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PERSPECTIVE

Biocompatible Conjugated Polymers for Bioelectronics

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Received: 22 October 2025 | **Revised:** 13 January 2026 | **Accepted:** 16 February 2026

Keywords: bioelectronic devices | biointerfaces | conjugated polymers

ABSTRACT

Bioelectronics, as a bridge between electronic devices and living systems, is rapidly advancing toward transformative applications in human–machine interfaces and intelligent healthcare. Conjugated polymers (CPs) are driving revolutionary advances in bioelectronics by offering a unique combination of high electronic conductivity and tissue-compliant mechanical properties. This perspective summarizes recent progress in the application of CPs as conductors or semiconductors in next-generation implantable bioelectronic devices, highlighting key strategies for enhancing the biocompatibility of CP-based devices, such as superior tissue–device interfacing, low cytotoxicity, and immune compatibility. We further review their roles in advanced bioelectronic applications, from signal acquisition to sensing, and discuss the key challenges of device integration, long-term stability, and degradability that must be addressed for clinical translation, and offer an outlook on the future development of CP-based bioelectronic systems.

1 | Introduction

Bioelectronics is the field that involves the development of interfaces between electronic devices and living systems, with the main objective of monitoring or modulating biological processes. Since Galvani's pioneering research on electrical stimulation of frog leg muscles in the 1780s, increasing efforts have been devoted to exploring the interactions between electronic and biological systems. Since the 21st century, research on brain-computer interfaces (BCIs) and neuromorphic computing has been flourishing, deepening our understanding of the brain's working mechanisms and advancing further exploration into the nature of intelligence [1]. At the same time, bioelectronics is revolutionizing healthcare by creating innovative therapies and diagnostics that restore functions like movement, speech, and vision, thereby dramatically improving patients' quality of life [2–5].

Bridging electronic systems with biological systems is essential for achieving effective human-machine interaction, yet a key challenge lies in constructing effective interfaces between electronic devices and biological tissues. Conventional bioelectronic devices typically employ electrodes made of inorganic materials [6–9], but these materials often suffer from mechanical mismatch with biological tissues and trigger immune responses that lead to performance degradation. These challenges highlight the urgent need for alternative materials that combine electronic functionality with mechanical and biological compatibility.

Organic electronic materials, particularly conjugated polymers (CPs), have emerged as a transformative platform. Beyond intrinsic properties like lightweight nature and mechanical flexibility, CPs possess structural tunability, which can be engineered to meet specific biocompatibility requirements, making them well-suited for bioelectronic interfaces [10]. Featuring π-conjugated

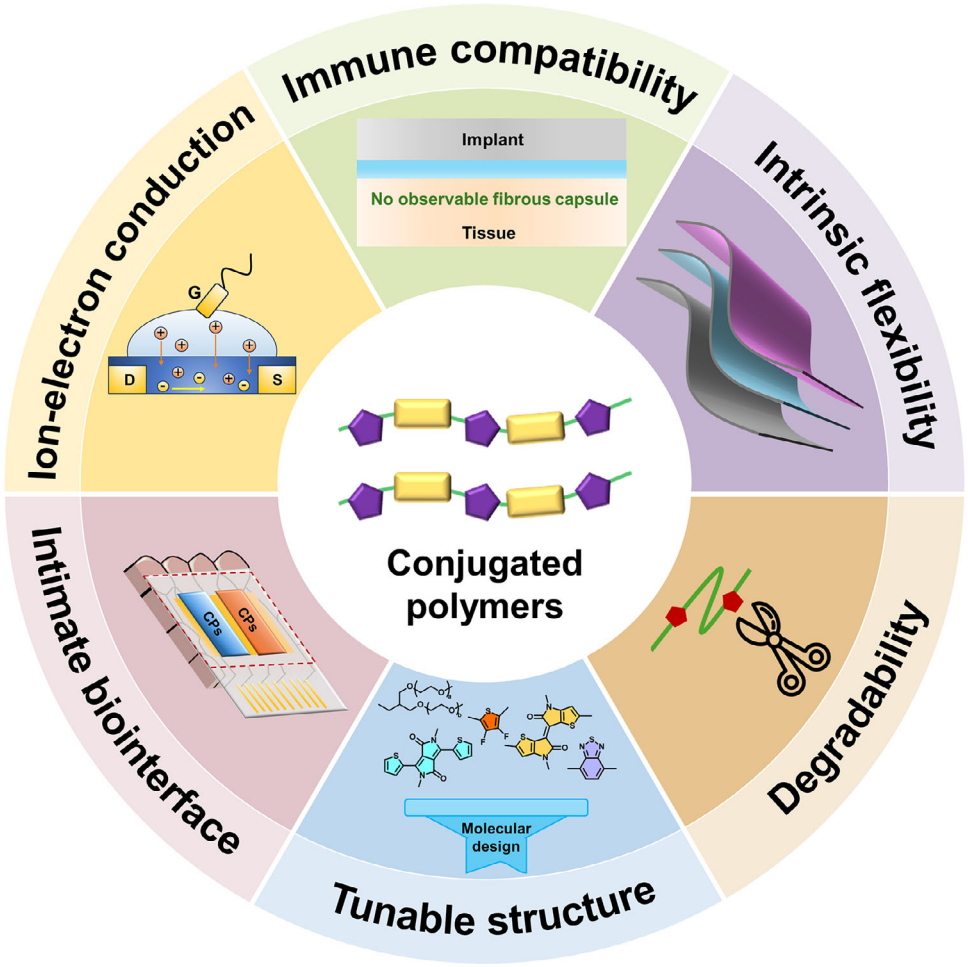

FIGURE 1 | Conjugated polymers (CPs) as the functional core for next-generation bioelectronics. The unique combination of mixed ionic and electronic conduction, intrinsic mechanical flexibility, and tunable molecular design in CPs enables the development of biointerfaces with seamless integration, immune compatibility, and programmable degradability.

backbones, CPs enable efficient charge transport comparable to inorganic semiconductors, allowing them to serve as the functional core of organic electronic devices (Figure 1) [11]. Critically, their mixed ionic and electronic conduction facilitates direct ionic signal transduction and enables stable operation in aqueous media—a hallmark of organic electrochemical transistors (OECTs)—which mirrors biological communication mechanisms and thereby significantly enhances biocompatibility [12]. Meanwhile, the element composition of CPs—primarily carbon, hydrogen, nitrogen, oxygen, and sulfur—closely resembles that of biomolecules. Combined with weak intermolecular van der Waals interactions, this biomimetic chemistry imparts intrinsic mechanical softness and flexibility that align more closely with those of biological tissues [13]. In addition, CP-based materials possess good solution processability and tunable molecular design, which not only reduces fabrication costs but also provides access to specialized functionalities such as self-healing and degradability [14, 15]. Beyond this foundation, CPs can be seamlessly integrated with soft organic materials, such as hydrogels and elastomers, to form composite systems with finely tuned electrical and mechanical properties, substantially expanding their potential for applications in complex biological systems [16, 17].

CPs have already demonstrated broad applications in bioelectronics. Many wearable and implantable devices based on these polymers have been developed to record diverse biosignals from tissues, including the skin, heart, spinal cord, and brain [18–20]. To achieve long-term stability under physiological conditions and minimize adverse effects on biological systems, enhancing material biocompatibility becomes essential. Despite considerable progress, to reach a better biocompatibility, several critical challenges remain to be addressed. These include the matching of interfacial properties (e.g., mechanical modulus and adhesion), interactions with living systems (e.g., cytotoxicity and immune responses), and degradability for sustainability (Figure 1).

