recording of biopotentials (EMG, ECG, and ECoG) in the absence of significant motion artifacts proves its potential for advanced bioelectronic interfaces, as shown in **Figure 4c**. For simultaneous determination of lactate and interleukin-6, Nandhakumar et al. [54] fabricated small bioelectronic sensor devices that used both enzyme- and aptamer-based methods. The utility of the device in performing real-time decentralized diagnosis of sepsis and associated disorders was underlined by its fast and crosstalk-free determination of the two analytes in human serum and interstitial fluids. As shown in **Figure 4d**.

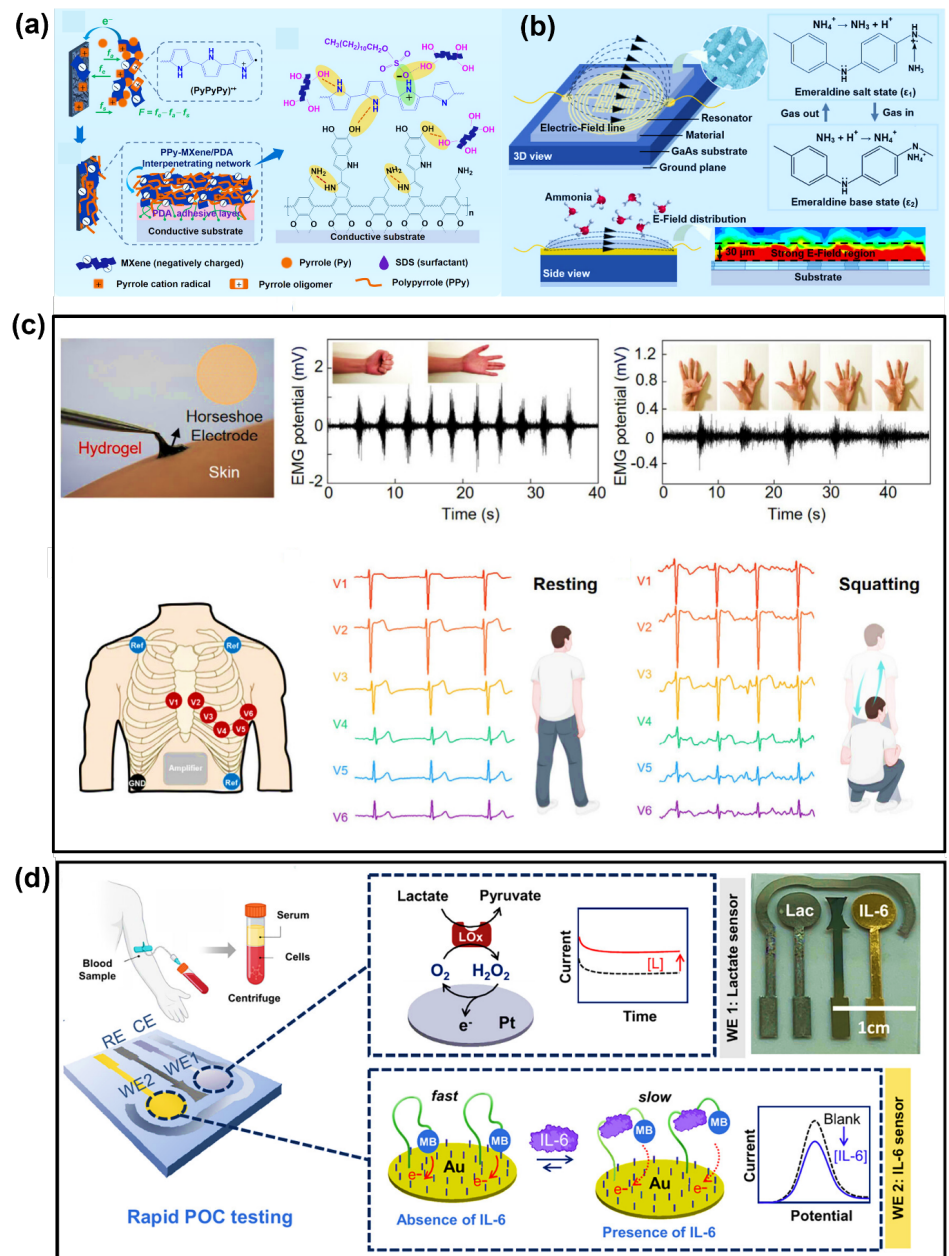


Figure 4. (a) Schematic diagram of electrodeposition migration, depicting the interpenetrating networks formed by PPy-MXene and PDA on a conductive substrate. Various molecular interactions present at the PPy-MXene/PDA interface, including hydrogen bonding, electrostatic attraction, polymer chain entanglement, and π - π stacking interactions; (b) Integrated Passive Device-Based Gas Sensor Combined with PANI/SnO₂ Composites for Ammonia Detection; (c) On-skin EMG and ECG monitoring. Image of an EPAD bioelectronic device for EMG and ECG monitoring. EMG signals generated by fist clenching and extension of different fingers; (d) Schematics of a POC sensor chip showing the two working electrodes for the IL-6 and lactate sensors, with an Ag/AgCl RE and Pt CE. Enzymatic amperometric lactate measurements are carried out on the Pt-working electrode (WE1) kept at +0.6 V through enzymatic (LOx) oxidation and detection of the liberated H₂O₂ product. IL-6 recognition involved an MB-tagged aptamer in the Au working electrode (WE2) and with IL-6-binding inducing changes in the signaling aptamer probe, resulting in a decrease in measured voltammetric peak currents.

Source: **Figure 4a:** Reprinted with permission from Zeng et al. [51] Copyright 2026 American Chemical Society; **Figure 4b:** Tang et al. [52] Copyright 2023 American Chemical Society; **Figure 4c:** Lao et al. [53] Copyright 2025 American Chemical Society; **Figure 4d:** Nandhakumar et al. [54] Copyright 2025 American Chemical Society.

3.1. Nanoscale considerations in bioelectronic coupling

In the bio-nano interface, the nanoscale properties of the engineered nanomaterials play a crucial role in determining the efficacy of the bioelectronic coupling [55]. These include the surface properties of the nanomaterials, the medium used for the interface, and the biological materials they interact with. These surface characteristics include elemental composition, charge, size, morphology, functional groups, and porosity, which determine the interaction between the nanomaterials and the lipid molecules, proteins, and cell membrane [56]. The nanoparticles with diameters larger than 200 nm have shown the ability to induce changes in the structure of the proteins that are adsorbed. This may have a significant influence on signal transmission and biocompatibility [57]. The state of oxidation, e.g., in cerium oxide nanoparticles, also plays a critical role in the interaction between the nanoparticles and the biological environment as well as their toxicity. Environmental factors also determine the interaction between the nanomaterials and the biological environment. Temperature, pH, ionic strength, and the presence of biomolecules may influence the ability of the nanoparticles to aggregate, adhere to surfaces, and dissolve [58]. Finally, the biological effect, particularly the effect via the adsorbed biological molecules such as lipids and proteins, can also dynamically change the surface property of the nanoparticle, thus controlling its interaction with the tissue and the cell [59]. Therefore, the nanoscale design, considering all three parameters, is very important for the development of a stable and safe bioelectronic system. In a recent study, silver nanoparticles synthesized using *Gymnema Sylvestre* by Keerthiga et al. [60] have been used as a strong antibacterial and antibiofilm material. These nanoparticles were found to be spherical and polydispersed (50–100 nm) and possessed a unique peak of SPR at 398 nm. They showed antibacterial activity against four different bacteria, such as *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Escherichia coli*, and *Klebsiella pneumoniae*, having a maximum zone of inhibition of 19 mm. Furthermore, the antibiofilm efficiency of GS-AgNPs was found to be highly effective, up to 94.6%. Core-shell aluminium oxide (Al_2O_3) nanoparticles were developed by Singh et al. [61] using the extract of *Bauhinia variegata* in a green process. The developed nano-bioengineered electrode on the indium tin oxide exhibited excellent selectivity and stability along with sensitivity ($23.44 \mu\text{A} \mu\text{M}^{-1} \text{cm}^{-2}$) and detection limit ($0.463 \mu\text{M}$) to sodium azide. Besides, the nanoparticles proved to be potential candidates for environmental and clinical applications owing to their efficient photocatalytic degradation of crystal violet under visible light irradiation.

