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Review

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Implantable flexible neuroelectrodes: advances in material innovation, structural design, and performance optimization

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Abstract: In recent years, implantable neuroelectrodes have been widely applied in various fields, including deep brain electrical stimulation, neuroprosthesis, and recording neuronal electrical activity in neuroscience research. However, with the rapid advancement of neuroscience and brain–computer interface technology, the limitations of traditional rigid neuroelectrodes have become increasingly evident. Flexible neuroelectrodes constructed from soft materials are emerging as a key research focus in the neural interface field. This review presents a systematic classification of the material selection, structural design, and key performance of implantable flexible neuroelectrodes and analyzes the optimization of achieving electrode flexibility in avoiding tissue damage and immune response. Furthermore, we summarized the contemporary challenges in performance optimization and material innovation, proposing potential solutions. By integrating and reviewing existing innovative approaches to flexible implantable neuroelectrodes, this review aims to provide an important theoretical foundation and technical guidance for the development of high-performance implantable neuroelectrodes.

Key words: Implantable; Neuroelectrode; Electrode material; Electrode structure; Electrode key performance

1 Introduction

Neural interface technology is an essential bridge connecting the human nervous system with external devices and holds substantial potential for application in the fields of brain–computer interface, neuroprosthesis, and neuromodulation therapy, thereby enabling the treatment of epilepsy (Khodagholy et al., 2011; Fan et al., 2019; Ahmed Taha et al., 2024), Parkinson's disease (Mahlknecht et al., 2018; Jia et al., 2024; Shah et al., 2024; Cui et al., 2025), deafness (Boisvert et al., 2020; Tian et al., 2023), blindness (Palanker and Goetz, 2018; Mirochnik and Pezaris, 2019), and other neurological disorders. Electrode arrays such as cochlear implants for hearing restoration and prostheses for vision reconstruction are currently in use. Neuroelectrodes are core technological components that accurately record bioelectrical signals as information or transmit stimulatory electrical signals to neural tissues to modulate biological functions (Stieglitz et al., 2000; Zhang et al., 2019; Park et al., 2022). Early neuroelectrodes predominantly used rigid materials such as metal- and silicon-based materials. Although they provide excellent conductivity, their physical properties and biocompatibility have limited their technological development. First, the Young's modulus of rigid materials is much higher than that of brain tissue. After implantation, mechanical stress can be easily generated owing to physiological pulsation, resulting in nerve cell damage and glial scar formation, making it difficult to realize long-term and stable signal acquisition (Luo et al., 2011; Sharafkhani et al., 2022; Hu et al., 2023; Ren et al., 2024; Khan et al., 2025). Second, adapting rigid structures to 3D surfaces is difficult, limiting the accurate localization of deep or irregular areas. The emergence of flexible neuroelectrodes has solved the

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inherent limitations of rigid electrodes through the dual breakthrough of material innovation and structural design. Switching from rigid to softer electrode materials, such as hydrogels, or designing traditional planar structures into lattice-like structures can help mitigate mechanical damage and immune-reactivity, thereby achieving long-term recording stability. Breakthroughs in material science and flexible electronics have transitioned neuroelectrodes from high modulus, low biocompatibility, short-term applicability, and single function to low modulus, high biocompatibility, long-term and stable applicability, and multifunctional integration. Such a novel flexible electrode expands the application of traditional rigid electrodes, plays an important role in the long-term management of neurodegenerative diseases, and helps sensory function reconstruction.

These flexible neuroelectrodes can be implanted in the nerve tissue to achieve a high degree of fit, reducing the mechanical damage and immune response to the surrounding tissues. The flexibility of electrodes can generally be divided into two categories: material flexibility, mainly owing to the soft and bendable properties of the material used; structural flexibility, achieved through an electrode with a unique structural design, for example, ultrathin electrodes and mesh structures. Although the material is relatively rigid, the fabricated electrode exhibits good flexibility and deformability owing to the design of these special structures, which can better fit tissues and cause minimal damage.

While recent reviews have extensively covered individual material classes or fabrication techniques, a comprehensive understanding of how to balance conflicting design requirements for long-term implantation remains limited. Unlike the literature, this review establishes a multidimensional framework to address the chronic reliability of neural interfaces. First, at the material level, this review provides a systematic classification of flexible conductive materials and evaluates their intrinsic physical and chemical characteristics for achieving mechanical compliance with neural tissue. Second, at the structural level, this paper reviews the engineering of neuroelectrodes across 1D, 2D, and 3D configurations to optimize tissue integration. Finally, in terms of performance, this paper focuses on two core pillars. The first involves electrical properties required for high-fidelity recording and safe stimulation, while the second centers on long-term stability strategies, such as biocompatible coatings, to ensure reliability within harsh physiological environments. By integrating material selection, structural design, and performance optimization, this review provides a roadmap for overcoming the bottlenecks of current flexible neural electrodes and achieving stable and long-term neuroprosthetic function (Fig. 1).

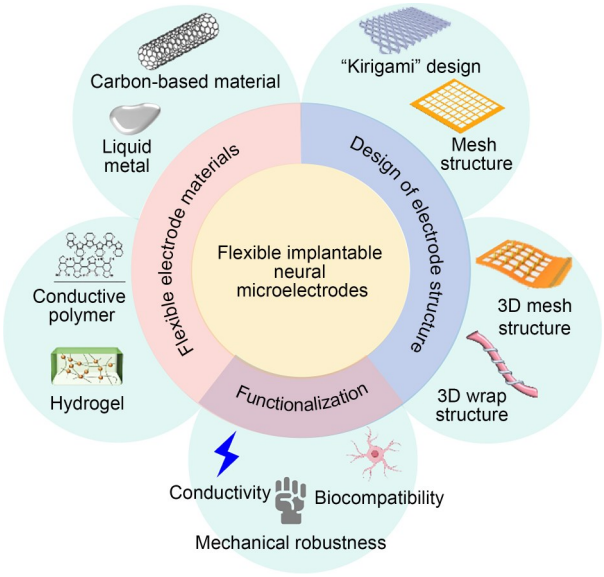


Fig. 1 Construction of flexible implantable neuroelectrodes from material and structural viewpoints

2 Core conductive material selection

The core function of implantable flexible neural electrodes lies in enabling the long-term and stable recording of neural electrical signals as well as precise and safe stimulation. This places multiple stringent demands on their core conductive materials, including intrinsic mechanical properties compatible with neural soft tissue, outstanding intrinsic conductivity and electrochemical activity, good intrinsic biocompatibility and long-term in vivo stability, and formability and interfacial bonding capabilities suitable for micro- and nanofabrication processes. Currently, the conductive materials widely used in related research are primarily classified into three major categories: metallic materials, carbon-based materials (Deng et al., 2011; Zhang and Lieber, 2016; Ryu et al., 2017; Wang et al., 2019; Saunier et al., 2020), and conductive polymer (CP) materials (Cui and Martin, 2003; Castagnola et al., 2015; Pranti et al., 2018; Yang et al., 2023). The following sections

will provide a systematic analysis of the intrinsic properties and research progress of representative materials within each category.

2.1 Metallic materials

Metal-based electrodes are the first large-scale commercial implantable electrode materials to have been clinically translated and are currently the most widely used. However, conventional systems primarily consist of bulk pure metals (e.g., Pt and Au), whose inherent high stiffness easily causes mechanical mismatch and tissue damage after implantation. To meet the growing demand for flexible implantable electrodes, it is essential to maintain high electrical conductivity while significantly reducing the effective modulus. Currently, research focuses on two main strategies to address this challenge. The first strategy transforms traditional bulk metals into nanostructures (such as nanoparticles (NPs) and nanowires (NWs)), while the second directly utilizes emerging liquid metals (LMs) that combine excellent conductivity with extreme deformability.

First, traditional bulk metals can be transformed into nanoscale architectures to overcome the inherent mechanical limitations of conventional planar metals. One approach involves developing nanostructured metal coatings to replace rigid solid metal films. These nanostructures not only significantly enhance the material surface area and density of electrochemically active sites but also offer better structural compliance than continuous rigid films. For example, Boehler et al. (2020) designed a nanostructured Pt electrode coating (Fig. 2a), and Wu et al. (2024) constructed a PEDOT/3-MPA-AuNP layer, where PEDOT is the poly(3,4-ethylenedioxythiophene) and 3-MPA is the 3-mercaptopropionic acid (Fig. 2b). However, these delicate nanostructures are prone to detachment during chronic micromotion, potentially causing inflammation. To fundamentally enhance the intrinsic mechanical durability of the conductive network, an alternative nanoscale approach is to transform bulk metals into high-aspect-ratio structures (such as AuNWs). Rather than relying on surface coatings, this approach utilizes the bending flexibility of 1D materials to balance the continuity of the conductive path with mechanical toughness. Seufert et al. (2024) developed a novel flexible electrode fabricated using high-aspect-ratio AuNWs (Figs. 2c and 2d). This strategy enables the electrode to maintain conductive pathways even under bending or slight stretching, making it suitable for surface arrays attached to the cerebral cortex. Although metal NWs balance conductivity with fatigue resistance, their fabrication complexity often limits electrode density.