In this perspective, we reflect on the essential functions that biocompatible bioelectronic materials must fulfill and explore potential approaches to achieve these capabilities. We begin by discussing the conductivity of CPs, which is central to signal acquisition and transmission in bioelectronic devices, introducing various conductive and semiconductive CP materials along with their applications. Subsequently, we discuss the favorable biointerfacing properties of CPs and evaluate their stability when interacting with biological systems under physiological

conditions. Finally, we discuss ongoing challenges and future opportunities. Through this perspective, we seek to underscore the critical role of CPs in driving the evolution of bioelectronics and shaping the next generation of biomedical technologies.

2 | From Conducting to Semiconducting CPs

The defining structural feature of CPs is their alternating single and double bonds, which form an extended conjugated backbone. This configuration narrows the bandgap compared to insulating non-conjugated polymers, thereby endowing the material with conducting or semiconducting properties depending on specific doping state. Furthermore, the conductivity, solubility, and stability of the polymer can be tuned through molecular design, allowing for the rational design of materials tailored for specific bioelectronic roles. Here, we describe the progression of CPs in bioelectronics, from their use as highly conductive electrode materials to their role as semiconducting channel materials in active transistors, highlighting how this transition in operating regime underpins increasingly sophisticated bioelectronic functionalities.

2.1 | Conducting CPs and Passive Bioelectrodes

The discovery in the 1970s that doped polyacetylene exhibited remarkably high electrical conductivity paved the way for the development of conductive polymers [21]. Subsequently, an increasing number of conductive polymers were discovered, such as polyaniline (PANI), polypyrrole (PPy), and poly(3,4-ethylenedioxythiophene) (PEDOT) [22–24]. Among them, the PEDOT family, particularly poly (3,4-ethylenedioxythiophene):polystyrene sulfonate (PEDOT:PSS), has emerged as one of the most widely studied and used conducting polymers, owing to its favorable combination of high electrical conductivity, ease of processing, flexibility, non-toxicity, and good thermal stability [25–27]. The conductivity of PEDOT:PSS can be significantly enhanced through treatments such as thermal annealing, light exposure, organic solvents, ionic liquids, surfactants, salts, zwitterions, and acids, achieving a maximum conductivity of over 4000 S cm^{-1} [28, 29]. The combination of better mechanical compatibility—surpassing conventional metal electrodes—and an efficient mixed conduction mechanism makes the PEDOT family a highly effective material for advanced passive bioelectrodes.

PEDOT-based electrodes have demonstrated utility across diverse fields, from wearable electronic devices such as electronic skins, flexible energy materials such as organic thermoelectrics, to biosensing and electrophysiology monitoring (Figure 2a) [30, 31]. As a passive electrode, PEDOT:PSS has been widely used for acquiring bioelectrical signals [32]. For example, Ouyang et al. reported in 2020 a fully organic, self-adhesive dry electrode composed of a PEDOT:PSS, waterborne polyurethane (WPU), and D-sorbitol blend. This dry electrode demonstrated superior performance in long-term, motion-robust monitoring of epidermal bioelectrical signals—such as electrocardiogram (ECG), electromyogram (EMG), and electroencephalogram (EEG)—with lower skin-contact impedance and noise than conventional Ag/AgCl gel electrodes and other dry electrodes (Figure 2b) [33]. Beyond single-channel detection, highly integrated electrode arrays offer enhanced spatial resolution and information capture capabilities. In 2022, a high-density stretchable PEDOT:PSS electrode array with cellular-scale feature sizes was reported, which not only adhered robustly to dynamically moving muscles for surface electromyography (sEMG) recording but also formed seamless biointerfaces on the rat brainstem without significant inflammatory responses (Figure 2c) [34].

2.2 | Semiconducting CPs and Transistors

While passive CP electrodes represent a significant advancement over traditional metal electrodes, they can only record signals without amplification, thus resulting in a limited signal-to-noise ratio (SNR). Furthermore, passive electrodes face a fundamental spatial constraint: although increasing electrode density and reducing individual size can enhance selectivity, the consequent reduction in contact area raises interfacial impedance, thereby degrading signal sensitivity [35, 36]. This results in an inherent trade-off between sensitivity and selectivity. The separation between signal acquisition and processing in such systems also leads to increased energy consumption and signal quality degradation [37].

At the materials level, these limitations arise because conductive CP-based electrodes operate in a permanently and doped regime, where the polymer functions as a static electronic conductor rather than a switchable semiconducting medium. In contrast, when CPs are operated in a gate-controlled semiconducting regime, they facilitate a paradigm shift toward active bioelectronics, providing a potential solution to these challenges.

As the channel material in transistors, including OECTs and organic field-effect transistors (OFETs), CPs allow for local signal amplification and processing through switching between doping ("ON") and depoing ("OFF") states, overcoming the SNR limitations of passive electrodes and unlocking advanced functionalities [38]. Besides, the core electrical signal in transistors is the source-drain current, which remains independent of interfacial impedance and is not constrained by device size, thereby enabling higher spatial resolution. To further clarify the distinction between passive and active bioelectronics devices, we provide a direct comparison in Table 1.

These transistor architectures integrate multiple functional components (Figure 3a): semiconducting CP channels for signal acquisition and transduction, flexible substrates for mechanical compatibility with tissues, electrolytes (OECT) or dielectric layers (OFET) for gating, and encapsulation materials (such as Parylene-C, PaC) for operational stability. Since the substrate and encapsulation layers constitute a considerable proportion of the overall device and are in direct contact with biological tissues, their mechanical compliance and biocompatibility are critical determinants of overall device performance. Accordingly, the substrate and encapsulation layers are often engineered to be flexible [39], stretchable [40], degradable [41] or hydrogelation