3.2. Interface engineering: Surface chemistry, topography, and charge

Engineering of the bioelectronic device-biological entities interface requires careful control of topography, chemistry, and charge, as these play an important role in determining interactions, signal quality, and long-term device performance [62]. Topography, especially micro- and nanometer-scale roughness, can affect cell behavior by regulating adhesion, orientation, and migration. Nonhomogeneous, porous, or patterned surfaces can offer more surface area for interaction with biomolecules, which can be very beneficial for bioelectronic devices, especially sensors and neural

interfaces [63]. Moreover, nanometer-scale roughness can also control protein adsorption kinetics as well as organization, which can have an impact on subsequent cell behavior. Surface chemistry plays an important role in regulating the adsorption of biomolecules, especially proteins, on bioelectronic devices. The presence of particular functional groups, such as (-OH, -COOH, or -NH₂), is responsible for regulating adhesion, protein structure, and biofunctionalization for better interactions. Surface charge is also an important factor for bioelectronic devices, especially for electrostatic interactions with other biological entities [64]. Positively charged surfaces have been reported to enhance protein as well as cell adhesion, but can also trigger inflammation when applied in bioelectronic devices. Negatively charged or zwitterionic surfaces have been reported to resist nonspecific adsorption, thus offering better stability for bioelectronic devices [65]. Finally, charge density is also an important aspect of electrostatic interactions with biological species. More specifically, positively charged surfaces can facilitate protein and cell adhesion but can also trigger inflammation pathways. On the other hand, negatively charged or zwitterionic surfaces can resist non-specific adsorption, thus offering excellent stability in biofluids. In summary, it is clear that interface engineering enables us to design bioelectronic devices that are intelligent, flexible and tissue-friendly by offering tailored surface chemistry, morphology, and charge density.

3.3. Functional requirements: Softness, conformability, and signal fidelity

The properties of softness, conformability, and signal integrity are crucial for the successful integration of bioelectronic interfaces with soft and dynamic tissues. Rigid materials, which have been traditionally used, have been proven to create a mechanical mismatch, which leads to poor interface, irritation, and device failure [66]. However, soft and elastomeric materials, such as hydrogels, silicones, and polymers, have been able to mimic the mechanical properties of tissues, which are typically in the range of 1–100 kPa, thereby reducing tissue strain and improving long-term tissue biocompatibility. Conformability enables the interface to have close contact with irregular shapes of tissues, which is crucial for the stimulation and sensing of tissues [67]. Flexible materials, thin films, and mesh structures have been proven to have the best interface contact with tissues, even during movement. Signal integrity enables the interface to have a low-impedance interface that can accurately sense and transmit weak signals from the tissues without being interfered with by noise [68]. This is achieved by the matching properties of mechanical softness and electrical conductivity, which is typically achieved by the use of hybrid materials with the incorporation of nanomaterials. These properties together facilitate implantable, internal connections between electronics and biology for use in applications such as neural recording, wearable diagnostics, and cardiac monitoring.

4. Classes of advanced nanomaterials

Nanomaterials are essential in the progress of bioelectronic devices, as they present particular physicochemical properties that can improve their sensitivity, flexibility, and multifunctionality for biomedical applications [69]. Metallic

nanoparticles, including gold and platinum, are utilized as powerful electron wires that can facilitate rapid electron transfer between biological molecules, like enzymes, and electrodes, thus increasing the efficiency of biosensors and biofuel cells. Their elevated surface-to-volume ratios can improve the effective electrode surface area, thus allowing for better bio-catalyst immobilization. Biopolymers' nanomaterials are naturally bio-compatible, thus creating micro-environments that are appropriate for maintaining biological activities, thus allowing for better and more consistent bioelectronic devices' performance. Moreover, these nanomaterials can enable bioelectronic devices to be miniaturized to micro- and nano-scales, thus allowing for less invasive devices that can interact with sensitive biological tissues [70]. Nanomaterials, when integrated into hydrogels, elastomers, and composites, can enable bioelectronic devices to be more flexible, thus allowing for their application in wearable bioelectronics, including biosensors that can stretch with body movements [71]. There are various classes of nanomaterials depending on their dimensions and their bioelectronic applications, as shown in **Figure 5**.

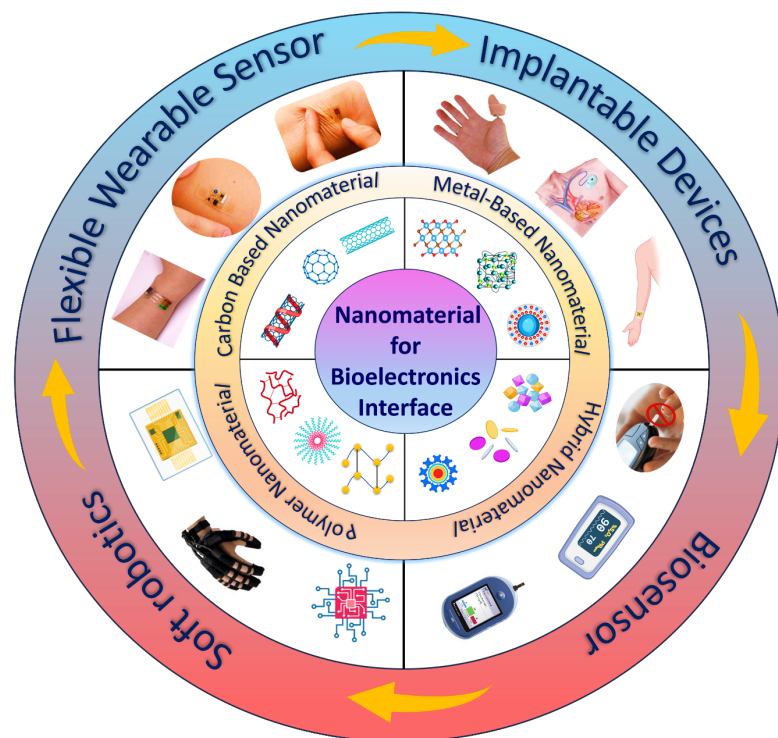


Figure 5. Schematic representation of various nanomaterial-based systems and their applications in the bioelectronics interface.

4.1. Carbon-based nanomaterials

Carbon-based nanomaterials have been recognized as a new class of materials with great promise for revolutionizing bioelectronics, offering key properties that are highly advantageous for interacting with biological systems. The nanometer scale of these materials enables them to be closely integrated with biological molecules and structures, thereby enabling the development of highly sensitive and selective biosensors, drug delivery systems, wearable devices, and innovative therapeutic strategies [72]. The continuous advancements in micron-sized and nanometer-scale

material synthesis and control have made it possible to create advanced functional materials with unique properties [73]. These materials also possess electronic properties, high surface area, and biocompatibility. In particular, carbon nanotubes (CNTs), graphene, carbon dots (CDs), and other carbon-based nanostructures have attracted a lot of attention [74]. When creating a sensitive composite with biomolecules, CNTs, graphene, and its derivatives, such as graphene oxide (GO) and reduced GO, are particularly effective due to their excellent biocompatibility and readily adjustable surface characteristics [75]. Carbon nanoparticles have been mixed with different kinds of stimulus-sensitive materials in numerous studies to fabricate carbon nanomaterial-mediated bioelectronic systems that respond to multiple external stimuli [76]. These materials help create novel gadgets that combine electronics with biology, improving their use in environmental monitoring, diagnosis, and treatment [77]. The application for commercialization is the primary developmental focus of current research in carbon nanomaterial-mediated bioelectronic devices. Many types of carbon nanomaterials can be used in bioelectronic devices, but to move forward with commercialization, they need to operate across a variety of configurations [78]. Graphene nano inks capable of undergoing structural modification, along with GO-based hydrogels, represent two prominent examples of carbon nanomaterial-based complexes developed for application in flexible and stretchable bioelectronics. Given their exceptional electrical, mechanical, and chemical properties, it is anticipated that the number of studies reporting wearable bioelectronic devices incorporating carbon nanomaterials will continue to grow in the near future [79]. Hazarika and Dutta [80] developed a novel electrochemical sensor based on a composite of chitosan-block-polyaniline (CHIT-b-PANI), α -manganese dioxide (α -MnO₂), and carboxylated multi-walled CNT (COOH-MWCNT). In this design, α -MnO₂ was coated with CHIT-b-PANI and encapsulated within COOH-MWCNTs. When dropped onto indium tin oxide (ITO), the sensor exhibited excellent creatinine sensing performance with a wide linear range (1–243.48 μ M), a low limit of detection (1.02 μ M), a high sensitivity (3,204.02 μ A \cdot mM⁻¹), and strong selectivity, stability, and repeatability [80]. Han et al. [81] developed a multifunctional electroconductive hydrogel (ECH) by integrating CNT-cellulose nanofiber (CNFs) nanohybrids into a polyvinyl alcohol-borax (PVAB) matrix. The CNFs enabled uniform CNT dispersion, forming a dual-network structure that significantly enhanced conductivity, mechanical strength (~93 kPa), and elasticity (~7.12 kPa). The resulting CNT-CNF/PVAB hydrogel demonstrated fast self-healing (~20 s), high water content (~95%), excellent moldability, and pH responsiveness [81]. Similarly, Ma et al. [82] developed conductive scaffolds by incorporating carboxylated MWCNT (1–5 wt%) into a sodium alginate/gelatin (Alg/Gel) matrix via freeze-drying, targeting neural tissue engineering. Moreover, the optimized scaffold (Alg/Gel–1%C) exhibited high hydrophilicity, as the contact angle decreased to 60°. Also, the conductivity and mechanical strength were found to be 1.32×10^{-3} S/cm and 1.40 MPa, respectively. Additionally, the optimized scaffold showed better cell proliferation, cell cycle, and morphology, indicating its potential use in nerve regeneration applications. Lv et al. [83] prepared a multifunctional conductive hydrogel based on polyacrylamide