Second, in contrast to solid metals, LMs offer a fundamental solution to fracture risks due to their unique fluidity. However, the primary challenge for LMs is the risk of leakage. To mitigate leakage, advanced encapsulation and structural confinement strategies are essential. Chung et al. (2024) designed a 3D stimulation electrode by integrating a flexible ultrathin phototransistor and eutectic gallium–indium (EGaIn) alloy. The alloy was 3D-printed as a high-resolution stimulation electrode and encapsulated with parylene C (PC). This pinhole-free polymer coating serves as a robust physical barrier to effectively prevent LM leakage into surrounding tissues (Fig. 2e). Zhou et al. (2025) developed a LM fiber mat as an implantable physiological electrode, combining high durability, breathability, and long-term biocompatibility; it was based on AgNPs, LMs, and porous poly(styrene block chain diene-methylene-methylene pen) (pSBS) fiber mats. In this design, leakage is prevented through the structural confinement provided by the porous pSBS network and the stabilization effect of AgNPs, which anchor the LMs within the fiber matrix (Figs. 2f and 2g). Dong et al. (2021) fabricated highly stretchable neural electrode arrays mainly employing LMs and polydimethylsiloxane (PDMS). This approach addresses the leakage issue through a sandwich encapsulation strategy, where the LM channels are fully sealed within the biocompatible PDMS elastomer, ensuring isolation from the biological environment (Figs. 2h and 2i). LM electrodes eliminate fracture risks but trade fabrication resolution for extreme stretchability. The primary challenge lies in ensuring long-term encapsulation safety to prevent leakage, which restricts high-density micropatterning. Consequently, LMs are less suitable for high-channel-count cortical recording but are ideal for high-strain environments, such as spinal cord or muscular interfaces, where mechanical compliance is critical.

2.2 Carbon-based materials

Carbon-based materials exhibit high electrical conductivity, exceptional chemical stability, and excellent biocompatibility, making them highly compelling

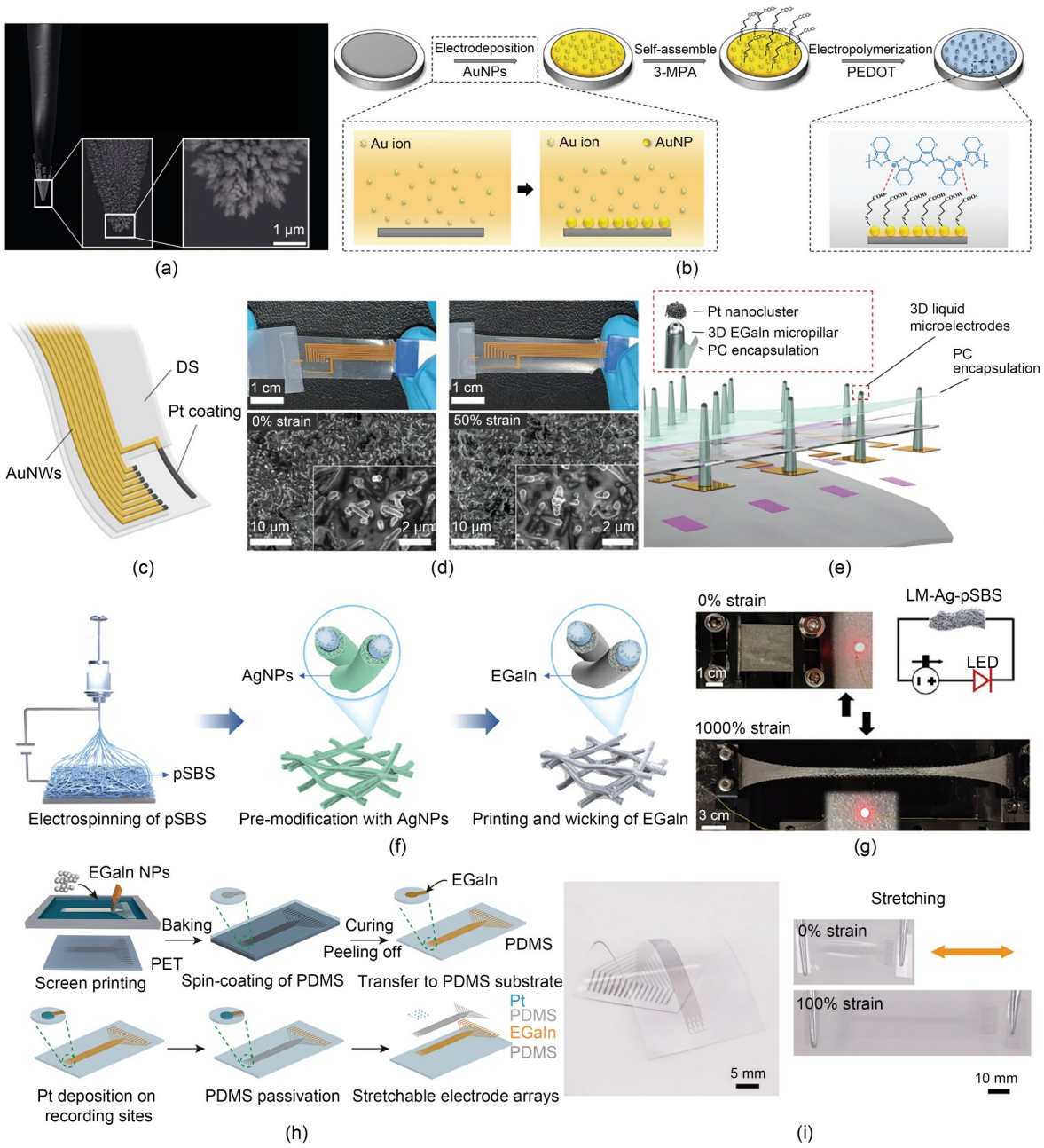


Fig. 2 Flexible neuroelectrodes based on metallic materials: (a) nanostructured Pt electrode coating on conical probes (reprinted from (Boehler et al., 2020), Copyright 2020, with permission from American Chemical Society); (b) schematic indicating the preparation process of the PEDOT/3-MPA-AuNP neural electrodes (reprinted from (Wu et al., 2024), Copyright 2024, with permission from John Wiley and Sons); (c) schematic of the multielectrode cuff based on soft AuNW–silicone composite; (d) photographs and SEM characterization of the multielectrode cuff in relaxed and stretched states (Seufert et al., 2024); (e) schematic of an artificial retina based on integrating a phototransistor with 3D LM microelectrodes (electrode structures are shown in the upper left corner) (Chung et al., 2024); (f) fabrication process of LM-Ag-pSBS physiologic electrodes; (g) digital photos illustrating the deformation of LM-Ag-pSBS under 0% and 1000% strain (reprinted from (Zhou et al., 2025), Copyright 2025, with permission from John Wiley and Sons); (h) schematic indicating the fabrication of stretchable electrode arrays utilizing screen printing; (i) optical microscopy images of LM neural electrodes and their photographs after stretching under 0% and 100% strain (reprinted from (Dong et al., 2021), Copyright 2021, with permission from John Wiley and Sons). DS is the dextran sulfate; SEM is the scanning electron microscopy; MeOH is the methanol; PSS is the poly(styrene sulfonate); PDA is the polydopamine; LED is the light-emitting diode; PET is the poly(ethylene terephthalate)

candidates for fabricating flexible neural interfaces. The carbonaceous materials most commonly employed in this domain include graphene, carbon nanotubes (CNTs), and polymer-derived carbon. The following sections systematically review the structural designs and fabrication strategies associated with these distinct carbon-based microelectrodes.

Graphene-based materials are highly valued in neural engineering for their exceptional intrinsic properties and remarkable versatility in physical form factors. While graphene can be synthesized through various mainstream approaches—such as mechanical exfoliation, oxidation–reduction techniques, and chemical vapor deposition (CVD)—the chosen synthesis method fundamentally dictates the resulting design of the electrode. For instance, Viana et al. (2024) developed thin-film microelectrodes using nanoporous graphene (NPG) grown via CVD (Figs. 3a and 3b). To further enhance