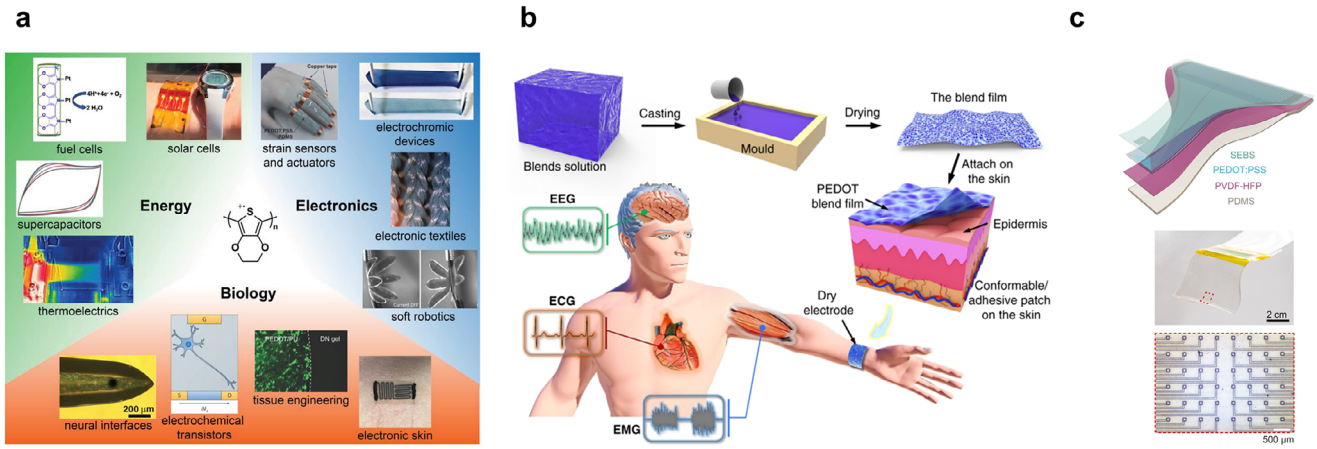

FIGURE 2 | Applications of conducting CPs in bioelectronics. (a) Schematic diagram showing applications of PEDOT across energy, electronics, and biology. Reproduced with permission [27]. Copyright 2019, WILEY-VCH. (b) Electrodes based on PEDOT:PSS blends for ECG, EMG, and EEG acquisition. Reproduced under terms of the Creative Commons CC-BY license [33]. Copyright 2020, published by Springer Nature. (c) Highly stretchable flexible electrode arrays based on PEDOT:PSS [34]. Reproduced with permission [32]. Copyright 2024, Royal Society of Chemistry.

TABLE 1 | Comparison between conducting CP-based passive electrodes and semiconducting CP-based active transistors.

Parameter	Passive electrodes	Active transistors
Material state	Permanently doped, highly conductive	Gate-controlled doping and dedoping, switching between "ON" and "OFF" states
Function	Transduce ionic currents in tissues into electronic signals	Provide both signal transduction and amplification through gate-modulated channel conductance
SNR	Unable to amplify signals; limited by electrode impedance	In situ amplification yields higher SNR
Spatial resolution	Typically constrained by size, trade-off between sensitivity and selectivity	Less constrained in size, high spatial resolution can be achieved through a high density of transistors
Power consumption	Low intrinsic power demand, but relies on external electronics	Requires biasing and gate control, leading to higher but still moderate power consumption
Sensitivity	Depends on electrode area, surface chemistry, and impedance	High sensitivity arising from amplification in the transistor channel
Stability challenges	Mechanical mismatch can induce motion artifacts and tissue damage	Additional challenges from repeated doping/de-doping, swelling, and material degradation

[42] to better match the mechanical properties of biological tissues and improve biocompatibility. Additionally, polymers can be introduced as monomers and polymerized in vivo to derive "impregnated", substrate-free electrodes with long-range conductivity [43].

Notably, among these components, CPs are the functional core of bioelectronic devices, enabling signal acquisition and transduction at the tissue-device interface. Specifically, while both OFETs and OECTs utilize CPs as channel materials, their operational mechanisms differ fundamentally. OFETs operate through field-effect modulation of charge carriers at the semiconductor-dielectric interface, whereas OECTs function via bulk ion-mediated electrochemical doping of the CP channels [44, 45]. This mixed charge transport characteristic qualifies OECT materials as organic mixed ionic–electronic conductors (OMIECs), which exhibit higher transconductance and lower operating voltages, albeit with slower response speeds. These characteristics determine their respective applications: OFETs' stability makes them suitable for wearable devices, which usually require strict encapsulation, while OECTs' ability to operate in aqueous environments makes them ideal for implantable bioelectric interfaces [46].

The development of high-performance semiconducting CPs has been crucial for advancing transistors. While PEDOT:PSS is

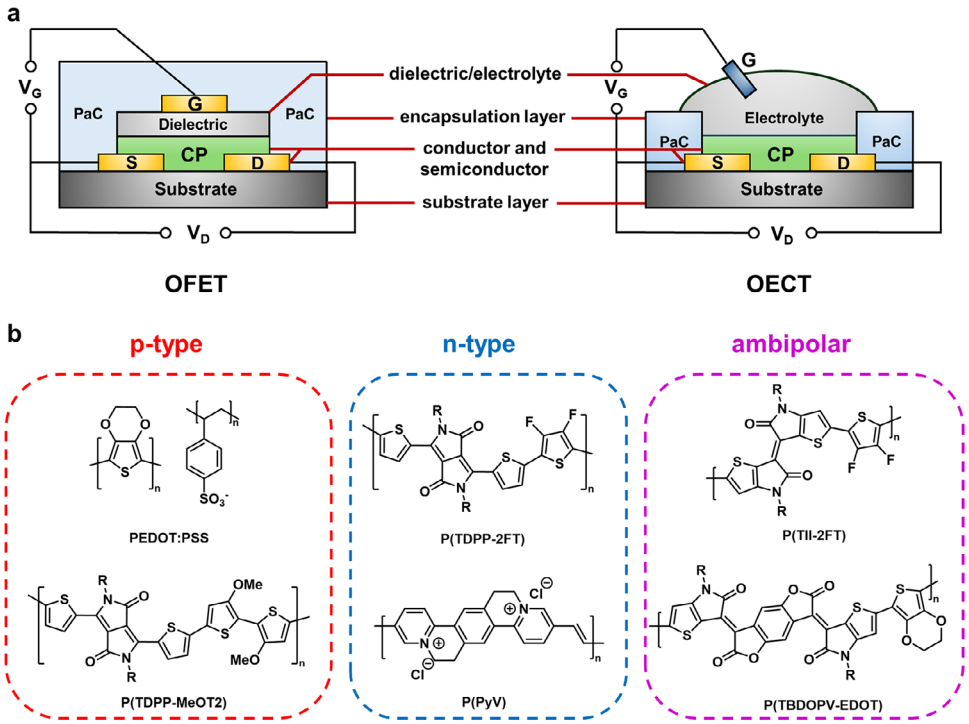

FIGURE 3 | Semiconducting CPs and their applications as transistors. (a) Schematic diagrams of the device structure for OFET and OECT. (b) Representative polymer structures of p-type, n-type, and ambipolar semiconducting CPs for OECTs.

widely known for its applications as a conducting polymer in passive electrodes, it also functions as an effective p-type semiconductor in transistors. For example, in OECTs, PEDOT:PSS can undergo dedoping when a gate voltage is applied, switching from a conductive to a non-conductive state, thus operating as a semiconductor [45]. Currently, p-type CP semiconductors are relatively well-developed, with materials such as polythiophene and its derivatives, along with some donor-acceptor (D-A) type CPs, demonstrating high device performance (Figure 3b) [47]. However, in n-type materials, the electron carriers occupy relatively high-energy states after doping, making them unstable and highly susceptible to parasitic reactions with water and oxygen. Therefore, the development of n-type semiconductor materials for bioelectronics has long lagged far behind due to challenges in achieving stable doping in aqueous, physiological environments.

Recent advances have addressed this gap through novel molecular designs. Current strategies for optimizing n-type materials mainly include introducing electron-withdrawing groups into the backbone to lower the lowest unoccupied molecular orbital (LUMO) energy level [48], as well as tuning side chains to optimize ionic-electronic transport balance [49]. In addition, other factors—such as the stability of the doped state [50], backbone planarity [51], polaron distribution [52], and film morphology [53]—also play critical roles in improving the performance of n-type OECT materials. Based on this, our research group has developed a series of n-type diketopyrrolopyrrole (DPP)-based CPs [52] and side chain-free cationic backbone CPs [16], as well as a series of ambipolar OECT materials that exhibit both high and balanced p-type and n-type semiconducting performance (Figure 3b) [54, 55]. The advance of organic semiconductor materials has made it possible to construct organic electronic devices with higher integration density and more complex functionalities.