(pAAm), chitosan (CS), silver nanowire (AgNW), and carboxylated multi-walled carbon nanotubes (c-MWCNTs) via in situ polymerization without the use of any cross-linking agents. The hydrogel exhibited excellent mechanical strength (503.64 kPa), ultra-stretchability (16,000%), and toughness ($22.8 \text{ MJ}\cdot\text{m}^{-3}$). The AgNW/CS synergy showed high antibacterial properties, and the AgNW/c-MWCNT synergy showed high conductivity, response time (200 ms), and strain sensitivity ($\text{GF} = 10.42$). The hydrogel also showed high performance in the detection of human motion sensors, suggesting in flexible wearable electronics. A multifunctional conductive hydrogel was synthesized by Dou et al. [84] using heparin-polydopamine-reduced graphene oxide (Hep-PDA-rGO) as a basis. The hydrogel exhibits remarkable antibacterial, antioxidative, and angiogenesis-promoting capabilities, along with conductivity enhancement (3.63 S m^{-1}) along with dispersion capability, and high sensitivity for monitoring motion in real time, making it suitable for chronic wound treatment and epidermal sensing. To prove the effectiveness of skin adhesion ($\sim 6.5 \text{ kPa}$), electrical conductivity ($\sim 0.11 \text{ S m}^{-1}$), biocompatibility ($>90\%$ cell viability), and measurement of electrophysiological signals such as EOG, EMG, and ECG while in motion in humans, Kim et al. [85] designed RGO-based conductive hydrogel bioelectrodes using polyvinyl alcohol (PVA), RGO flakes, and polyacrylic acid (PAA).

4.2. Metal-based nanomaterials

Metal-based nanomaterials have been found to be of critical importance in the field of bioelectronics owing to their distinctive properties, such as superior conductivity, compatibility, and mechanical properties [86]. Nanostructures of gold, silver, nanostructured metal oxides, and metallic nanoparticles doped with strontium, among other elements, are being used to improve the efficacy of bioelectronic devices [87]. NPs are typically synthesized using metals such as gold (Au), silver (Ag), aluminium (Al), zinc (Zn), copper (Cu), cadmium (Cd), cobalt (Co), lead (Pb), and iron (Fe). These metal-based nanomaterials offer tunable optical, electrical, and chemical properties that are highly crucial for sensing, signal transmission, and therapeutic applications in advanced wearable bioelectronics systems [88]. These nanomaterials can be cylindrical or spherical in shape, crystalline or amorphous in structure, and tiny in size (10–100 nm). The incorporation of these nanoparticles with biomaterials results in the formation of bio-nanohybrids, which are critical for overcoming the limitations of traditional biomaterials in bioelectronics. Such nanomaterials have been widely used as catalysts and fillers in different types of chemical transformations. Their intrinsic properties, such as geometry, specific surface area, sites (edges, corners, faces, kinks, and steps), and electronic configuration, offer a wide range of interactions with the reagents and products of catalytic processes [89]. Furthermore, the nature of the metal and the support (MNPs are frequently supported on solids or immobilized in liquid phases) have a significant impact on their catalytic behavior and recycling potential. For instance, gold nanomaterials such as gold nanocrystals and nanowires are being used in soft bioelectronics due to their high conductivity and high biocompatibility [90]. In addition, Sami et al. [91] constructed a highly sensitive and selective colorimetric biosensor by using copper nanoparticles for detecting urinary albumin, showing a

wide dynamic range (25–250 mg/L), high sensitivity (6.5 mg/L), good specificity, and practical application. This approach can be considered an efficient tool for early CKD diagnosis. A wireless and passive strain sensor made from hydrogel containing zinc oxide nanoparticles (ZnO-gel) was developed by Jiang et al. [92] wherein the ZnO nanoparticles were embedded in the poly(DMA-co-MAA) matrix, making it stronger and highly flexible (strain rate of ~260%). The ZnO nanoparticles were efficient ultrasound contrast agents, and hence could be used to monitor strain remotely using ultrasonic imaging. The optimized hydrogel, which had 10 wt% ZnO, showed imaging visibility, linear dimension changes, and high biocompatibility. A nanohybrid piezoelectric strain sensor was fabricated by Panth et al. [93] through the growth of vertically aligned zinc oxide nanowires on graphene without using seeds via a hydrothermal method, which ensures lower defects at the interface, enhancing electrostatic gating performance. This nanohybrid sensor demonstrated enhanced performance with increased sensitivity ($3.15 \times 10^{-2} \text{ kPa}^{-1}$) and faster response (0.10 s) compared to sensors produced using seeded methods.

4.3. Conductive polymer-based nanomaterials

The creation of multifunctional and adaptable nanomaterials that smoothly link the realms of electronics and biological systems is speeding up the progression of the next generation of bioelectronics. In this regard, conductive polymer-based nanomaterials have witnessed significant interest owing to their inherent electrical conductivity, mechanical flexibility, stretchability, and superior tissue-compatibility characteristics [94]. The conductive polymers, such as PEDOT: PSS, polypyrrole (PPy), and polyaniline (PANI), are revolutionizing the field of bioelectronics by improving the electrical characteristics and tissue compatibility of bioelectronic devices [95]. Recent advancements have led to the creation of ‘smart’ materials, which include the integration of conductive polymers with two-dimensional materials, such as metal-organic frameworks (MOFs), and biological-derived hybrid nanostructures, to improve the electrical properties, mechanical properties, and versatility of the materials for biomedical applications [96]. These materials, particularly when integrated with nanostructures such as graphene and MXenes, have superior electrical properties, biocompatibility, and stability, thus offering a wide array of bioelectronic device opportunities. Nanomaterial-doped conducting polymers are a new and innovative type of composite material that combines the properties of nanoparticles and conducting polymers, thus offering a wide array of opportunities for application in various fields. For instance, the integration of MXenes into composites based on CP has the ability to improve the conductivity and sensing properties of the composites, thus offering a wide array of opportunities for wearable electronics [97]. Conductive polymers can be prepared controllably from different monomers, and during polymerization, different nanomaterials with unique physical and chemical properties can be doped into conductive polymer composites [98]. In a recent study, Wan et al. [99] developed a bioelectronic interface based on a hydrogel, fabricated using a 3D printer, with PEDOT: PSS, which offers high conductivity and tissue adhesion, thus allowing precise measurement of bio-signals using electromyography. The hydrogel was

found to exhibit outstanding printability, mechanical flexibility, and concomitant skin-contact stability, thus allowing precise acquisition of bio-signals. The PEDOT:PSS bioelectronic interface was found to enable precise measurement of bio-signals, thus offering promising prospects for future bioelectronics and human-machine interfaces next-generation wearable bioelectronics and human-machine interface. In a recent study, a very flexible and conductive composite nanofiber was prepared from thermoplastic polyurethane (TPU) by electrospinning and in-situ PANI polymerization, showing a high sensitivity to strain variation from 0–160%, fast response time, and high stability. Moreover, the composite showed high resiliency, ability to conform to curved surfaces, and temperature-independent electrical conductance, thus allowing it to detect sensitive and quick human body movements through flexible strain sensors [100]. The CMC-PANI/PEI/PAAM double network hydrogel developed by Li et al. [101] exhibited a high mass content, high specific capacitance (approximately 679 mF cm^{-2}), high energy density, and excellent cycling stability with only a 2% loss after 5,000 cycles. Its mechanical flexibility, ability to operate over a wide range of temperatures (-30 to $70 \text{ }^\circ\text{C}$), and reliable electrical response made it ideal for use in flexible electronics for human motion detection and strain sensors. For instance, Zhang et al. [102] synthesized the composite membranes of CNFs coated by conducting polymers PANI, Ppy, and PTh through in-situ synthesis, which led to improved conductivity and strain sensing capability when compared to plain CNFs. Among the three composites, CNF/Ppy performed better than the other two composites in terms of sensitivity, repeatability, and stability, enabling the accurate measurement of small and large deformations. Chen et al. [103] fabricated highly sensitive, low-drift, reversible, and durable pressure sensors based on polypyrrole-modified polyetherimide fibers. The sensors demonstrated excellent sensitivity, low drift, high reversibility, and a lifespan of nearly 30,000 cycles. The sensors worked efficiently under temperatures between -70 to $150 \text{ }^\circ\text{C}$. By integrating the technology with an IoT framework, the innovation enabled accurate, non-destructive, and instantaneous detection of cracks in historical designs, consuming minimal energy to function for over one year.