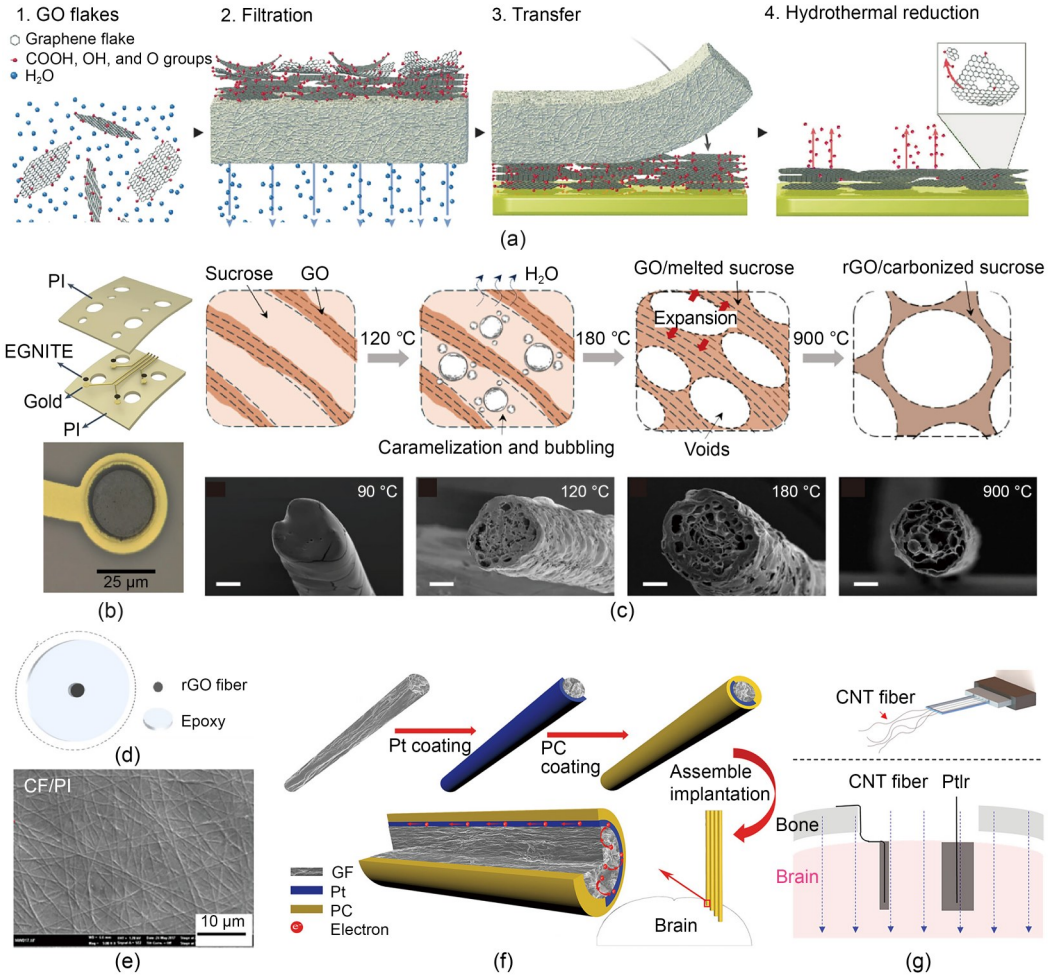


Fig. 3 Flexible neuroelectrodes fabricated using carbon-based materials: (a) schematic indicating the preparation of the porous and reduced GO film, EGNITE; (b) schematic (up) describing the fabrication of the EGNITE flexible microelectrode array and a micrograph (down) of 25 μm diameter EGNITE microelectrodes (Viana et al., 2024); (c) schematic representation (up) of the mechanism underlying the evolution of GO/sucrose hydrogel fibers during heat treatment and the microstructures (down) of the GO fibers solidified in a 50% weight sucrose bath (GO-50) after vacuum drying at 90, 120, 180, and 900 °C, respectively; (d) fabrication of a single recording electrode by employing rGO–epoxy fibers (reprinted from (Dong et al., 2025), Copyright 2025, with permission from American Chemical Society); (e) SEM image of a CF mat embedded in PI (reprinted from (Vomero et al., 2020), Copyright 2020, with permission from John Wiley and Sons); (f) schematic indicating GF-Pt microelectrode fabrication (reprinted from (Wang et al., 2019), Copyright 2019, with permission from John Wiley and Sons); (g) schematic of the soft and MRI-compatible CNT fiber electrode (reprinted from (Lu et al., 2019), Copyright 2019, with permission from American Chemical Society). GO is the graphene oxide; PI is the polyimide; EGNITE is the engineered graphene for neural interface; rGO is the reduced graphene oxide; CF is the carbon fiber; GF is the graphene fiber; PtIr is the platinum–iridium alloy; MRI is the magnetic resonance imaging

these planar structures through interface engineering, Dong et al. (2025) proposed flexible graphene-based microelectrodes with tunable porous structures through optimized synthesis and posttreatment, significantly enhancing neural recording performance (Figs. 3c and 3d). Furthermore, to achieve extreme mechanical compliance, Wang et al. (2019) utilized wet-spinning strategies to prepare 1D graphene fiber-based microelectrodes, offering the extreme flexibility needed to accurately capture weak neuroelectric signals (Fig. 3e). However, the widespread implementation and clinical translation of graphene are often hindered by the complexities and scalability of these precise manufacturing processes. Despite these fabrication challenges, its outstanding electrochemical characteristics, tunable physical forms, and superior tissue conformability make graphene a highly promising candidate for developing high-resolution and conformal neural interfaces and ultraflexible microelectrodes.

Owing to their unique 1D morphology and exceptional mechanical properties, CNTs have emerged as highly compelling candidates for flexible neural interfaces. Although individual CNTs are typically synthesized at the nanoscale via CVD, arc discharge, or laser ablation, translating these nanomaterials into functional implantable devices fundamentally relies on assembling them into macroscopic architectures. For instance, Lu et al. (2019) developed soft and MRI-compatible neural electrodes from CNT fibers fabricated through solution spinning and twisting processes (Fig. 3f). Furthermore, beyond 1D fibers, the high electrical conductivity, large electroactive surface area, and extraordinary mechanical flexibility of macroscopically assembled CNTs make them equally suitable for fabricating highly sensitive cortical surface microelectrode arrays. Despite these functional advantages, the biosafety of CNT-based neuroelectrodes remains a controversial issue. While surface-functionalized and properly dispersed CNTs generally exhibit favorable biocompatibility, unmodified or heavily agglomerated CNTs can induce oxidative stress, severe inflammatory responses, and potential cytotoxicity in neural tissues. Consequently, rigorous surface engineering and dispersion controls are essential prerequisites for their safe clinical translation.

Polymer-derived carbon materials, such as glassy carbon and PI-based carbon, offer a compelling combination of electrical conductivity, excellent biocompatibility, and compatibility with standard microfabrication processes. These properties enable the creation of structurally stable and customizable carbon-based neuroelectrodes. For example, Vomero et al. (2020) developed a flexible bioelectronic device featuring micropatterned monolithic CF pads on a PI substrate, achieved through the pyrolysis of photoresist precursors (Fig. 3g). However, the physical assembly of individual microscopic CFs into dense arrays is highly labor-intensive, which severely restricts their lateral spatial resolution. Consequently, such assembled CF arrays are less viable for high-density flexible surface electrocorticography (ECoG), although they remain exceptional tools for targeted deep-brain recordings where insertion trajectory precision and a minimal footprint are critical. To overcome the scalability limitations of individual fibers, researchers have increasingly turned to photolithographically patterned glassy carbon. In a separate study, Vomero et al. (2017) developed a novel glassy carbon electrode material that features an ultrasmall footprint and sufficient structural stiffness to optimally facilitate tissue penetration while minimizing acute insertion trauma. Similarly, Castagnola et al. (2025) utilized photolithography to fabricate a glassy carbon microelectrode array capable of multimodal neural monitoring, enabling simultaneous electrophysiological recording and neurotransmitter detection. Despite these advanced microfabrication capabilities, photolithographically derived glassy carbon is inherently brittle and susceptible to cracking under significant dynamic deformation. Therefore, rather than being applied in highly dynamic environments (such as peripheral nerves), polymer-derived carbon is optimally suited for cortical surface arrays subjected to minimal mechanical strain or as structurally robust penetrating probes for long-term and stable chronic implantation.

2.3 Conductive polymer materials

Surface chemical modification of CP materials is highly adaptable; they also possess good biocompatibility and inherent softness, making them attractive candidates for bridging the mechanical gap between soft neural tissue and electronic devices (Cui and Martin, 2003; Marzocchi et al., 2015; Wang et al., 2017; Aqrawe et al., 2018; Feig et al., 2018; Liu et al., 2018; Yang et al., 2023; Lee et al., 2024; Ma et al., 2024). Based on their structural composition and conductive mechanisms, CPs applied in neural electrophysiology can be broadly

classified into two main categories: intrinsically conductive polymers (ICPs) and conductive polymer composites (CPCs).

ICPs achieve electronic conduction through delocalized π bonds in their main chains. The most common ICPs used for fabricating electrodes are PEDOT (Cui and Zhou, 2007; Venkatraman et al., 2011; Green et al., 2012; Khodagholy et al., 2013; Mandal et al., 2014), polypyrrole (PPy), poly(5-nitroindole) (PIN-5NO$_2$), and polyaniline. Through electrochemical polymerization or film-forming processes, it is possible to create extremely thin and flexible interfaces that adhere closely to biological tissues. For instance, Abidian and Martin (2008) developed an implantable neuroelectrode modified with PPy and PEDOT nanotube polymers (Fig. 4a). Middya et al. (2025) developed a