2.3 | Applications of Semiconducting CPs in Bioelectronics

Detection of chemical biomarkers and bioelectrical signals provides critical insights into health and disease, as their concentration or temporal dynamics directly reflect underlying physiological or pathological processes, holding profound clinical importance [56]. Since molecular-level abnormalities often precede the onset of clinical symptoms, the early and precise detection of these signals is of irreplaceable value for disease prevention, diagnosis, and treatment. OFETs and OECTs possess inherent signal amplification capabilities, offering higher sensitivity than conventional electrochemical methods [57]. Through the modification and integration of transistor devices, it is possible to achieve chemical biomarker sensing as well as in situ acquisition and processing of bioelectrical signals. Biosensing functionality is typically achieved through functionalization of gate, channel, or electrolyte (Figure 4a) [58]. Electron transfer arising from redox reactions at the gate electrode, or capacitive changes induced by selective binding events on the functionalized gate surface, results in a shift of the effective gate potential and modulates device output [59, 60]. On the other hand, channel surface or bulk functionalization enables interaction with target analytes, which can lead to structural changes or voltage drops at the channel interface, thereby modulating channel conductivity [61]. In 2020, Shi et al. reported the first OECT array capable of detecting neurotransmitters in rat brains [62]. So far, CP-based chemical sensors have demonstrated high sensitivity in detecting a wide spectrum of targets, including small molecules, biomacromolecules, and even whole cells—such as dopamine [63], lactate [64], glucose [65], adrenaline [66], cortisol [67], DNA [68], proteins [69], glycans [70], and bacteria [71] thus exhibiting considerable promise in disease prediction, screening, diagnosis,

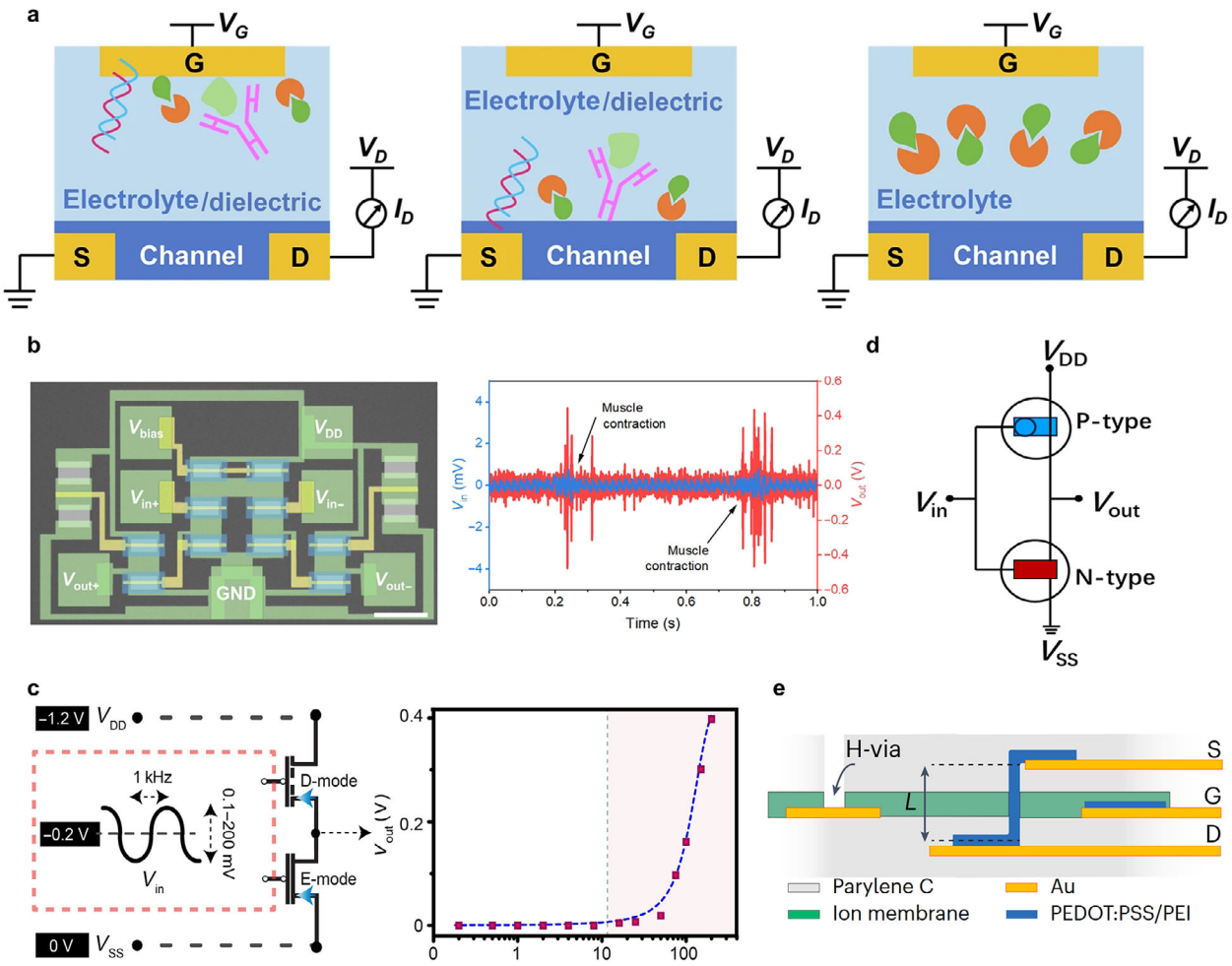

FIGURE 4 | Applications of semiconducting CPs in chemical signal and bioelectrical signal sensing. (a) Biosensing mechanisms of bioelectronic devices based on CPs, by gate functionalization (left), channel functionalization (middle), and electrolyte functionalization (right). Reproduced under terms of the CC-BY-NC-ND license [58]. Copyright 2025, The Authors, published by Springer Nature. (b) An ultrathin differential amplifier based on CNTFETs with an optical microscope image (left, scale bar, 100 μm) and its performance in amplifying EMG signals from the surface of the forearm skin of an adult male. Reproduced with permission [72]. Copyright 2024, American Association for the Advancement of Science. (c) Signal processing with a common-mode rejection (CMR) circuit using combined enhancement and depletion mode OECTs. The left side illustrates applied V_{in} corresponding to each V_{in} (offset at −0.2 V) with various pulse amplitudes between 100 μV and 200 mV. Right side shows the resulting V_{out} response pulse. Reproduced with permission [73]. Copyright 2024, American Association for the Advancement of Science. (d) Schematic circuit diagrams of a complementary inverter, consisting of a p-type transistor and an n-type transistor. (e) Schematic diagram of the cross-section for a vertical-channel internal-ion-gated transistor (IGT) consisting of a vertical channel length (L) defined by the thickness of the interlayers between the source and drain contacts. PEDOT:PSS-based channel contains sugar alcohol (d-sorbitol) to create a depletion-mode (normally ON) transistor, with the addition of poly-ethylamine (PEI) to generate an enhancement-mode (normally OFF) transistor. Reproduced under terms of the CC-BY license [74]. Copyright 2023, The Authors, published by Springer Nature.

and treatment. Currently, enhancing the detection limit and long-term stability of implantable devices remains a potential challenge in this field.