4.4. Soft and hybrid nanomaterials

Soft and hybrid nanomaterials are at the forefront of bioelectronics, which facilitates the development of flexible, stretchable, wearable, and biocompatible devices that can smoothly integrate with biological tissues [104]. These materials can transform conventional rigid electronics into soft devices that can conform to complex and dynamic biological surfaces, including skin, heart, and brain, thus allowing for advanced applications. Soft nanomaterials like hydrogels, conductive polymers, elastomers, and nanocomposites have mechanical properties close to soft tissues in the body and provide a stable biointerface. The special flexibility and stretchability of these materials allow them to conformally integrate with dynamic and complex organs in the body, enhancing signal quality and reducing irritation. Some examples include gold nanomembranes, carbon-based nanomaterials like graphene and CNTs, and metal nanoparticles in soft materials, which provide a promising base for high-performance bioelectronics [105]. Such advanced nanomaterials give flexibility and stretchability,

allowing devices to adhere to the skin without causing discomfort or damage [106]. Hybrid materials are nanomaterials that integrate different material types, such as combining inorganic nanostructures and organic materials, such as polymers and hydrogels, for improved multifunctionality, mechanical malleability, and device performance. For example, hybrid hydrogels integrate the electrical properties of nanoparticles and the intrinsic softness, malleability, and biocompatibility of hydrogels, making hybrid hydrogels suitable for wearable and implantable bioelectronic devices. Moreover, flexible hybrid electronics integrate the properties of soft and deformable materials and rigid materials, such as electronic sensors, biosensors, and processors for conformal contact and interaction with tissues and biological materials, ensuring device performance and integrity [107]. In a recent study, using a one-pot synthesis technique, Patel et al. [108] fabricated an integrated conductive hydrogel that had excellent printability, higher mechanical properties, rapid self-recovery ability, and high electrical conductivity. The conductive hydrogel was composed of carboxymethyl chitosan (CMCS) and functionalized carbon nanotubes (f-CNTs). The hydrogel exhibited remarkable biocompatibility, antimicrobial performance against *Escherichia coli* bacteria, and high adhesion properties toward various surfaces, including human skin. Additionally, it also exhibited high strain sensitivity ($GF = 2.4$ at 210% strain), making it suitable for wearable electronics applications. For instance, Zou et al. [109] developed a highly functional hydrogel via physical crosslinking and immersion in glycerol, which has great mechanical stability, anti-freezing properties (up to $-60\text{ }^{\circ}\text{C}$), minimal water loss, and multi-modal sensing capability (contact and non-contact) of temperature, humidity, strain, and stress parameters, making it possible to monitor physiological parameters and human motion accurately. By using the free radical crosslinking process of allyl cellulose, Tong et al. [110] developed ionic hydrogels based on cellulose that were highly stretchable, compressible, ion-conductive, highly transparent (with a transmission of $\sim 89\%$), and mechanically strong (stretchability of $\sim 126\%$ and compressibility of $\sim 80\%$). Furthermore, they exhibited tunable nature through controlled crosslinking densities and anti-freezing characteristics (effective at $-20\text{ }^{\circ}\text{C}$). Moreover, they proved to be useful for various electrical applications by demonstrating themselves as robust strain sensors for monitoring human motion. He et al. [111] developed a conductive hydrogel using a one-pot synthesis technique that includes gelatin-PVA along with Tara tannin and carbon nanotubes. This hydrogel shows remarkable mechanical properties, such as elongation ($\sim 760\%$), adhesion ($\sim 16\text{ kPa}$), and strain gauge factor ($GF \approx 6.79$). Moreover, the hydrogel exhibits quick healing properties ($\sim 99\%$) as well as adhesion repeatability under dry as well as wet conditions. It has shown promising results as a biocompatible material for different bodily motions, including finger movement, and also underwater. Comparative overview of different nanomaterial types, key properties, and applications in bioelectronic interfaces as mentioned in **Table 1**.

Table 1. Comparative overview of different nanomaterial types, their categories, composition matrices, electrical conductivity, key properties, and applications in bioelectronic interfaces.

Nanomaterial types	Categories	Composition matrix	Key properties	Application	References
Carbon-based nanomaterial	Graphene Oxide (GO)	GO layered with AuNPs and GdHCF	Large surface area, high biocompatibility, high adsorption capability	Electrochemical biosensor	Kumar et al. [112]
Carbon-based nanomaterial	CNT composite	CNT/PDMS composite	High electrical conductivity, tunable mechanical elasticity, high sensitivity (0.59 kPa^{-1}), low detection limit (12 Pa), fast response (25 ms), excellent cycling stability ($>1,700$ cycles),	Flexible piezoresistive pressure sensor	Qiao et al. [113]
Carbon-based nanomaterial	Graphene-based polymer nanocomposite	Graphene nanoplatelets (GNPs)/PDMS elastomer nanocomposite	High strain sensitivity ($GF = 140$), pressure sensitivity (260), stretchability (up to 20% strain), good cyclic stability and dynamic response	wearable electronics, artificial skin, human motion detection	Niu et al. [114]
Carbon-based nanomaterial	Carbon black	Chitosan-Carbon Black Composite (CH-CB)	High electrical conductivity, flexibility, stretchability, and biocompatibility	Wearable bioelectrodes, glucose biosensor	Buaki-Sogó et al. [115]
Metal-based nanomaterial	CuNPs	(SarOx/CH/CuNPs/c-MWCNT/Au) composite	High sensitivity ($277.5 \mu\text{A}/\mu\text{M}/\text{cm}^2$), ultra-low detection limit (0.1 pM), rapid response (2 s), excellent stability (180 days), and good reproducibility	Biosensor prostate cancer diagnosis	Narwal et al. [116]
Metal-based nanomaterial	ZnNPs	PEGylated Zinc Nanoparticles (ZnNPs)	Eco-friendly synthesis, excellent dispersion, and stability, nanoscale size (33.6–78.1 nm), strong antifungal activity, and biocompatibility	Biosensor,	Ammar et al. [117]
Metal-based nanomaterial	AgNPs	Ag@PDMS composite	High conductivity, excellent stretchability (up to 70% strain), high gauge factor (10.08), fast response time, good durability and repeatability,	human motion detection sensor	Soe et al. [118]
Metal-based nanomaterial	AuNPs	(AuNPs/CNTs/PDMS) composite	Ultra-high sensitivity (gauge factor 366.7), improved conductivity, and a wide linear strain range (0–15%) with excellent flexibility and stability.	Flexible strain sensor for wearable electronics and human motion detection	Zhao et al. [119]
Conductive Polymer	PANI	Carbon nanofiber (CNF)/polyaniline (PANI)/silicone rubber nanocomposite	Enhanced sensitivity (gauge factor 14 at 2% strain, 2.8 at 20%), good linearity, negligible hysteresis, high electrical conductivity, and flexibility.	Capacitive strain sensor for wearable electronics	Hosseini et al. [120]
Conductive Polymer	PEDOT:PSS	PEDOT: PSS/PDMS composite conductor	Good electrical conductivity, excellent flexibility and stretchability, tensile strength, transparency, and piezoresistive behavior	Wearable strain sensor for real-time human motion monitoring	Luo et al. [121]
Conductive Polymer	PPY	PPy polymerized in situ on FeCl_3 -PPy@PVA composite	High stretchability (up to 309.5% strain), good mechanical strength (32.8 MPa), moderate sensitivity (gauge factor ~ 5.07), flexibility,	Wearable strain sensor for physiological monitoring	Shi et al. [122]
Conductive Polymer	PEI	PEI/CNTs/polymer sponge composite	Enhanced adhesion between CNTs and the substrate, uniform conductive network formation, high sensitivity (0.57 kPa^{-1} at 0–20 kPa; 1.34 kPa^{-1} at 20–117 kPa), fast response (~ 160 ms), and excellent stability (8,000 cycles)	Flexible 3D pressure sensor	Cheng et al. [123]
Soft ionic material Hydrogel	Chitosan-Based Conductive Hydrogel	Double cross-linked P(AAm-co-AA)/CS- Fe^{3+} hydrogel	High mechanical strength (550 kPa), ultra-high stretchability (800%), good toughness, fast self-recovery (30 min), low hysteresis ($<100\%$), good conductivity, and high strain sensitivity ($GF = 6.6$)	Flexible wearable strain sensor for human motion monitoring	Li et al. [124]