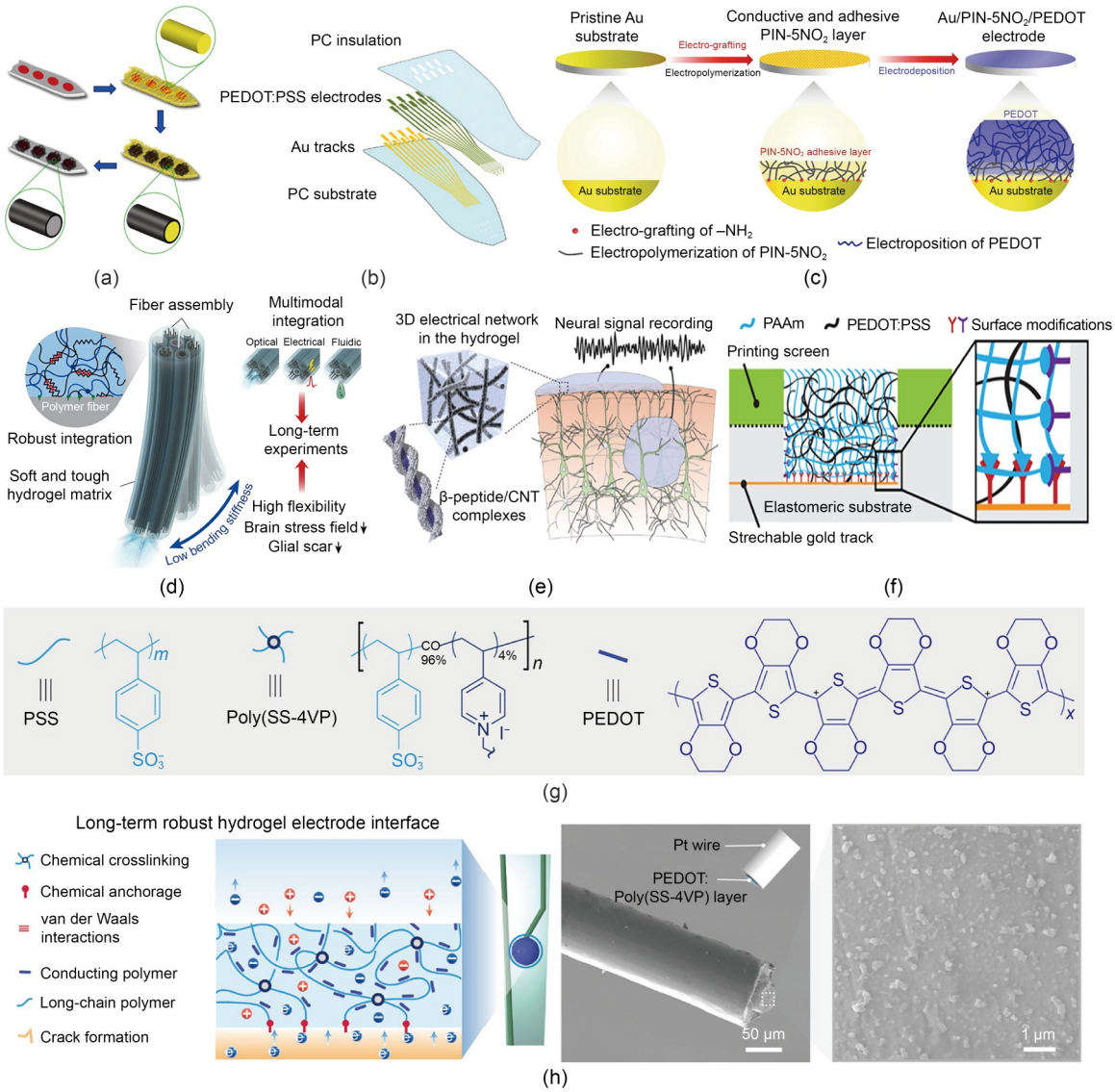


Fig. 4 Flexible neuroelectrodes fabricated using CPs: (a) schematic describing the preparation of CP nanotubes (Abidian and Martin, 2008); (b) schematic of the PEDOT:PSS-based ECoG array (Middya et al., 2025); (c) schematic representation of the Au/PIN-5NO$_2$/PEDOT electrode fabrication process (reprinted from (Yang et al., 2021), Copyright 2021, with permission from John Wiley and Sons); (d) design of an adaptive and multifunctional hydrogel hybrid probe (Park et al., 2021); (e) schematic of the supramolecular, β-peptide, and hydrogel-based electrode (reprinted from (Nam et al., 2020), Copyright 2020, with permission from American Chemical Society); (f) schematic of the PAAm-PEDOT:PSS-based hydrogel electrode (Shur et al., 2020); (g) conceptual diagram of the CP hydrogel coating; (h) SEM image of the PEDOT:Poly(SS-4VP) layer present on the Pt wire (reprinted from (Zhang JJ et al., 2023), Copyright 2023, with permission from John Wiley and Sons). PAAm is the polyacrylamide; Poly(SS-4VP) is the poly(4-styrenesulfonate-co-4-vinylpyridine)

PEDOT:PSS-based ECoG array that enables simultaneous electrophysiology and MRI studies (Fig. 4b). Furthermore, Yang et al. (2021) designed robust PEDOT neural interfaces using a PIN-5NO_2 film as an interfacial layer (Fig. 4c). However, ICPs tend to be quite brittle and are prone to cracking under large deformations, which limits their application in highly dynamic environments.

CPCs refer to composite systems formed by embedding conductive fillers into flexible polymer matrices (such as hydrogels or elastomers) to achieve a critical balance between high mechanical toughness and electrical conductivity. Depending on the desired electrochemical and mechanical profiles, various filler materials can be utilized. One primary approach involves metal-based composite fillers, where metal NPs or NWs are incorporated into a polymer matrix. This strategy leverages the high intrinsic conductivity of metals to construct a low-impedance interface. As a demonstration of this concept, Park et al. (2021) used Sn as the core conductive phase to prepare multielectrode fibers via a polymer thermal stretching process. Following surface functionalization, these fibers were seamlessly integrated into a hydrogel matrix to create a robust metal–polymer composite conductive interface (Fig. 4d). Alternatively, carbon-based composite fillers can be employed to enhance the structural integrity of the interface. By taking advantage of the superior electrical and mechanical properties of carbon materials, these composites simultaneously improve the electrical conductivity and mechanical toughness of the host polymer matrix. For example, Nam et al. (2020) developed a flexible neural interface composed of nonprotein hydrolyzed β-peptides and CNTs assembled in a hierarchical structure. Within this design, the β-peptide and conductive nanomaterials formed a 3D electrical network that effectively enhanced brain signal acquisition (Fig. 4e). Beyond metallic and carbonaceous materials, another effective strategy is the development of ICP–filler composites. Illustrating this approach, Shur et al. (2020) reported a screen-printable PAAm-PEDOT:PSS conductive hydrogel (Fig. 4f). By blending inherently CPs with soft insulating polymer networks, researchers can mimic the hydrated microenvironment of biological tissues while maintaining efficient charge transport and elastic mechanical properties. Building on similar principles, Zhang JJ et al. (2023) prepared a PEDOT:Poly(SS-4VP) interpenetrating network hydrogel to modify a bioelectrode, achieving long-lasting and stable electrophysiological recordings and electrical stimulation (Figs. 4g and 4h). While the integration of substantial amounts of insulating polymers inevitably leads to a trade-off by reducing the overall electrical conductivity, these composite strategies remain essential for long-term chronic implants in dynamic environments. Their tissue-like modulus significantly mitigates mechanical mismatch, accommodates brain micromotions, and minimizes foreign body responses, thereby ensuring the enduring stability of the neural–electrode interface.

3 Structural design

Selecting electrode materials with a low Young's modulus and flexible polymer substrates can significantly reduce the stiffness of nerve electrodes. However, the electrode structure design is also crucial to enhance the electrode flexibility and deformability through a proper structural design to better fit the complex curved surface of the nerve tissue.

3.1 One-dimensional structure

Silicon-based probes, represented by classic Michigan arrays, have long served as the standard for intracortical recording. These rigid shanks allow for precise depth insertion but often suffer from mechanical mismatch with soft brain tissue (Wise et al., 2004). Extensive research has shown that reducing the size and stiffness of nerve probes can dramatically suppress the trauma caused during insertion. Ultraflexible and micron-sized electrodes are well adapted to curved blood vessels, effectively reducing the risk of bleeding during penetration. They can work normally without causing significant interference to the surrounding tissue. Luan et al. (2017) designed and fabricated subcellular-sized and ultraflexible nanoelectronic wires (NET-50 and NET-10) that can stably detect and track neural activity over long periods and enable seamless subcellular integration with local cell and vasculature system networks (Fig. 5). While traditional 1D probes offer established fabrication processes, emerging 1D and implantable neuroelectrodes possess high temporal resolution and signal quality, with a significantly reduced chronic immune response. Moving from rigid shanks to ultraflexible threads represents a trade-off

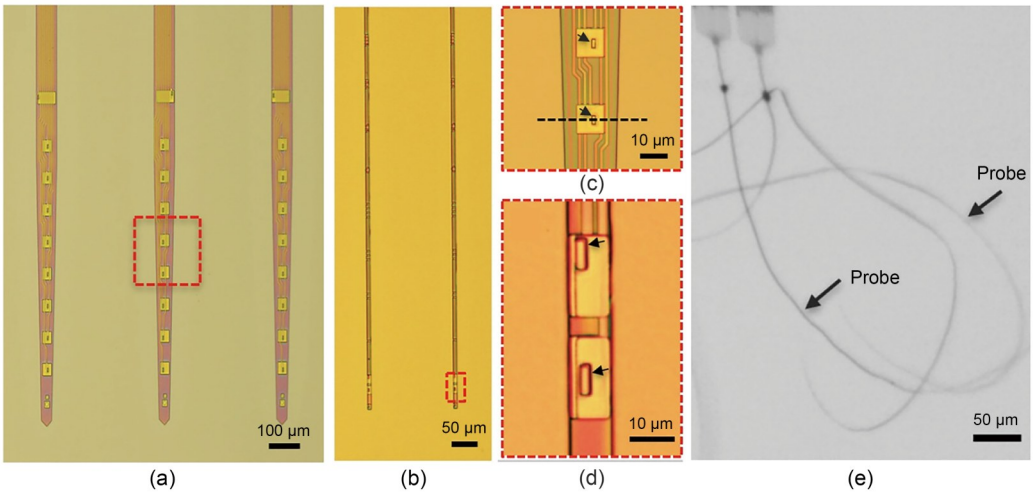


Fig. 5 One-dimensional electrodes comprising a nanoelectronic wire nerve probe: (a) NET-50 probe view; (b) NET-10 probe view; (c and d) magnified views of the two electrodes marked by red dashed boxes in (a) and (b), respectively; (e) multiple NET-10 probes suspended in water (Luan et al., 2017)

between insertion feasibility and chronic biocompatibility. While traditional probes (e.g., Michigan arrays) offer easy depth targeting but cause chronic tissue damage, subcellular-sized threads minimize inflammation at the cost of requiring complex insertion aids (e.g., stiff shuttles). Thus, ultraflexible 1D designs are superior for long-term and stable neural tracking, where minimizing the foreign body response outweighs the initial surgical complexity.

3.2 Two-dimensional structures

3.2.1 Flexible film electrodes

Planar electrodes are widely employed for ECoG to record macroscopic field potentials from the cortical surface. Ultrathin electrodes have a certain degree of flexibility, allowing conformal attachment to the curved surfaces of the neural tissues for the long-term recording of ECoG and local field potential (LFP). Lee et al. (2023) designed an ultrathin and minimally invasive neural probe (NeuroWeb) consisting of hexagonal boron nitride (h-BN) and graphene, with a total thickness of 100 nm (Figs. 6a and 6b). Khodagholy et al. (2013) designed an organic electrochemical transistor embedded in an ultrathin organic film based on PEDOT:PSS, Au, and PC (Figs. 6c and 6d). Ultrathin planar films prioritize noninvasive conformability over depth resolution. While excellent for minimizing cortical compression and mapping macroscopic network dynamics (ECoG/LFP), they fundamentally trade off single-unit specificity for safety. Consequently, solid film designs are limited to applications requiring broad surface monitoring, as they cannot access deep neural spiking or facilitate fluid exchange across the blood–brain barrier, such as open-mesh structures.