Complementary to chemical biomarkers, bioelectrical signals provide a real-time, dynamic reflection of neural and physiological activity, offering crucial information for understanding disease mechanisms and guiding clinical interventions. These signals originate from the coordinated activity of neurons, essentially reflecting changes in membrane potential driven by transmembrane ion flux. Such electrophysiological activities can be captured by OFETs or OECTs and processed in situ through integrated circuit systems. However, the presence of complex noise in biological systems often obscures key physiological signals, making direct signal recording challenging.

To address this, in situ processing strategies, such as signal amplification or using common-mode rejection (CMR) via differential amplifiers, have been developed. For instance, differential amplifiers (Figure 4b) based on OFETs and carbon nanotube field-effect transistors (CNTFETs) have been successfully implemented to suppress environmental noise, thereby improving the fidelity of ECG and EMG recordings [18, 72]. Compared to OFETs, OECTs are better suited for bioelectrical sensing due to their ionic-to-electronic signal transduction mechanism, high transconductance, and biocompatibility, enabling stable

interfacing with biological tissues. The application of OECTs in bioelectronics is progressing rapidly, even though current OECT-based implantable devices are still largely simplistic and characterized predominantly employing inverters. In 2018, Fabiano et al. developed a high-performance n-type OECT material, poly(benzimidazobenzophenanthroline) (BBL), and reported the first complementary inverter that consists of a pair of p-type and n-type OECT (Figure 4d) [75]. Owing to the extremely narrow transition region, small variations in the input signal can induce large changes in the output signal, thereby enabling effective amplification of weak signals. In 2020, Torricelli et al. demonstrated, for the first time, the application of a complementary PEDOT:PSS/BBL-based inverter for highly sensitive ion detection [76]. Shepard et al. developed an OECT device with differential functionality, which employs two serially connected p-type transistors (one depletion-mode and one enhancement-mode) to eliminate noise (Figure 4c) [73]. Our group recently realized a single-component ambipolar inverter with an ultrahigh gain exceeding 800 V/V at an input voltage step of 0.1 mV, enabling in situ signal acquisition and amplification directly on biological tissues [55].

Scaling OECTs into large and densely integrated circuits faces fundamental challenges that extend beyond fabrication and patterning. While CPs are generally compatible with solution processing and photolithography workflows, the primary bottlenecks in OECT integration arise from device-level physics. Since OECTs require a gate electrode immersed in a shared electrolyte solution, where ion migration can simultaneously modulate multiple transistors, creating significant crosstalk that impedes large-scale circuit integration. Moreover, ion transport in both the electrolyte and the channel reduces the response speed of OECTs, restricting their ability in high-frequency signal processing [77].

In recent years, Khodagholy et al. addressed these limitations by internal ion-gated organic electrochemical transistors (IGTs) [74, 78–80]. In the IGT architecture (Figure 4e), ion reservoirs are embedded within the channel, substantially shortening ion transport pathways and enabling operation at the MHz frequency range. Furthermore, since each transistor has an independent gate, interference-free control of densely integrated devices becomes feasible. Replacing liquid electrolytes with solid-state electrolytes also represents a promising strategy to achieve independent gate control in OECTs. Fabiano et al. [81] reported a photo-patternable hydrogel solid-state electrolyte composed of ι-carrageenan (ι-CGN) and poly(ethylene glycol) diacrylate (PEGDA), enabling the incorporation of one of the largest numbers of OECTs reported in a complementary OECT-based circuit, demonstrating an unprecedented level of integration. These advances indicate that the scalability of OECT-based circuits is governed more by device architectures than by processing constraints, highlighting device design as a key lever for advancing organic bioelectronic integration.

3 | Interface Engineering for Biocompatible Electronics

The performance of bioelectronic systems is strongly influenced by the characteristics of the device–tissue interface. A biocompatible interface enables efficient bidirectional signal transmission and preserves tissue integrity, whereas poor compatibility can lead to adverse effects. Interface engineering aims to establish a stable and minimally invasive biointerface by matching key mechanical properties—such as Young's modulus, stretchability, and bending stiffness—between devices and tissues, complemented by robust bioadhesion to ensure conformal and immobilized contact. This holistic approach is crucial for preventing tissue damage, suppressing immune rejection, and guaranteeing the long-term fidelity of bioelectronic signals. With the advancement of CP-based bioelectronic devices, enhancing their biocompatibility has become increasingly important.

3.1 | Mechanical Compatibility

Traditional bioelectronic devices are typically fabricated from rigid materials with Young's moduli on the GPa scale, in stark contrast to the much softer biological tissues—skin ranges from 10 to 100 kPa, while brain tissue is even lower (100 Pa and 10 kPa) [82]. For non-implantable devices, this stiffness disparity creates a non-conformal interface that generates motion artifacts, severely compromising recording accuracy [83]. For implantable devices, the mismatch in Young's modulus and bending stiffness can cause acute or chronic damage to tissues and trigger immune responses, leading to encapsulation of the implanted device by glial or fibrous cells [84–87]. As a result, the interface impedance of the device increases significantly, limiting the lifespan and long-term stability of these implants [88]. Beyond mechanical mismatch, a fundamental electrical incompatibility exists. Since traditional electronic devices based on inorganic semiconductors rely on electrons as charge carriers while biological systems utilize ions, efficient signal transduction across the interface is impeded [89, 90]. The inherent differences in the mechanisms of electrical signal conduction restrict the sensing capabilities at the device-tissue interface [12].

Compared to inorganic materials, CPs possess intrinsic flexibility, enabling closer mechanical alignment with biological tissues. This inherent softness allows CPs to form conformal and seamless biointerfaces, thereby minimizing tissue damage and underscoring their considerable promise for biocompatible bioelectronics. Although CPs exhibit significantly greater biocompatibility than conventional inorganic materials, their Young's modulus (1 MPa —1 GPa) remains much higher than that of biological tissues. To further reduce the modulus and impart tissue-like softness and stretchability, it is necessary to introduce greater chain disorder or free volume into the polymer structure. Such structural modifications, however, tend to disrupt molecular stacking and crystallinity, which can detrimentally affect electrical conductivity—highlighting a fundamental trade-off between mechanical compliance and electrical properties of CPs [32]. Several methods have been employed to modulate the mechanical properties of conductive polymers. Taking PEDOT:PSS as an example, these approaches include incorporating small-molecule additives (such as dimethyl sulfoxide (DMSO) [91] or surfactants [92]), blending with soft polymeric matrices (such as polydimethylsiloxane (PDMS) [93], polyurethane (PU) [94], polyethylene glycol (PEG) [95], etc.), or chemically modifying of PSS [96] (Figure 5a). While these strategies can, to