Table 1. *Cont.*

Nanomaterial types	Categories	Composition matrix	Key properties	Application	References
Soft ionic material Hydrogel	Alginate-Based Conductive Hydrogel	PEDOT: PSS integrated with polyacrylamide (PAAm)-sodium alginate (SA) composite hydrogel	High stretchability (up to 500%), high sensitivity (GF = 11), ultra-low hysteresis (1.52%), strong interfacial adhesion, excellent mechanical stability, and good conductivity	Flexible wearable strain sensor	Cao et al. [125]
Soft ionic material Hydrogel	Gelatin-Based Conductive Hydrogel	Fish gelatin (FG) integrated with AgNPs, forming FG-Ag hydrogel	Ultra-high stretchability (2,600%), good sensitivity (GF ≈ 4), strong self-adhesion, excellent biocompatibility, antibacterial activity (against <i>E. coli</i> and <i>S. aureus</i>), and self-powered capability	Wearable strain sensor for human motion monitoring	Yan et al. [126]

5. Applications of nanomaterials in bioelectronics

Nano-bioelectronics is the synergistic interaction between nanotechnology and the miscellaneous nature of biological systems, which is a rapidly developing platform that combines nanomaterials and biology with flexible electronics, which offers the possibility of addressing the challenges in the field of bioelectronics [127]. Nanomaterials greatly increase the efficiency and performance of bioelectronic devices, from their large and rigid structure to their ultrathin structure. The special properties of nanomaterials, such as their conductivity, compatibility with biological systems, and their mechanically stable and flexible properties, allow versatile applications in the area of bioelectronics, ranging from biosensors to therapeutic devices [128]. The following sections will highlight the major uses of nanomaterials in the area of bioelectronics.

5.1. Nanoengineered neural interfaces and brain-computer integration

Over the past three decades, the field of neurotechnology has witnessed remarkable advancements. The use of nanomaterials in the field of bioelectronics has increased the efficacy of conventional approaches that incorporate microelectrode arrays for electrical connections, allowing the production of tiny and efficient neuroelectronic devices [129]. Neural interfaces function as crucial bridges between tissues and external devices, allowing the modulation and recording of neural activities through electrical, chemical, and optical methods. Neural interfaces (NIs) serve as essential links between biological tissues and external devices, facilitating the modulation and recording of neural activity using chemical, electrical, and optical techniques. The enhanced electrical properties of nanoscale materials have played a significant role in improving traditional neural interfaces. Recent advancements in neurotechnology have revealed applications of nanomaterials that extend beyond merely modulating or recording neural membrane potentials [130]. Brain-computer interfaces (BCIs) mimic the human ability to read and write through stimulation (also known as writing) and recording (reading using metamorphic/image or symbol) of the brain, as shown in **Figure 6**. For instance, Zhang et al. [131] designed novel polymeric micelles with a dual pH/chemically reducible switch using the disulfide-functionalized CPA as the backbone. The efficiency of these micelles in targeting tumors effectively, due to their capability of achieving charge reversal,

enhanced cellular uptake, and intracellular release of doxorubicin, was shown in enhancing anticancer efficacy while minimizing side effects, as shown in **Figure 6a**. Hu et al. [132] demonstrated that combining nanomaterial integration with nanoscale engineering in soft nanobioelectronics leads to marked improvements in conductivity, compliance, and biointerface performance, enabling robust multimodal operation and efficient bidirectional communication with central and peripheral neural systems, as shown in **Figure 6b**.

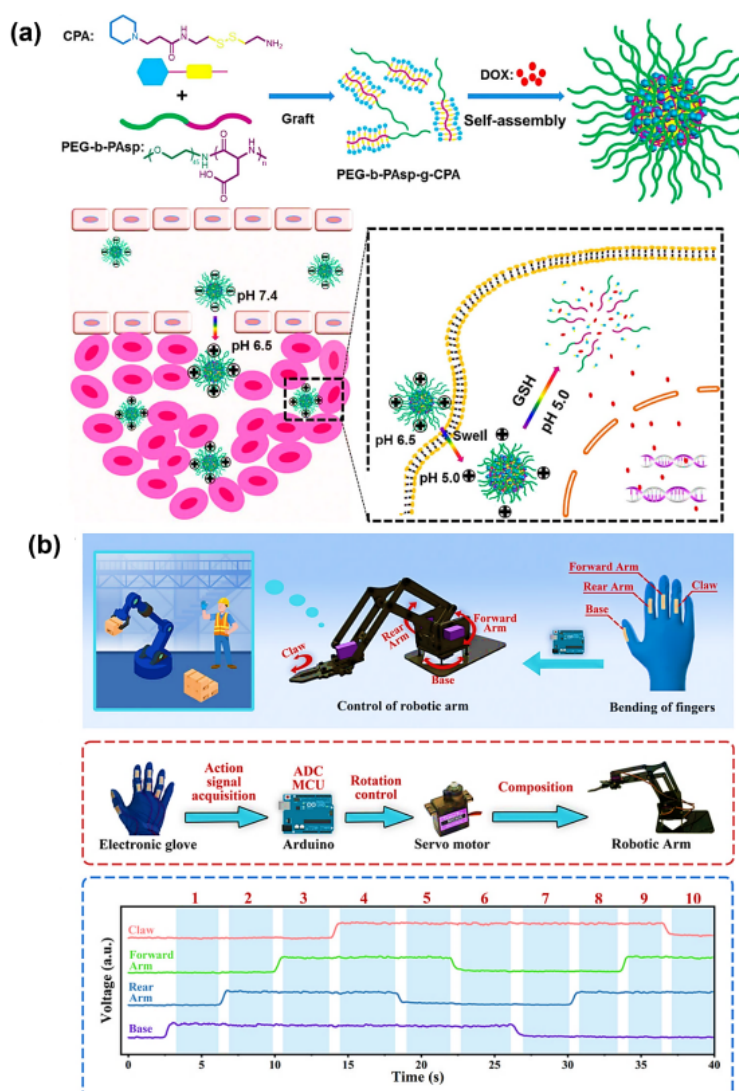


Figure 6. Schematic Illustration of the (a) Synthesis Procedures of PEG-b-PAsp-g-CPA/DOX Polymeric Micelles and the Processes of DOX Delivery; (b) Schematic illustration of the smart glove for human-machine interaction with a workflow diagram of the smart glove and data curves during the execution of a set of actions using the smart glove.

Source: **Figure 6a**: Reprinted with permission from Zhang et al. [131] Copyright 2021 American Chemical Society; **Figure 6b**: Hu et al. [132] Copyright 2025 American Chemical Society.

There are non-invasive data-driving sources such as electrocortigraphy (ECoG) and electroencephalography (EEG) [133]. Various studies have been published related to the monitoring and treatment of neurological disorders, e.g., Parkinson's disease and schizophrenia, in which dopamine (DA) is considered a major analyte in the neural system [134]. The level of DA can be tracked with high spatial and temporal precision, which is essential for comprehending, monitoring, diagnosing, and

tracking the progression of various diseases, as well as for formulating treatments. Carbon fiber electrodes in conjunction with fast scan cycle voltammetry have become the gold standard for dopamine detection *in vivo* due to their ability to provide detailed temporal resolution, enhanced sensitivity, and monitor the dynamic changes of neurotransmitters [135].