3.2.2 Mesh and kirigami

The grid-like design provides more detection sites, enabling the electrodes to simultaneously record nerve signals from multiple sites and facilitate a better fitting of the electrodes to the nerves. Morikawa et al. (2018) designed an electrode consisting of a PC polymer as a substrate and a nonstretchable metallic material, Pt/Ti, as an electrode material; it possessed the properties of high stretchability and deformability after patterning into a kirigami structure (Figs. 7a–7c). Li et al. (2022) designed a stretchable mesh-based microelectronic system employing conductive hydrogel electrode arrays consisting of PEDOT:PSS and the elastomer poly(styrene-ethylene-butadiene-styrene) (SEBS) as a substrate and encapsulant (Figs. 7d–7f). Zhang AQ et al. (2023) designed a polymer-based and ultraflexible microvascular endovascular (MEV) nerve probe loaded into a flexible microcatheter. The mesh structure relaxed and unfolded after injection; the microcatheter was then retracted, allowing the MEV probe to remain in place (Figs. 7g and 7h). Furthermore, Ryu et al. (2024) prepared multifunctional and nanogrid-structured electrodes based on a three-layer material of PC, Au, and PEDOT:PSS (Figs. 7i and 7j). Mesh and kirigami architectures solve the fluid permeability and

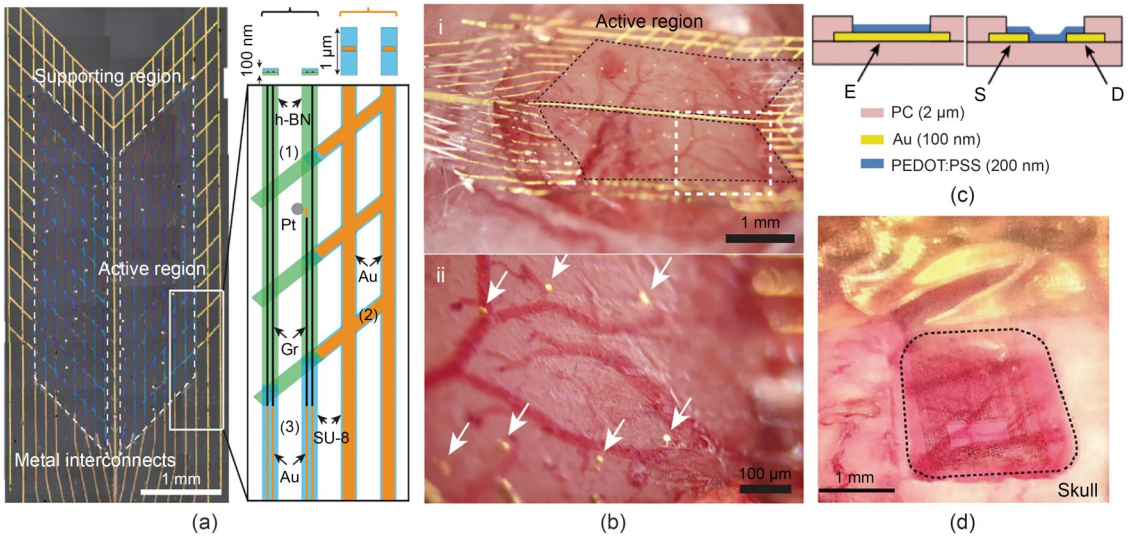


Fig. 6 Flexible thin-film electrodes: (a) optical microscopy images of the artificial neural nets; (b) (i) magnified image of the active region of the neural net (black dashed line) and (ii) magnified image of the white dashed box in (i); (c) structure of the ECoG probe; (d) optical micrograph of the ECoG probe placed on the somatosensory cortex (Khodagholy et al., 2013). (1), (2), and (3) in Fig. 6a denote the active region, supporting region, and metal interconnects, respectively, including h-BN (green), Gr (black), Pt (gray), SU-8 (blue, epoxy negative photoresist), and Au (orange). E, S, and D in Fig. 6c denote the electrode, source, and drain pad, respectively

stretchability limitations of solid films, enabling true tissue integration. The critical trade-off lies in deployment complexity and structural fragility. Expanding these delicate networks often necessitates specialized delivery tools. Therefore, these open designs are superior for endovascular approaches.

Compared to 1D neuroelectrodes, 2D structured electrodes have a higher spatial resolution and cover a wider neural area. However, it is difficult to accurately distinguish and record signals from nerve cells distributed at different depths and varied locations using 2D electrodes.

3.3 Three-dimensional structures

Three-dimensional electrodes allow for the all-around and 3D recording of neural activity. The Utah array is the most prominent example of a 3D electrode, consisting of rigid silicon microneedles that enable high-density population recording (Campbell et al., 1991). However, such rigidity limits conformity to soft tissues. To overcome this, novel 3D designs focus on accurate localization and selective stimulation while enhancing flexibility. Lee et al. (2025) developed a one-step and microelectrothermoforming (μETF) technology to fabricate flexible microelectrodes into neural interfaces with 3D microstructures for improved neural recording and stimulation (Fig. 8a). Hiendlmeier et al. (2023) designed an electrode that can self-fold into a nerve cuff during insertion. It incorporates a sodium acrylate hydrogel, which swells maximally when immersed in an aqueous solution, allowing the electrode to gently fold around the nerve (Fig. 8b). Zhu et al. (2024) developed helical electrodes for peripheral nerves using a bilayer rollable silk protein membrane and a micro-electromechanical system (MEMS) process (Figs. 8c and 8d). Xiang et al. (2016) fabricated biocompatible, microneedle, and 3D electrodes utilizing stretch lithography (Fig. 8e). Dong et al. (2024) developed a cuff that actively wraps around nerves when driven by a voltage (V) of a few hundred millivolts. This smart nerve cuff uses dodecylbenzene sulfonate-doped polypyrrole (PPy(DBS)) as the actuating material, which can significantly change its volume under electrochemical stimulation. As the process is reversible, the cuff can withstand hundreds of folding and unfolding cycles within the physical environment and be adjusted multiple times to fit the nerve better (Figs. 8f–8h). Although 3D electrodes enable comprehensive neural recording, they rely heavily on high-precision micromachining and entail greater invasiveness than surface arrays. The evolution from rigid Utah arrays to soft 3D architectures fundamentally trades implantation simplicity for chronic biocompatibility. Despite the elevated fabrication and surgical