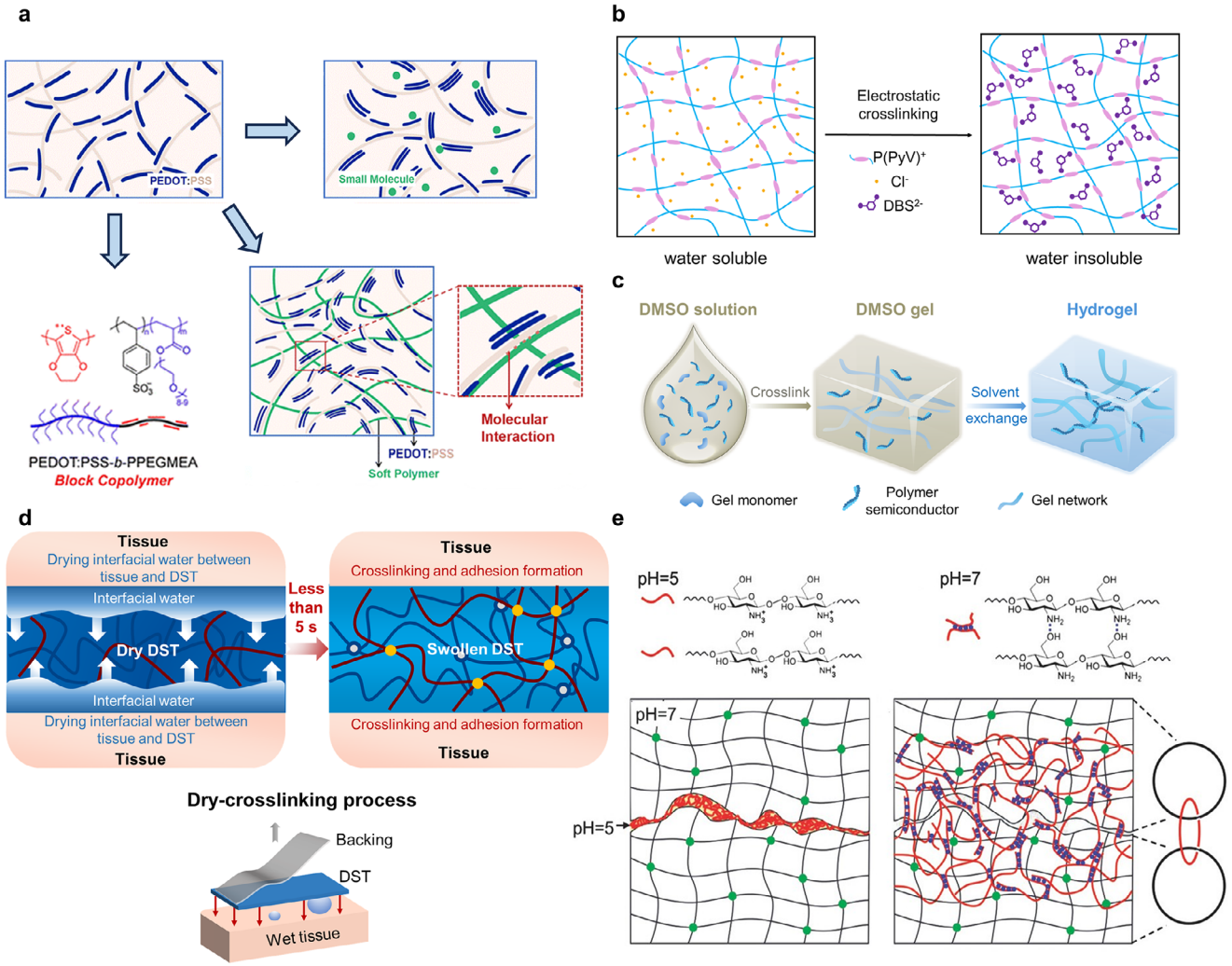

FIGURE 5 | Engineering the biointerface through CP-based composites. (a) Tuning the mechanical properties via modification of PEDOT:PSS. Redrawn according to ref. [32]. (b) Water-soluble CPs directly form hydrogel structures through counterion electrostatic crosslinking. Redrawn according to ref. [16]. (c) Water-insoluble CPs form hydrogel structures through solvent exchange. Redrawn according to ref. [97]. (d) Achieving tissue adhesion of hydrogels through double-sided tape (DST). Redrawn according to ref. [98]. (e) Adhesion mediated by pH-regulated topological chain entanglement. Reproduced with permission [99]. Copyright 2018, WILEY-VCH.

some extent, enhance mechanical compliance, they also show much higher modulus than soft tissue, such as brain, and could lead to issues such as small-molecule leakage and polymer-phase separation, which might compromise electrical conductivity and long-term operational stability.

Hydrogels, consisting of a three-dimensional polymer network permeated with water or aqueous electrolytes, possess tissue-mimetic mechanical properties and can substantially reduce immune rejection, making them a promising alternative for biointerface applications [100]. Traditional hydrogels are ionically conductive but lack electronic conductivity, and they have been used to construct viscoelastic interfaces between electrode array devices and tissues [101, 102]. CPs can be incorporated into hydrogel networks to impart electronic conductivity. To date, a variety of conductive hydrogels have been developed based on CPs such as PPy [103], PANI [104], and PEDOT:PSS [105]; however, the electrical conductivity of these composites is often compromised by the insulating nature of the hydrogel matrix. Furthermore, their general lack of semiconducting properties limits their application in advanced electronic devices.

To overcome these limitations, our group developed the first semiconducting hydrogel through electrostatic crosslinking of a water-soluble n-type semiconducting polymer, P(PyV) (Figure 5b) [16]. This approach yielded a single-network hydrogel, which can be further developed into a multi-network structure via composite reinforcement. The multi-network hydrogels could combine both good mechanical properties, biocompatibility, and bioadhesive features, enabling the construction of semiconductor-like circuits and the formation of intimate biointerfaces. An in situ amplifier fabricated based on the semiconducting hydrogel successfully recorded mouse cortical electrical signals with an improved SNR. By integrating the functionalities of semiconductors with the biocompatibility advantages of hydrogels, the semiconducting hydrogel offers great potential for implantable bioelectronic devices to achieve long-term stability and in situ signal processing. Likewise, water-insoluble polymer semiconductors

can also be processed into hydrogel-semiconductor composites through organic solvent-induced gelation and solvent exchange (Figure 5c) [97]. This method is applicable to some polymer semiconductors with polar side chains. For example, P(g2T-T) was crosslinked with acrylic acid in DMSO and subsequently converted into a hydrogel via solvent exchange. The resulting material maintains efficient charge transport properties while exhibiting a low modulus, significantly enhancing tissue compatibility and reducing foreign body responses.

3.2 | Bioadhesive Interfaces

In addition to mechanical matching, adhesion between bioelectronic materials and biological tissues is equally critical. For devices, strong adhesion avoids device migration and detachment, improves signal quality and sensitivity, and ensures long-term operational stability [106]. For biological tissues, it helps mitigate inflammation and fibrotic encapsulation [107]. Based on semiconducting hydrogels, surface modification strategies can be employed to endow materials with bioadhesive properties.

Until now, achieving strong adhesion on wet surfaces has remained challenging, as interfacial water molecules often weaken molecular interactions. To overcome this, Wang et al. reported a double-network structured bioadhesive polymer semiconductor formed by a bioadhesive brush polymer and a redox-active semiconducting polymer [108]. In particular, the brush component incorporated a side group that could absorb interfacial water upon initial contact, which locally dehydrates the tissue surface to promote adhesion. The resulting semiconducting film can form rapid and strong adhesion with wet tissue surfaces together with high charge-carrier mobility, high stretchability, and good biocompatibility.