5.2. Implantable biosensors

Implantable biosensors are advanced medical devices that are employed for insertion into the human body to monitor biomarkers, physiological parameters, or health conditions for the treatment of patients [136]. The integration of various nanomaterials (carbon-based nanomaterials, metal-based nanomaterials, polymer-based nanomaterials) into implantable biosensors has significantly improved their performance, sensitivity, stability, biocompatibility, and utility for medical diagnostic applications. These nanomaterials have enabled the tracking of biological markers in real-time sensing, which is important for personalized medicine [137]. These forms of nanomaterials are biodegradable and generate minimal immune reactions, because they safely disintegrate within the body after the purpose has been accomplished, thereby avoiding difficulties that are critical for sustaining sensor functionality within live organisms [138]. The advancement of biosensors using nanomaterials has presented itself as an effective means of addressing the aforementioned issues and improving the detection and monitoring of periodontitis, an infection of the gums that affects the tissues surrounding the teeth. Nano-sensors, which incorporate particles such as silver and zinc oxide, show promising antimicrobial properties against commonly occurring oral pathogens such as *Aggregatibacter actinomycetemcomitans* and *Porphyromonas gingivalis*, which may help prevent the colonization of microbes responsible for periodontitis [139]. Recent developments in biosensors based on 2D NMs, such as graphene, enable the detection of various biomarkers, including pathogens, proteins, and nucleic acids. These graphene-based biosensors can be utilized to detect infectious agents, biomarkers of cancer, and environmental pollutants, which are a very sensitive and selective platform for diagnostic applications [140]. Thus, NMs-based biosensors can provide various benefits, including faster response rates, higher sensitivity, and miniaturization, compared to conventional biosensors and the fabrication of composite PLLA nanofiber scaffolds by the electrospinning technique, as shown in **Figure 7a**. For instance, the multielectrode array was fabricated by Truong et al. [141] using a flexible wide bandgap nanomembrane material and employed in implantable devices. Along with the ability to monitor properties such as temperature, stress/strain, and impedance, it exhibited exceptional bendability, chemical non-reactivity, and durability. It also succeeded in the *ex vivo* animal pacing of hearts, indicating its application as a reliable bioelectronic device, as shown in **Figure 7b**. For instance, Sun et al. [142] incorporated both chemically cross-linked and stimuli-responsive physical forces to develop an Upy/Tyr-modified gelatin-based conductive hydrogel that is compatible with living tissues. Due to the inclusion of PEDOT:PSS, the conductive hydrogel displayed excellent tissue adherence, elasticity, high conductivity, and self-healing

capacity. The potential of the hydrogel in next-generation wearable and implantable medical devices was highlighted through multimodal sensing of motion, temperature, and urea, and by functioning as a bidirectional neural interface, as shown in **Figure 7c**. A comparative overview of advanced sensing technologies, their applications, development stages, and associated challenges is presented in **Table 2**.

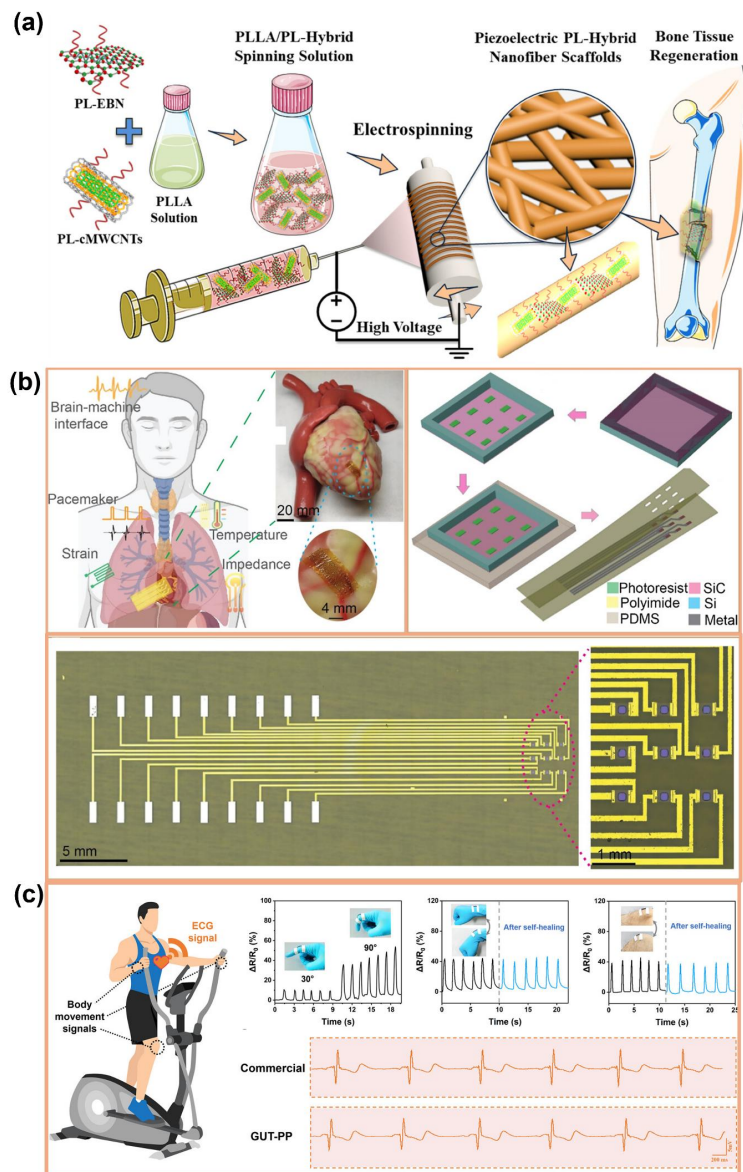


Figure 7. (a) Schematic representation of the fabrication of composite PLLA nanofiber scaffolds by the electrospinning technique; (b) Device overview: Schematic illustration of a chronic flexible MEA for multisensing and heart pacemaker with inset highlights the free-standing flexible MEA and flexible MEA on a phantom heart model. Main steps for fabrication of flexible chronic MEA, fabrication of free-standing membranes, backside photolithography, (iii) the transferring the membranes to a soft PDMS substrate for reactive ion etching (RIE), to (iv) soft transfer printing and achieving an MEA with three layers: the bottom PI substrate, the functional layer of metal interconnect and SiC electrodes, and the top encapsulation PI; (c) Multimodal tracking application of GUT-PP hydrogels as wearable sensors for physiological signal detection. Physiological and movement signal detection for fitness monitoring: schematic finger, wrist, and knee motions; wireless ECG signals.

Source: **Figure 7a:** Reprinted with permission from Ramasamy et al. [37] Copyright 2022 American Chemical Society; **Figure 7b:** Truong et al. [141] Copyright 2025 American Chemical Society; **Figure 7c:** Sun et al. [142] Copyright 2023 American Chemical Society.

Table 2. Comparative overview of advanced sensing technologies, their applications, development stages, and current challenges.

S. No.	Technology	Application area	Development stage	Challenges	References
1.	Graphene-based Sensors	Glucose, sweat analysis	Lab → Prototype	Scalability, reproducibility	Abdelfattah et al. [143]
2.	AI-integrated Wearables	Predictive health analytics	Early commercialization	Data privacy, algorithm bias	Patel [144]
3.	Gold Nanoparticle Sensors	Cancer biomarkers	Clinical trials	Cost, toxicity concerns	Hemdan et al. [145]
4.	Microfluidic Lab-on-Chip	Multiplex biomarker detection	Prototype → Early trials	Complexity, integration & fabrication	Cai et al. [146]
5.	Wearable Hydrogel Sensors	Strain, motion detection	Prototype	Long-term durability	Uyanga et al. [147]
6.	Electrochemical Paper Sensors	Point-of-care (POC) diagnostics	Prototype	Stability & mass production	Nayak et al. [148]
7.	Flexible Patches	Continuous monitoring	Early commercialization	Data accuracy, skin compatibility	Ferreira et al. [149]
8.	Optical Biosensors (Photonic)	Pathogen detection, blood analysis	Prototype	Sensitivity, miniaturization	Joshi et al. [150]
9.	Smart Textiles	Health monitoring	Research stage	Integration complexity	Wang et al. [151]
10.	Millimeter-wave Radar Sensors	Cardiopulmonary activity, vital signs	Dataset validation stage	Signal processing, clinical translation	Ahmed and Cho [152]
11.	Wireless Implantable Sensors	Long-term physiological monitoring	Pre-clinical/early trials	Power supply, biocompatibility	Ahamad et al. [153]