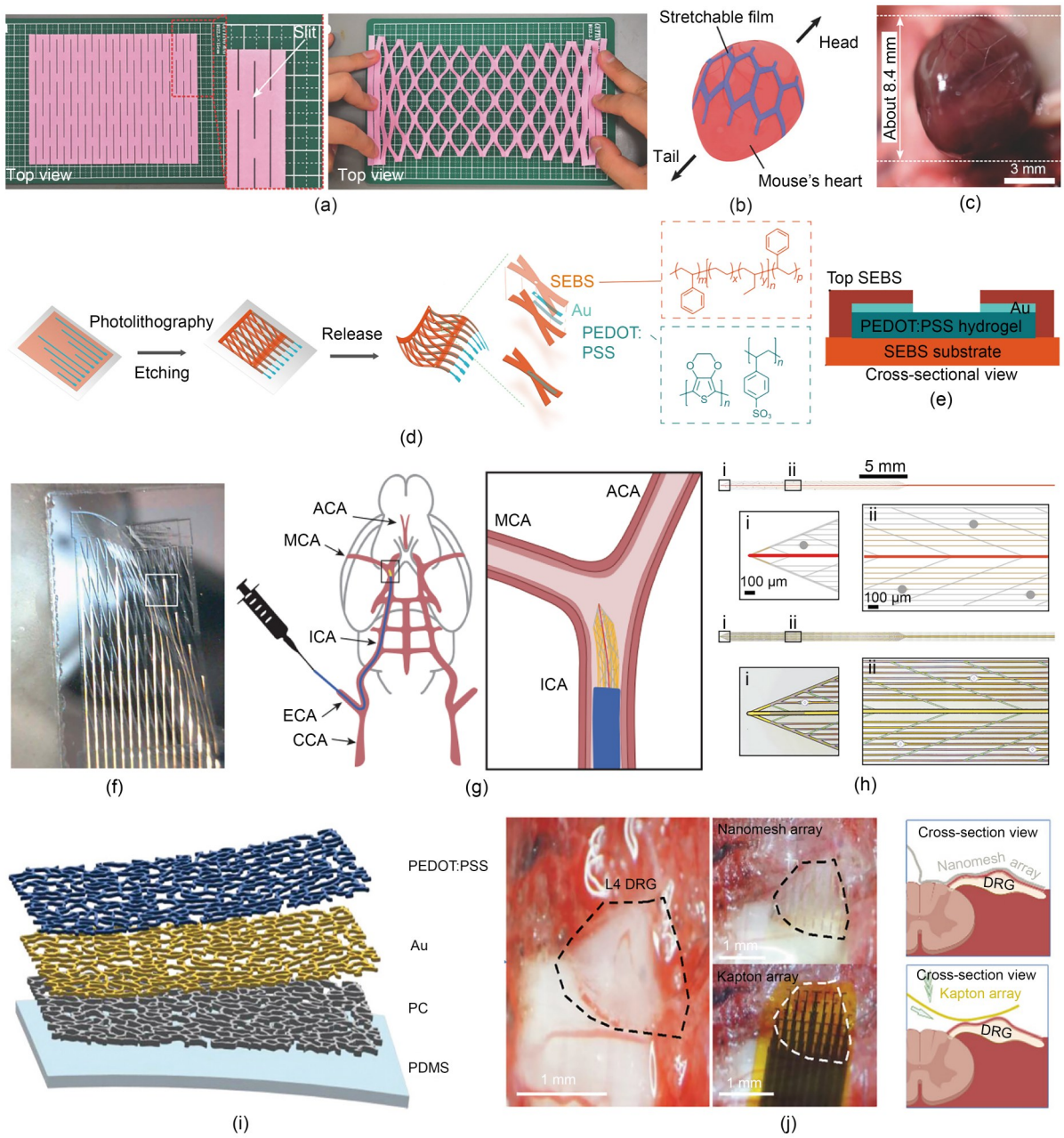


Fig. 7 Flexible mesh planar electrodes: (a) photographs and schematic diagrams of the stretched kirigami paper (120 mm× 160 mm); (b and c) schematic diagram and photograph of artificial PC films placed on a beating mouse heart (reprinted from (Morikawa et al., 2018), Copyright 2018, with permission from John Wiley and Sons); (d) stretchable SEBS and PEDOT: PSS materials patterned into a grid-like shape and their fabrication process; (e) cross-sectional view of the electrode design; (f) photograph of the mesh electrode (Li et al., 2022); (g) schematic of the endovascular implantation procedure; (h) enlarged view of the MEV probe tip (up) and recording electrode (down) (Zhang AQ et al., 2023); (i) detailed view of the multifunctional and nanonet-composed film; (j) in a similar design, a 64-ch nanomesh elastic electrode and 64-ch Kapton arrays placed in the same DRG region and the nanoweb elastic electrode arrays that were more conformal (reprinted from (Ryu et al., 2024), Copyright 2024, with permission from John Wiley and Sons). ACA, MCA, ICA, ECA, and CCA are the anterior cerebral, middle cerebral, internal carotid, external carotid, and common carotid arteries, respectively; L4 DRG is the 4th lumbar dorsal root ganglion

complexity, these conformal designs remain essential for high-fidelity volumetric mapping and dynamic peripheral interfaces, offering significant advantages in signal quality over planar alternatives.

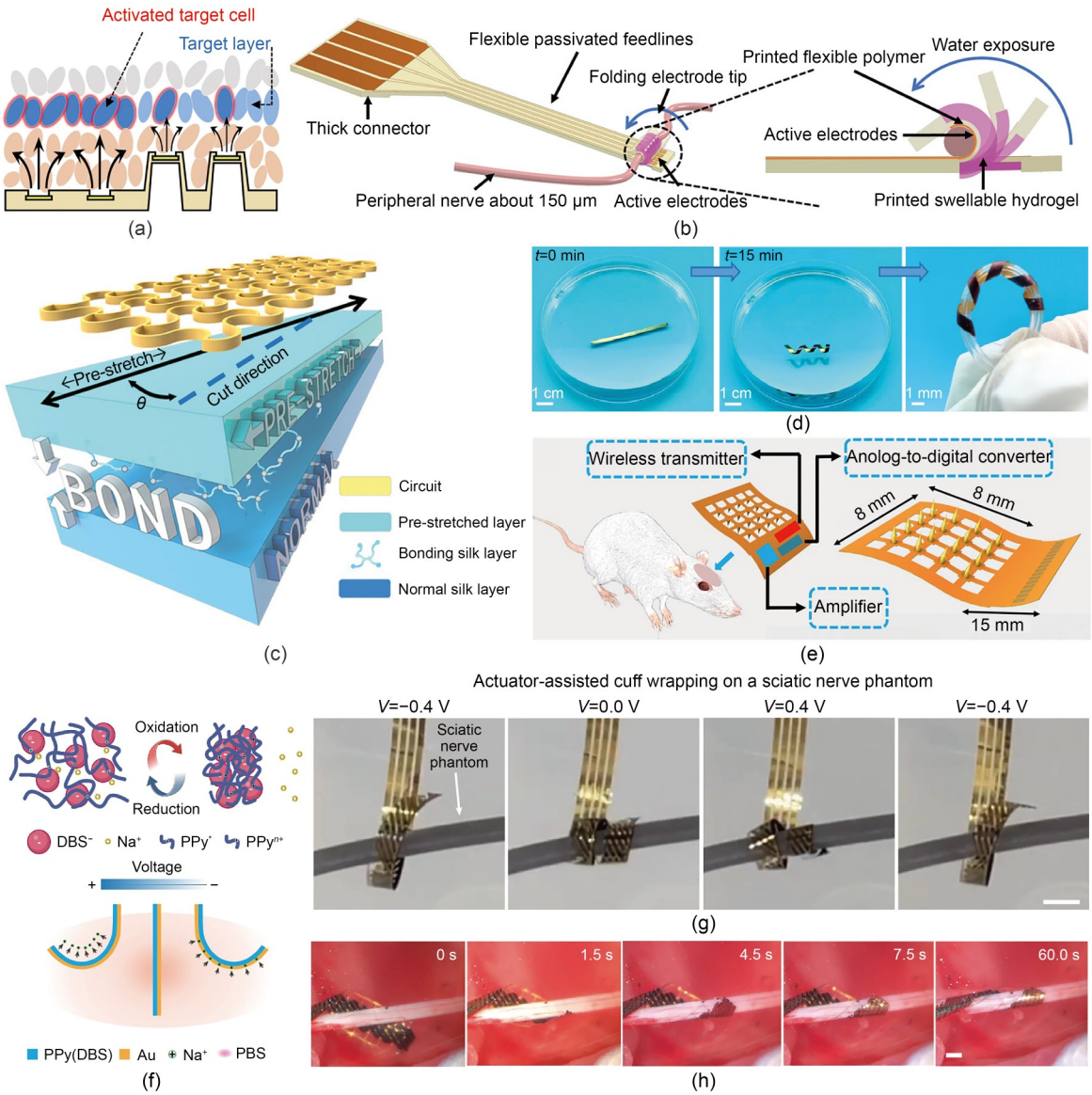


Fig. 8 Flexible 3D electrodes: (a) benefits of localized neural interfaces achieved through 3D structures (Lee et al., 2025); (b) schematic of the cuff electrode with a collapsible tip and a close-up side view of the electrode tip (Hiendlmeier et al., 2023); (c) schematic representing the standard reconfigurable silk bioelectronic device concept; (d) photographs of a neural cuff during deformation and the bending of a silicone tube over time (t) (reprinted from (Zhu et al., 2024), Copyright 2024, with permission from John Wiley and Sons); (e) design and geometry of a flexible microneedle electrode (Xiang et al., 2016); (f) schematic indicating the volume changes in PPy(DBS) and the reversible bending motion in PBS solution induced by binding to Au; (g) nerve cuffs at different voltages; (h) nerve envelope automatically wrapping the sciatic nerve when the voltage is switched from −0.5 to 0.0 V over time (Dong et al., 2024). θ is the angle between the pre-stretching direction and the cutting direction; PBS is the phosphate buffered saline

4 Vital properties of the implantable neuroelectrodes

Implantable neuroelectrodes act as the key interface connecting the nervous system and electronic instruments. Their performance directly determines the accuracy of neural signal acquisition, reliability of long-term implantation, and safety in clinical applications. The performance requirements for flexible microelectrodes have currently shifted to multidimensional synergistic optimization. In the following sections, this paper will focus on two key

parameters, namely, electrical performance and long-term stability.

4.1 Electrical properties

Electrical performance is the core element that determines the functioning of an electrode. While low impedance and high signal-to-noise ratio (SNR) are essential for recording (Lim et al., 2021; Neto et al., 2021; Zeng et al., 2022; Horváth et al., 2024), parameters related to electrical stimulation, specifically charge storage capacity (CSC) and charge injection limit (CIL), are equally critical for therapeutic applications. A high CSC ensures sufficient charge delivery within safe voltage limits, while the CIL defines the maximum charge density that can be injected reversibly without inducing harmful faradaic reactions or tissue damage. Table 1 summarizes the electrochemical properties of various neuroelectrodes reported in recent studies.

To push the boundaries of recording and stimulation efficacy, contemporary electrode designs rely heavily on a dual approach: maximizing the effective electrochemical surface area and integrating advanced pseudocapacitive materials. First, surface nanostructuring significantly increases the electrochemical surface area, thereby boosting the CSC. For example, Zeng et al. (2022) developed platinum-iridium oxide (Pt-IrO_x) neuroelectrodes based on a nanocone array structure, which provided a large surface area for charge transfer, and the CSC and CIL reached (52.44±2.53) and (4.39±0.36) mC/cm^2, respectively. In a related study, the same group demonstrated that electrodepositing iridium oxide (IrO_x) onto Pt nanocones could achieve a low impedance of 2.45 kΩ·cm^2 at 1 kHz and a high CSC of 22.29 mC/cm^2 (Figs. 9a and 9b) (Zeng et al., 2017). Fiáth et al. (2018) developed a silicon-based neural probe integrated with densely packed low-impedance titanium nitride (TiN) microelectrodes, enabling ultrahigh-resolution in vivo neural electrophysiological recording (Fig. 9c). Second, incorporating CPs and carbon nanomaterials creates hybrid composites with exceptional CSCs. For instance, Chen et al. (2020) designed a nanotunnel-like coating of PEDOT and CNTs, which markedly reduced impedance and increased CSC by facilitating ion transport (Figs. 9d–9f). Reddy et al. (2019) and Lee et al. (2019) demonstrated that PEDOT-based nanohybrids (with bionanotubes or GO) could significantly improve electrochemical stability and durability. Additionally, Huang et al. (2022) developed PDA-doped PEDOT interfaces to enhance bioactivity and electrochemical performance. The CSC of the PEDOT/PDAM-modified electrodes is approximately 21.00 mC/cm^2, reaching 2.3 times that of unmodified electrodes, where PDAM is the polydopamine melanin (Figs. 9g–9i). More recently, Yan et al. (2023) prepared PEDOT/PSS/PVA interpenetrating conducting polymer network (ICPN), where PVA is the poly (vinyl alcohol), which effectively combined the high conductivity of polymers with the soft mechanics of hydrogels, leading to robust electrical stability and enhanced charge storage performance (Figs. 9j and 9k).