In addition to absorbing water, effective bioadhesion relies on weak intermolecular forces such as hydrogen bonding between the material and tissue, as well as covalent linkages that are either stable (e.g., NHS esters) or dynamic (e.g., disulfide bonds) [109, 110]. These functionalities can be introduced into the material through chemical modification. For example, Zhao et al. reported a tissue-adhesive dry double-sided tape (DST) for hydrogel systems comprising poly(acrylic acid) grafted with N-hydroxysuccinimide ester (PAAc–NHS ester), crosslinked by biodegradable gelatin methacrylate, along with secondary biodegradable biopolymers (e.g., gelatin or chitosan) [98]. Upon contact with biological surfaces, the DST rapidly hydrates and swells to prevent water molecules from hindering adhesion, while PAAc–NHS ester interacts with the tissue surface, thereby enabling strong hydrogel–tissue interfacial adhesion (Figure 5d).

Beyond chemical modification, adhesion of wet materials can also be achieved through topological entanglement of polymer chains. Suo et al. developed a pH-triggered topological adhesion method, exploiting the solubility of chitosan in mildly acidic conditions (pH 5) and its crosslinking behavior at neutral pH (pH 7) [99]. The newly formed chitosan network bridges the hydrogel and tissue networks, resulting in robust adhesion under wet conditions (Figure 5e). This approach uses biocompatible polymer chains to achieve strong adhesion and retain softness, but requires no specific functional groups from the wet materials. The molecular suture can be designed to be permanent, transient, or removable on-demand. Such topological adhesion may open many opportunities in complex and diverse environments.

4 | Interactions With Biological Environments

The performance and longevity of CP-based bioelectronic devices are closely tied to their interactions with biological environments. Once implanted or interfaced with tissues, these materials encounter complex cellular and molecular activities that affect their stability and biocompatibility. Conversely, the intrinsic properties of CPs—such as surface chemistry, mechanical modulus, and degradability—directly influence surrounding tissues by triggering immune responses and affecting cellular behaviors. A comprehensive understanding of these bidirectional and dynamic interactions is essential for designing next-generation bioelectronic devices that can operate safely and stably in vivo.

4.1 | Cytotoxicity and Immune Compatibility

To achieve long-term stability and biosafety of CP-based bioelectronic devices, it is fundamental to investigate their interactions with biological systems. For chronic implantation, a comprehensive biocompatibility assessment must address not only cytotoxicity, but also sensitization, irritation, and systemic toxicity. Overall, since CPs are usually not soluble in water, most conductive CPs exhibit relatively low cytotoxicity (Figure 6a) [55] and limited adverse biological effects [111]. Moreover, their π-conjugated structures can neutralize reactive oxygen species (ROS) and free radicals, endowing them with potential antioxidant bioactivity [112]. Combining CPs with natural biomaterials can further enhance their biocompatibility [113]. For instance, the incorporation of collagen, gelatin, alginate, or hyaluronic acid (HA) provides cell-binding sites, modulates hydrophobicity, and improves cell adhesion [114]. The addition of extracellular matrix proteins also helps maintain progenitor cell viability and normal phenotypes [115].

In addition, CPs possess intrinsic antibacterial activity, which may reduce the risk of infection after device implantation. CPs can interact with microbial cell membranes, potentially disrupting cell wall or membrane integrity, leading to destabilization and eventual cell death. Furthermore, oxidative byproducts generated during CP oxidation can induce microbial oxidative stress, thereby enhancing antibacterial effects [116]. The incorporation of CPs with antimicrobial peptides, metallic nanoparticles (e.g., silver, copper), or antibiotic compounds can further improve the antimicrobial efficacy of CP-based materials (Figure 6b), offering a promising defense mechanism against a wide range of pathogens, including bacteria, fungi, and even certain viruses [117].

On the other hand, the implantation of electronic devices introduces foreign objects, which can trigger recognition by immune cells and lead to a foreign body reaction (FBR) over long term [118]. This immune-mediated response not only results in device failure but also poses health risks to the host. Therefore, the immune-compatible properties of materials are also of critical importance. Traditional silicon-based electronic devices typically