5.3. Wearable health monitoring devices

Wearable health monitoring devices can be defined as electronic gadgetry that can be worn in contact with the body, such as patches, wristbands, rings, smartwatches, and even smart clothing. These devices monitor, collect, and transmit health-related data about the patient. Wearable health monitoring devices have become vital in modern digital health, enabling remote patient monitoring, health management, and the detection of possible health concerns [154]. Wearable biosensors can effectively monitor the management and control of chronic diseases and mental health conditions such as diabetes, hypertension, and respiratory infections. Wearable biosensors can improve patient outcomes by providing real-time data and also monitoring stress and anxiety levels, thus providing biofeedback for self-regulation [155]. The advancements in digital health technology have also led to the use of nanomaterials to improve their biocompatibility, flexibility, and sensor technology in the real-time health monitoring process, as depicted in **Figure 8**. The use of nanomaterials such as nanocomposites, graphene, nanowires, carbon nanotubes, and quantum dots has provided a large surface area and unique electrical and mechanical properties, thus providing the detection of biomarkers and physiological parameters at low concentrations in bodily fluids [156]. Boschetto recently found that nanomaterials such as Carbon Nanotubes (CNTs) are used in sensors to monitor the respiratory rate and vital signs due to their high electrical conductivity and mechanical properties [157]. Additionally, graphene, being a two-dimensional material, provides remarkable flexibility and conductivity, which makes it suitable for wearable electrodes that monitor electrophysiological signals such as EEG and ECG [158]. The integration of nanomaterials with biosensors enhances sensing abilities and creates new opportunities for personalized medicine and remote patient monitoring. In a recent study Bi and Yuan [159] developed a

conducting hydrogel sensor that consisted of PVA/PEDOT: PSS, along with deep learning, which was used for motion disorder detection and continuous monitoring. The capability of being used in futuristic wearables for health care was established by this hydrogel because of its excellent conductivity, flexibility, anti-freezing nature, and biocompatibility. For instance, Tu et al. [160] synthesized an efficient dual network hydrogel that possesses excellent tensile strength (681 kPa), good flexibility (764%), and fast healing behavior (~99%). The hydrogel exhibits strong antimicrobial efficacy (~94%) against both *E. coli* and *S. aureus* bacteria and maintains stability throughout the large range of temperatures from -80 to 40 °C. Effective monitoring of movements under difficult circumstances is enabled by the gauge factor of the sensor of 2.32, along with fast response/recovery time (~200/300 ms).

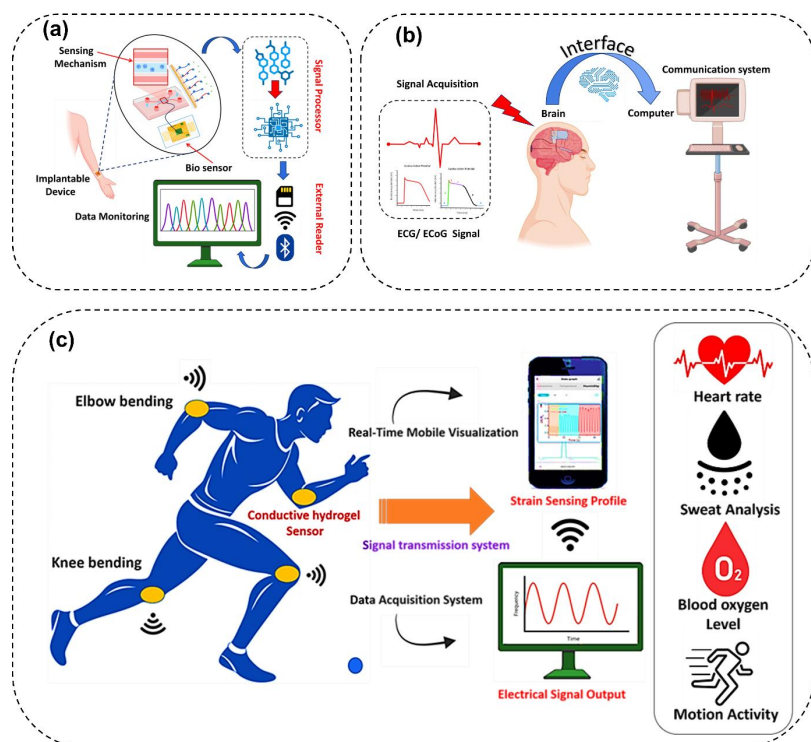


Figure 8. (a) Schematic diagram of a wearable health monitoring system with signal transmission; (b) Schematic flow of signal transmission in a brain-computer interface system; (c) Integrated schematic of an implantable biosensor with data acquisition and communication to an external monitoring unit.

5.4. Electrically active tissue scaffolds

Electrically active tissue scaffolds are specially designed structures that replicate the electrical microenvironment found in natural tissues. They facilitate cell growth, differentiation, tissue regeneration, and proliferation by delivering electrical signals. These scaffolds are especially important for tissues like skin, bone, nerves, and both cardiac and skeletal muscles, where electrical signaling is essential for proper function and healing [161]. Additionally, electrically active tissue scaffolds that utilize nanomaterials are sophisticated structures designed to offer both electrical conductivity and structural integrity, facilitating tissue regeneration by replicating the natural tissue microenvironment. These scaffolds are particularly important for tissues like muscle, nerves, and the heart, where electrical signaling plays a vital role in their function

and healing [162]. The tissue scaffolds created using 3D printing and electrospinning, which are functional and electrically conductive, along with nanomaterials, help in the creation of scaffolds with improved properties such as uniform thickness and porosity. These key properties are significant in tissue engineering, as they help provide a high surface area and porosity, thus promoting cell migration and growth, which in turn improves intercellular communication, which is significant in healing ischemic heart tissue and preventing arrhythmias. The tissue scaffolds created have shown promising results in both in vitro and in vivo experiments, thus indicating their possible application in clinical trials for regenerative medicine [163].

5.5. Smart drug delivery systems

Smart Drug Delivery Systems (SDDS) are innovative systems for the delivery of therapeutic agents with precision and control for better efficacy, reduced side effects, and dosage. Smart Drug Delivery Systems have been developed as an alternative to the conventional drug delivery systems (CDDS) techniques, which mostly involve the use of high doses and lack specificity. The SDDS systems make use of special delivery vehicles for the precise delivery of the medication [164]. In a recent study, Li et al. [165] incorporated thioketal bonds to form an SF/TK nanoparticle delivery system based on silk fibroin that responds to ROS. This system has shown itself to be highly efficient for intelligent and controlled delivery systems due to its responsiveness to ROS, which results in accelerated drug release under oxidation conditions, as shown in **Figure 9a**. The developments in nanotechnology have led to different applications of nanomaterial-based smart drug delivery systems, as shown in **Figure 9b**. In medicine, because of their targeted delivery and biocompatibility, and by making use of their responses to internal and external stimuli and their ability to target specific tissues or cells, nanomaterial-based smart drug delivery systems have numerous applications in medicine and healthcare [166]. This is because they have the potential for delivering drugs in a controlled manner, either through stimulus response, such as pH, enzymes, and temperature, or over a prolonged period of time. They take advantage of the unique properties of nanomaterials, such as surface characteristics, size, and encapsulation of drugs, to address the limitations of traditional drug delivery systems [167]. Son et al. [168] synthesized hyperbranched polyglycerol micelles using spiropyran as a light-activated drug delivery system. Their suitability for controlled drug delivery systems was emphasized through their reversible assembly and disassembly by photoisomerization, favorable CMCs, and good biocompatibility, as shown in **Figure 9c**. For instance, a novel UCAGMH nanoplatfom (60 nm) was designed by Yan et al. [169] to treat breast cancer and prevent its metastasis. In an acidic environment, the platform generated O₂ and Mn²⁺ ions, which facilitated multimodal imaging and synergistic PTT, PST, and CDT. Furthermore, angiogenesis, tumor progression, and liver metastasis were prevented due to HIF-1 α degradation, as shown in **Figure 9d**. The comparison of various biosensor platforms based on sensitivity, detection limit, stability, and response time is presented in **Table 3**.