4.2 Long-term stability

Neuroelectrodes must be stable for longer periods after surgical implantation, and their performance must meet certain standards. For long-term applications, a low Young's modulus may provide a certain degree of protection against loss of performance due to encapsulation by microglia. In the previous discussion, we introduced ways to achieve flexibility at the material and structural level. Next, we focus on other strategies that can enhance the long-term stability of electrodes. Specifically, surface engineering, such as implementing immuno-modulatory coatings to mitigate foreign body responses and reinforcing interfacial adhesion to prevent material delamination, is essential.

Table 1 Comparison of electrochemical properties of neuroelectrodes

Electrode material	Impedance at 1 kHz	CSC (mC/cm^2)	CIL (mC/cm^2)	Reference
Pt-IrO_x nanocones	(0.72±0.04) kΩ·cm^2	52.44±2.53	4.39±0.36	Zeng et al. (2022)
PEDOT/bionanotube	130 Ω	>11.00	N/A	Reddy et al. (2019)
PEDOT/CNT nanotunnels	(2.6±0.4) kΩ	26.30±2.40	N/A	Chen et al. (2020)
Electrodeposited IrO_x on Pt nanocones	2.45 kΩ·cm^2	22.29	N/A	Zeng et al. (2017)
PEDOT/PDAM	<100 Ω	≈21.00	N/A	Huang et al. (2022)
PEDOT-hydrogel ICPN	1.14 kΩ	216.54±9.61	N/A	Yan et al. (2023)

All impedances are tested at 1 kHz and are divided into two forms: absolute impedance (Ω or kΩ) and area-normalized interface impedance (kΩ·cm^2)

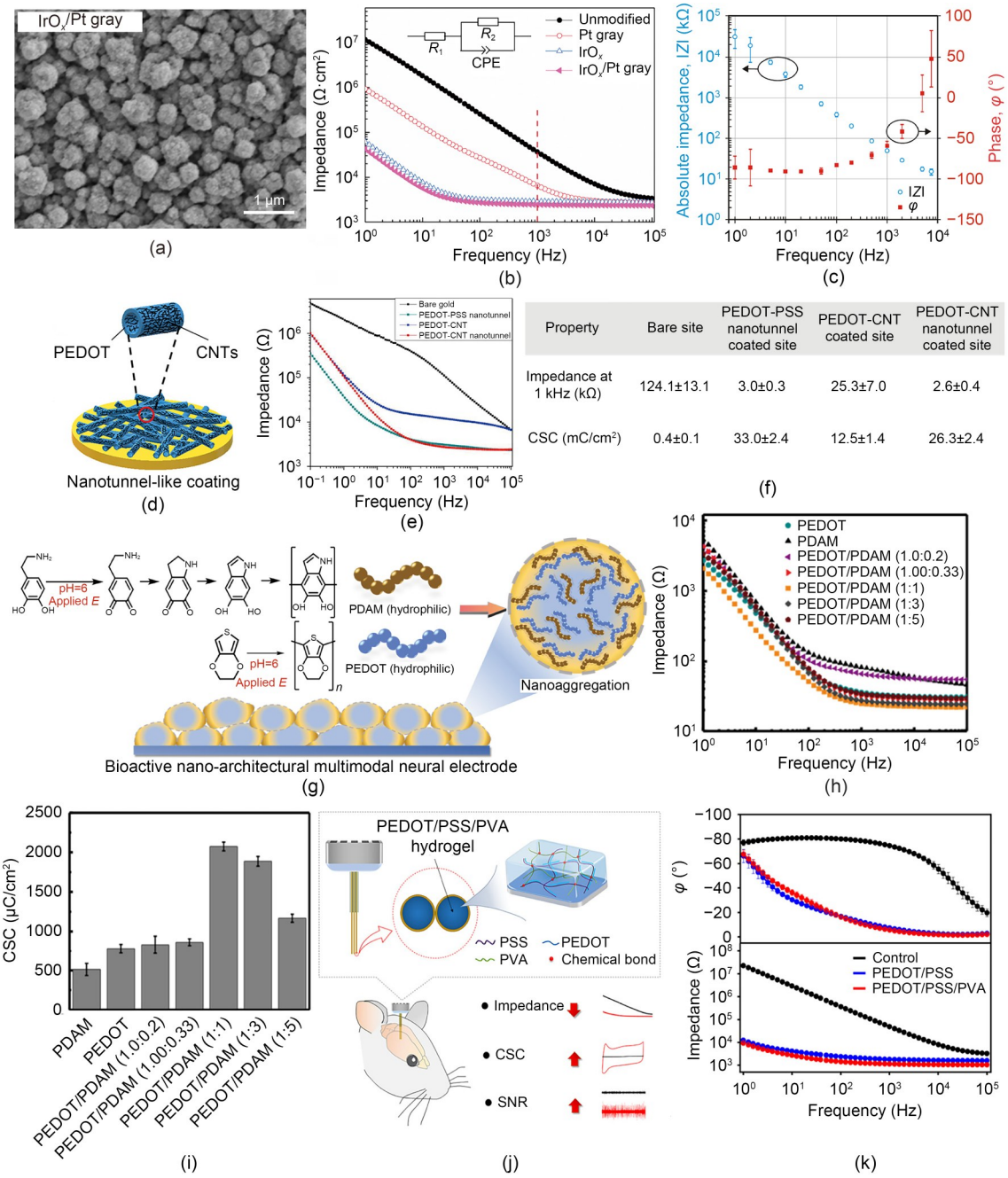


Fig. 9 Strategies to enhance the electrical performance of flexible neuroelectrodes: (a) SEM images of the IrO_x/Pt gray-coated microelectrodes; (b) Bode's plot indicating the electrochemical impedance of the IrO_x/Pt-coated microelectrodes (reprinted from (Zeng et al., 2017), Copyright 2017, with permission from Elsevier); (c) absolute impedance and phase values for TiN electrodes measured at 13 different frequencies (Fiáth et al., 2018); (d) schematic of the PEDOT-CNT nanotunnel-like coating; (e) alternating current impedance spectra of bare and coated electrodes; (f) electrochemical properties of bare and coated electrodes (reprinted from (Chen et al., 2020), Copyright 2020, with permission from American Chemical Society); (g) schematic diagram indicating the synthesis of the self-assembled nanostructured PEDOT/PDAM membrane; (h and i) measured impedance values and calculated CSCs at 1 kHz for membranes with different PEDOT/PDAM ratios (reprinted from (Huang et al., 2022), Copyright 2022, with permission from American Chemical Society); (j) schematic of the PEDOT/PSS/PVA ICPN; (k) Bode's plots of the electrochemical impedance of bare Pt, PEDOT/PSS-modified Pt, and ICPN-modified Pt electrodes (reprinted from (Yan et al., 2023), Copyright 2023, with permission from American Chemical Society). R_1 and R_2 are the solution resistance and charge transfer resistance, respectively; CPE is the constant phase element; E is the electric potential

The following studies highlight recent advancements in these two critical areas. To reduce immune rejection, Wang et al. (2022) developed a bioadhesive, immunoevasive, and hydrogel-integrated brain–machine interface (BMI) by introducing catechol functional groups into a hydrogel, which offers the possibility of long-term and stable operability (Figs. 10a and 10b). Similarly, targeting the tissue inflammatory response, Golabchi et al. (2019) developed an amphoteric ionic polymer/PDA coating, which could effectively reduce the acute inflammatory tissue reaction induced by neural implants (Fig. 10c). Furthermore, Lee et al. (2022) developed a polypyrrole/heparin (PPy/Hep) bionic electrode with an immune-compatible morphology that modulated macrophage responses, thereby inhibiting inflammation (Fig. 10d). In addition to biological compatibility, maintaining the physical integrity of the electrode coatings is equally important. Ouyang et al. (2017) proposed a method to effectively improve the adhesion of PEDOT to solid substrates, and an electrically grafted methylamine-functionalized 3,4-ethylenedioxythiophene (EDOT) derivative (EDOT-NH_2), which could withstand 1 h of sonication without significant cracking or delamination, was proposed (Fig. 10e). Inoue et al. (2020) proposed the use of a few-nanometer-thick hydrophilic and polymeric adhesive layer to achieve interfacial bonding between wet conducting polymers and various substrates (Figs. 10f and 10g). In summary, by combining biofriendly surface modifications with robust interfacial bonding techniques, these strategies effectively overcome both biological encapsulation and mechanical degradation, thereby providing a comprehensive framework for designing durable and reliable long-term neural implants.