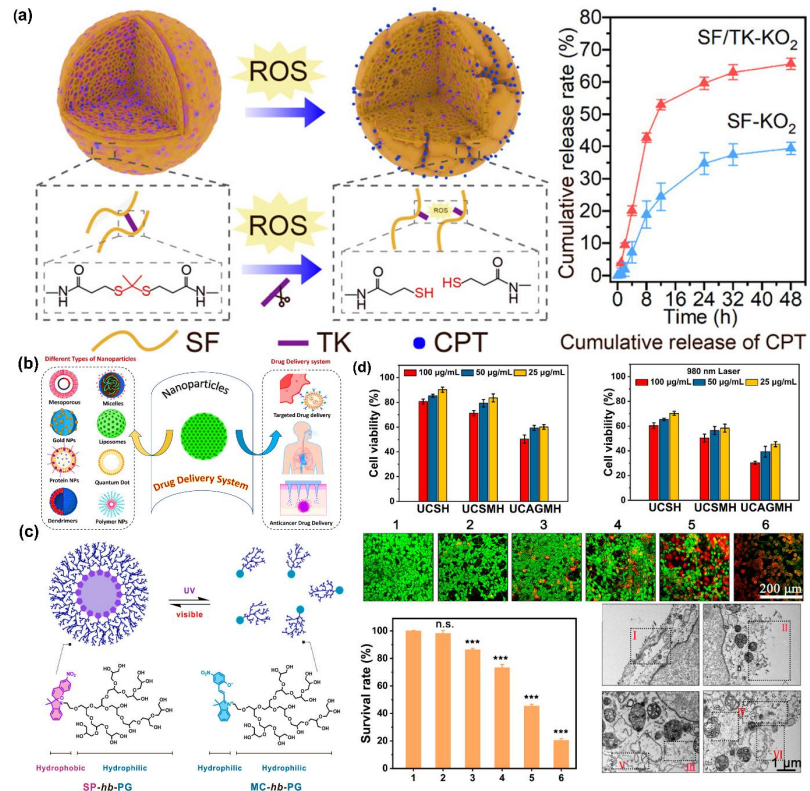


Figure 9. (a) ROS-responsive silk fibroin materials in smart drug delivery systems; (b) Illustrative diagram of different nanoparticle-mediated drug delivery pathways; (c) Light-responsive micelles of spiropyran-initiated hyperbranched polyglycerol for smart drug delivery; (d) Cellular cytotoxicity and treatment effect of UCAGMH. Cell viability (CCK-8) of 4T1 tumor cells of different materials at 12 h without or with a 980 nm laser, Calcein-AM/PI staining images of 4T1 cells, and fluorescence quantitative figures after various treatments, and a BioTEM image of cells incubated with UCAGMH for 6 h.

Source: **Figure 9a:** Reprinted with permission from Abdel-Karim [156] Copyright 2024 American Chemical Society; **Figure 9c:** Reprinted with permission from Boschetto et al. [157] Copyright 2014 American Chemical Society; **Figure 9d:** Reprinted with permission from Hossain et al. [158] Copyright 2022 American Chemical Society.

Table 3. Comparison of various biosensor platforms based on sensitivity, detection limit, stability, and response time.

S. No.	Sensor type	Sensitivity	Limit of detection (LOD)	Stability	Response time	References
1.	Electrochemical Sensors	High	nM–pM	Moderate–High	Fast	Patial et al. [170]
2.	Optical Sensors	Very High	pM–fM	Moderate	Moderate	Patial et al. [170]
3.	Wearable Strain Sensors	Moderate–High	Depends on the material	High	Very Fast	Ren and Cui [171]
4.	Enzymatic Biosensors	High	Low (µM–nM)	Limited (enzyme degradation)	Fast	Haque et al. [172]
5.	Non-enzymatic Sensors	Moderate	nM	High	Fast	Hassan et al. [173]
6.	Photonic Crystal Biosensors	Very High	fM	Moderate	Moderate	Gowdhami et al. [174]
7.	Nanomaterial-based Sensors	Very High	fM–aM	High (nanostructure stability)	Fast	Fritea et al. [175]
8.	Paper-based Biosensors	Moderate	µM–nM	Moderate (disposable format)	Fast	Das et al. [176]
9.	Field-Effect Transistor (FET) Biosensors	Very High	fM–aM	High (solid-state stability)	Very Fast	Zhou et al. [177]
10.	Piezoelectric Biosensors	High	nM–pM	High	Fast	Skládal [178]

6. Current challenges

In developing nanomaterials that can serve as the next generation of wearable bioelectronic interface materials, there are some barriers that are interrelated. The

most important issue is the problem of biocompatibility. Although nanomaterials provide excellent conductivity and mechanical flexibility, sustaining biocompatibility over time presents a difficulty [179]. While high surface areas of nanoparticles can help to increase efficiency in detection mechanisms, this same property makes them susceptible to parasitic reactions when used around biological fluids or electrolytes, especially at the early contact stage. Secondly, minimizing any inflammatory reactions when used for skin or implants is another important issue. Another area that presents considerable challenges is in relation to scalability and standardization within manufacturing processes. Although there has been success in developing techniques for use within the laboratory environment, scaling up to an industrial scale is challenging [180]. Moving from the laboratory bench to viable commercial applications requires more than simply technical improvements but also standardization of manufacturing procedures. Material consistency and cost-effectiveness are key issues that need to be addressed [181]. The problem with durability and environmental stability becomes even more prominent when the device is wearable. Flexible electronics and bioelectronics need to be able to withstand mechanical strains, temperature changes, moisture changes, and even corrosion in biological environments [182]. Drift signals, moisture effects, and the gradual decline of nanomaterial sensors greatly lower device reliability and performance. The mechanical stability of nanomaterials in repetitive mechanical strain is still a significant problem for devices that operate. Energy supply and power regulation are critical issues for true autonomy in wearable bioelectronics. Although energy generation using piezoelectricity, thermoelectricity, and triboelectricity is promising, the energy density obtained is inadequate for several applications. However, the implementation of such devices faces the challenge of ensuring reliable data and high-quality signals [183]. It becomes imperative for wearable sensors to achieve high signal-to-noise ratios even when working under conditions that have many variables affecting the process of taking measurements. There is also an additional challenge presented by the need to ensure real-time processing of the data collected and security during wireless transmission of the data within the healthcare system.

7. Future perspectives and emerging directions

The future of flexible bioelectronics lies in multifunctional and stimulus-responsive materials. Recent developments have been made toward the creation of nanomaterials that will provide functions such as sensing, energy generation, and treatment [184]. For example, MXene-based systems have great potential as intelligent bioelectronic systems that not only sense but also store energy. Self-healing and stimulus-responsive hydrogels are other avenues that could revolutionize the field of bioelectronics by providing adaptable and resilient devices [185]. The integration of AI and machine learning techniques with wearable bioelectronic technology can revolutionize the way diagnostics are performed. AI-assisted designs make it possible for calibration and intelligent interpretation of collected data, allowing for predictions regarding the health status of the subject [186]. The combination of nanotechnology and computational intelligence can provide new opportunities for medical diagnosis.

Nanomaterials that are eco-friendly and biodegradable are another important area of research focus. Current trends are toward making nanomaterials that are not only more sustainable but also environmentally friendly and based on biological substances, as opposed to implants that will never decompose [187]. Another interesting approach involves using biologically engineered materials along with piezoelectric systems made out of peptides to achieve greater biocompatibility and sustainability. The development of advanced manufacturing technologies is still ongoing, especially in the aspect of scalability and economic feasibility [188]. The photolithography techniques used in silicon electronics have shown much potential in fabricating high-resolution and replicable organic bioelectronics. It is possible to incorporate both additive and subtractive manufacturing techniques to manufacture complex multi-functional structures through hybrid manufacturing routes [189]. The creation of such fully integrated, closed-loop bioelectronic systems is an area of great exploration [190]. Instead of having independent sensors, in the future, it will be expected to have systems that can sense, process information, and give out treatments, thus forming a complete health care system in one device.

8. Conclusion

This review examined how next-generation nanomaterials are remaking the bioelectronic interface landscape. The future of bioelectronics is undoubtedly dependent on materials that are both technologically advanced and biologically compatible, as evidenced by the significance of softness, surface chemistry, and nanoscale interactions, as well as the development of materials that can bend, conform, and communicate with biological tissues. Nanomaterials are powering performance enhancements and opening up completely new capabilities in wearable monitors, smart medicine delivery systems, and brain devices. Bioelectronic systems that are not only smaller and smarter but also more patient-friendly, intuitive, and adaptable are the way forward. We anticipate devices that can understand, absorb information, and react in real-time at the intersection of digital health, AI, and nanotechnology, resulting in closed-loop systems that treat and monitor concurrently. Although it will be crucial to overcome the present manufacturing and regulatory challenges, there is exciting and achievable potential to revolutionize human-machine interaction, treatment, and personalized healthcare.

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