5 Summary and outlook

In summary, we have highlighted that the future of neuroelectrodes lies not only in softer materials but also in the synergistic optimization of the mechanical–electrical–biological interface. From a future perspective, research on implantable neuroelectrodes can be organized in several important directions (Fig. 11). The first is the innovation of bionic materials and structures. The use of biodegradable materials holds enormous promise due to the ability of these materials to avoid secondary damage to the brain tissue when the electrodes are removed at the end of treatment. However, this approach requires precise control of the material degradation rate to achieve maximal synchronization with the treatment cycle. Scientists can try to precisely control the degradation rate by exploring the use of degradable polymers, such as polylactic acid, as electrode materials, adjusting their molecular structure, or adding specific degradation regulators. Concurrently, constructing a material system with mechanical properties highly similar to brain tissue and designing the electrode as a 3D bionic structure via 3D printing technology can maximize the contact area between the electrode and brain tissue. It effectively reduces mechanical damage, lowers the immune response, prevents the electrode from being wrapped by gelatinous scarring, and prevents the loss of performance. Moreover, multimodal function integration is a crucial future research topic. Considering sensory simulation as an example, scientists can further improve the fineness of the simulation. As the number of retinal neurons is in millions, in terms of visual simulation, future studies must achieve a matching electrode density to provide a more detailed, realistic, and long-term stable simulation of the visual scene. This achievement requires breakthroughs in electrode materials, manufacturing processes, and signal processing algorithms to develop high-resolution and low-noise microelectrode arrays, which can be combined with advanced image processing and neural coding technologies to accurately convert visual information into electrical signals and stimulate retinal nerve cells. In addition, functional breakthroughs are expected in the field of energy self-supply. Using biocompatible piezoelectric materials or glucose biomicrofuel cells, a continuous energy supply can be achieved using tiny mechanical vibrations generated by cerebrospinal fluid or glucose flow around brain tissue. For example, they can convert the mechanical energy generated by the flow of cerebrospinal fluid into electrical energy to provide electrodes with the energy required to work, thus eliminating the requirement of a traditional wired power supply and improving the portability and long-term stability of implantable neuroelectrode systems. In contrast, glucose biomicrofuel cells can employ abundant glucose resources around brain tissues to generate electrical energy through biochemical reactions, providing stable energy for electrodes. Finally, for neuroscience applications, the remarkable heterogeneity of neural circuits can enable

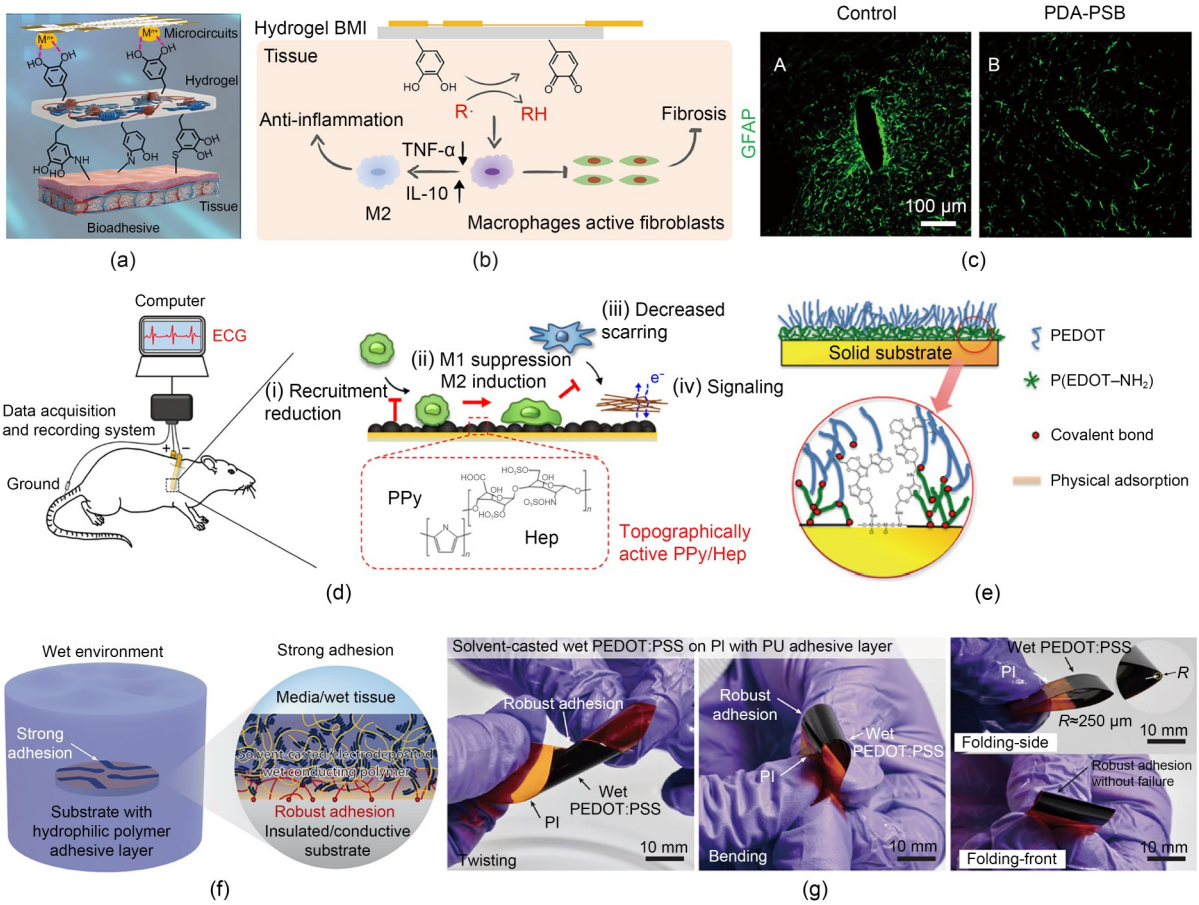


Fig. 10 Strategies for achieving the long-term stability of flexible neuroelectrodes: (a) mechanism of adhesion between hydrogel neural interfaces with soft tissues and metal substrates; (b) schematic representation of the potential mechanism underlying the immuno-evasive behavior of the dPEDOT-CA-PDA-PAAm hydrogel (Wang et al., 2022); (c) representative images of GFAP staining of reactive astrocytes one week after implantation of an uncoated probe (A) versus a probe coated with PDA-PSB (B) on a 100 μm scale (Golabchi et al., 2019); (d) schematic of PPy/Hep with optimal surface roughness exhibiting high performance and biocompatibility (reprinted from (Lee et al., 2022), Copyright 2022, with permission from American Chemical Society); (e) schematic representation of PEDOT deposited on the electrically grafted P(EDOT–NH_2) layer (Ouyang et al., 2017); (f) strong binding of the CP to the substrate via an adhesive layer in wet environments; (g) PEDOT:PSS capable of withstanding mechanical deformation, including twisting, bending, and folding around a substrate with a PU adhesive layer (Inoue et al., 2020). R· and RH are the phenoxy radical and hydrogen radical, respectively; TNF-α is the tumor necrosis factor-α; IL-10 is the interleukin-10; M1 is the pro-inflammatory type of macrophage; M2 is the anti-inflammatory and repair-type macrophage; dPEDOT and CA are the double-bond functionalized poly(3,4-ethylenedioxythiophene) and carrageenan, respectively; GFAP is the glial fibrillary acidic protein; PSB is the polysulfobetaine; ECG is the electrocardiogram; P(EDOT–NH_2) is the polymer of EDOT–NH_2; PU is the polyurethane; *R* is the radius of curvature

individualized treatment protocols for psychiatric disorders such as depression. The artificial intelligence (AI)-driven closed-loop feedback system can parse brain signals in real time and dynamically optimize the stimulation parameters. For example, machine learning algorithms are employed to analyze the collected electroencephalogram signals and identify the patterns of neural activity associated with depression. Then, the stimulation parameters of the electrodes can be precisely adjusted according to the brain status of individual patients in real time. These include stimulation intensity, frequency, and waveform to achieve personalized and precise neuromodulation therapy, providing new and effective means for treating depression and other neuropsychiatric diseases. These research directions can break through the current technical bottlenecks faced by implantable neuroelectrodes and provide solid and powerful technical support for improving the quality of life of patients with neurological disorders and expanding the boundaries of human–computer interaction applications.

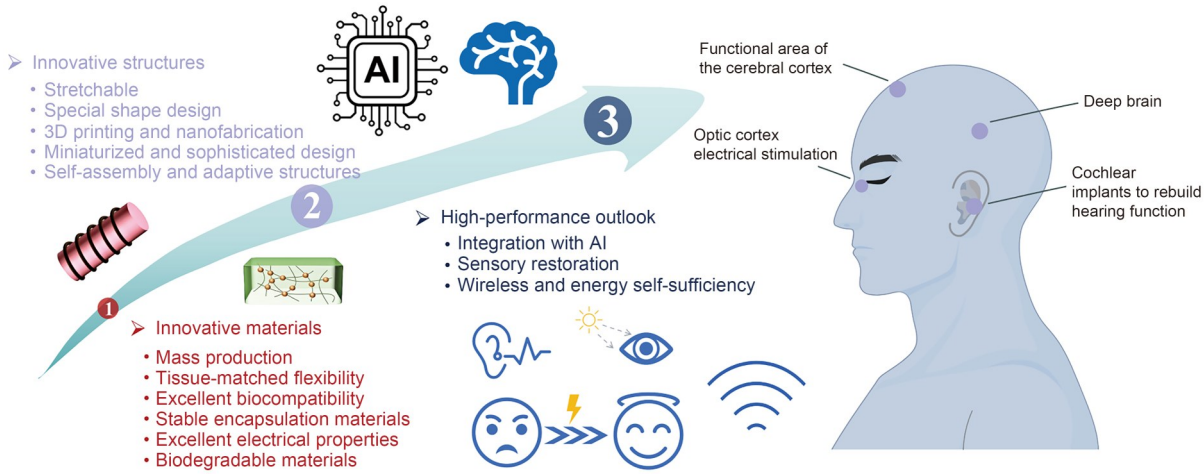


Fig. 11 Future perspectives concerning implantable neural interfaces

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Author contributions

Jiaqi SU: investigation, writing, and editing. Haomin WANG: conceptualization, writing, review, editing, supervision, and funding acquisition. Lu HAN, Rong CHENG, and Runfang HAO: guidance. Shengbo SANG: investigation. All authors have reviewed and approved the final version of this paper for publication.

Conflict of interest

Jiaqi SU, Haomin WANG, Lu HAN, Rong CHENG, Runfang HAO, and Shengbo SANG declare no competing interests.

Declaration on the use of generative AI tools

No generative AI tools were used in the preparation of this manuscript.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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