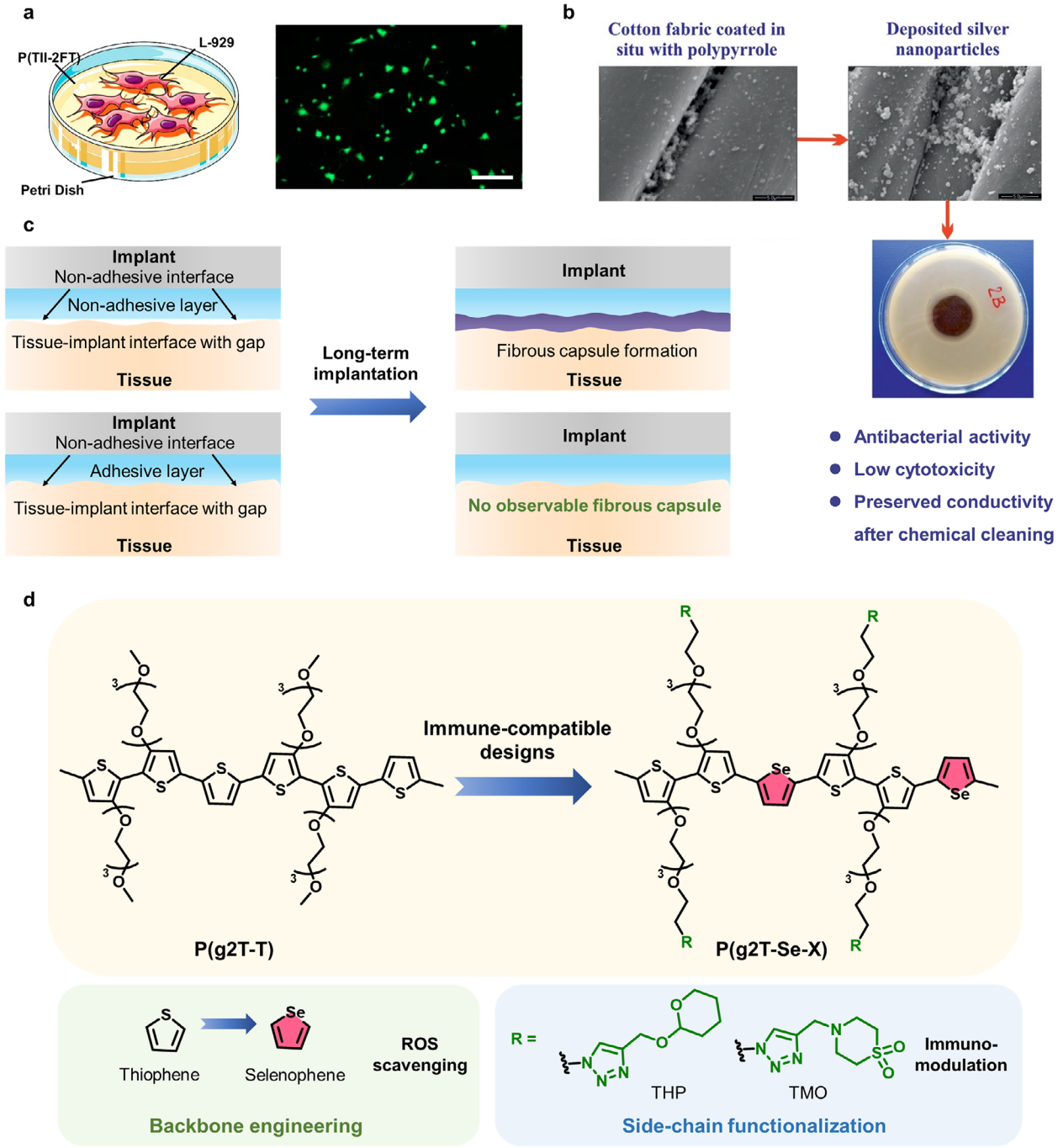

FIGURE 6 | Cytotoxicity and immune compatibility of CPs. (a) Schematic illustration and cell viability tests of P(TII-2FT) film via live (green fluorescence)/dead (red fluorescence) staining of mouse fibroblasts (L929) (scale bar: 100 μm). Reproduced under terms of the CC-BY-NC-ND license [55]. Copyright 2025, The Authors, published by Springer Nature. (b) Polypyrrole-coated cotton exhibits good antibacterial activity and low cytotoxicity, and the conductivity is preserved after chemical cleaning. Reproduced with permission [117]. Copyright 2016, Elsevier. (c) Adhesive layer prevents fibrous capsule formation at the implant–tissue interface during long-term in vivo implantation. Redrawn according to ref. [107]. (d) Backbone engineering through the substitution of thiophene with selenophene and side-chain functionalization with the immunomodulatory moieties THP and TMO to achieve reactive oxygen species (ROS) scavenging. Redrawn according to [85].

trigger chronic immune responses in the body, leading to the encapsulation of the devices by an endogenous protein fibrous capsule. This encapsulation gradually increases the electrode-tissue interface impedance, ultimately isolating the electronic device completely from the target tissue, even when favorable performance is observed in vitro [111]. In contrast, Urbanchek et al. demonstrated that introducing polymer PEDOT enabled neural interfaces to remain stable in vivo for over seven months [119], showcasing the superior immune-compatible properties of CP-based bioelectronic devices compared to traditional electronic devices.

To further enhance the immune-compatible properties of CP-based bioelectronic devices in vivo and achieve long-term

stability, a deeper understanding of the mechanisms by which implanted devices trigger immune responses is necessary. The potential modulus mismatch or friction between electronic devices and biological tissues can cause tissue damage, leading cells to release signaling molecules such as cell-free nucleic acids (cfNAs) and reactive oxygen and nitrogen species (RONS), which in turn trigger immune responses [120, 121]. Blending conductive materials with hydrogels, as discussed earlier, offers a promising strategy for achieving modulus matching between electronic devices and biological tissues. This approach can improve interfacial adhesion, minimize mechanical irritation, and thereby enhance the immune-compatible properties of materials and devices. For instance, Zhao et al. found that interfacial adhesion between biomaterials and tissues not only provides mechanical integration but also effectively reduces the formation of fibrous capsules by lowering the infiltration levels of inflammatory cells (Figure 6c) [107]. Additionally, immune-compatible properties can also be improved by clearing signaling molecules such as RONS and enhancing anti-protein adsorption capabilities. Liu et al. developed a double-layer gel system, where the inner layer achieves tissue adhesion through hydrogen bonding, and the outer layer employs zwitterionic and antioxidant properties to achieve immune resistance and anti-protein adsorption, thereby reducing the deposition of fibrous proteins caused by immune responses [122].

Currently, much research on immune-compatible properties focuses on hydrogel-based systems, while studies directly targeting the intrinsic immune-resistant functions of CPs remain relatively limited. Recently, Wang et al. reported an immune-compatible design strategy for CPs [85]. By replacing thiophene with selenophene in the polymer backbone, macrophage activation was effectively suppressed, alleviating FBR. Additionally, introducing immunomodulatory groups (such as triazole-tetrahydropyran (THP) and triazole-thiomorpholine-1,1-dioxide (TMO)) into the side chains further reduced FBR (Figure 6d). This approach ultimately achieved up to a 68% suppression in FBR and demonstrated satisfactory performance stability in the application of implanted OECT devices. This study inspires the possibility of achieving both high electronic performance and biocompatibility through chemical modifications of the CPs themselves, rather than relying entirely on systems such as hydrogels. Nevertheless, further in-depth investigation in this field is still needed.

4.2 | Degradability and Degradable CPs

Although CPs themselves exhibit low toxicity, their degradation products—such as small molecules and oligomers—may possess higher toxicity [123]. Therefore, it is generally necessary to minimize or avoid the biodegradation of CPs during long-term implantation. Unlike natural biomaterials such as sugars and proteins, the backbone of CPs primarily consists of carbon-carbon bonds, which are inherently difficult to degrade [41]. From another perspective, this non-degradable nature of CPs may lead to the accumulation of electronic waste from discarded devices [124]. In the field of inorganic devices, transient electronics—devices designed to physically disappear after use and/or disposal—have emerged as a promising solution [125, 126]. Beyond their environmental advantages, such devices can decompose in a controlled manner, rendering them untraceable and thereby enhancing security [127]. This concept is equally applicable to CP-based bioelectronic devices.

However, a critical challenge is to balance long-term operational stability under physiological conditions during their functional lifespan, while ensuring subsequent bio- or chemical degradability upon device decommissioning to prevent environmental accumulation. This dual requirement of sustained performance and controlled degradation represents a pivotal research focus in the field [128]. At the molecular level, this balance is difficult to achieve because electrical reliability in CPs relies on chemically robust backbones, stable π–π stacking, and doped states that withstand hydrolysis, oxidation, and ion-induced swelling. In contrast, degradability requires the presence of chemically cleavable motifs that can be cleaved in response to specific biological or chemical cues. Incorporating such cleavable units—whether in the backbone, side chains, or cross-linking motifs—must therefore be done in a way that does not compromise electronic delocalization, doping stability, or morphological integrity during long-term operation.

Compared with non-conjugated degradable polymers, the molecular design space for degradable CPs is highly limited, owing to the scarcity of available degradable molecular building blocks. In CPs, the double (–C═C–) and triple (–C≡C–) bonds that are essential for electronic conductivity possess high bond dissociation energies, which significantly constrain their biodegradability [129]. Given these challenges, numerous studies have focused on partially degradable CP-based materials. One approach is to incorporate organic conductive fillers into biodegradable polymer matrices (Figure 7a) [130–132]. Another strategy involves integrating (semi)conducting segments into the backbone of biodegradable materials (Figure 7b), or grafting CPs (Figure 7c) onto degradable substrates, via cleavable linkages. These approaches simultaneously impart electrical functionality and controlled degradability [132]. Nevertheless, these strategies exhibit intrinsic limitations: although the biodegradable polymer component may undergo decomposition in vivo, the conjugated segments remain non-degradable and may persist as residual deposits that are challenging to eliminate from the body. Additionally, the incorporation of degradable components may compromise the electrical conductivity, thereby influencing the overall device performance.

Introducing cleavable chemical motifs directly into the CP backbone offers a viable strategy to enable complete degradation into smaller fragments (Figure 7d). For instance, imine linkages (—C—N—) have been employed as reversible conjugated connectors: they remain stable under neutral pH conditions but undergo hydrolysis under mildly acidic environments. Based on this design principle, degradable OFETs and OECTs have been successfully developed [41, 133]. Such materials maintain structural stability, integrity, and biocompatibility, while their integration with biodegradable cellulose substrate enables the fabrication of fully degradable bioelectronic devices (Figure 7e). In addition to imine linkages, degradable heterocycles can also serve as linkers within CPs. Functionalized imidazole derivatives, for example, have been incorporated into thiophene- and DPP-based CP nanoparticles for biomedical imaging, where they undergo ROS-induced degradation [134, 135]. Currently, however, such

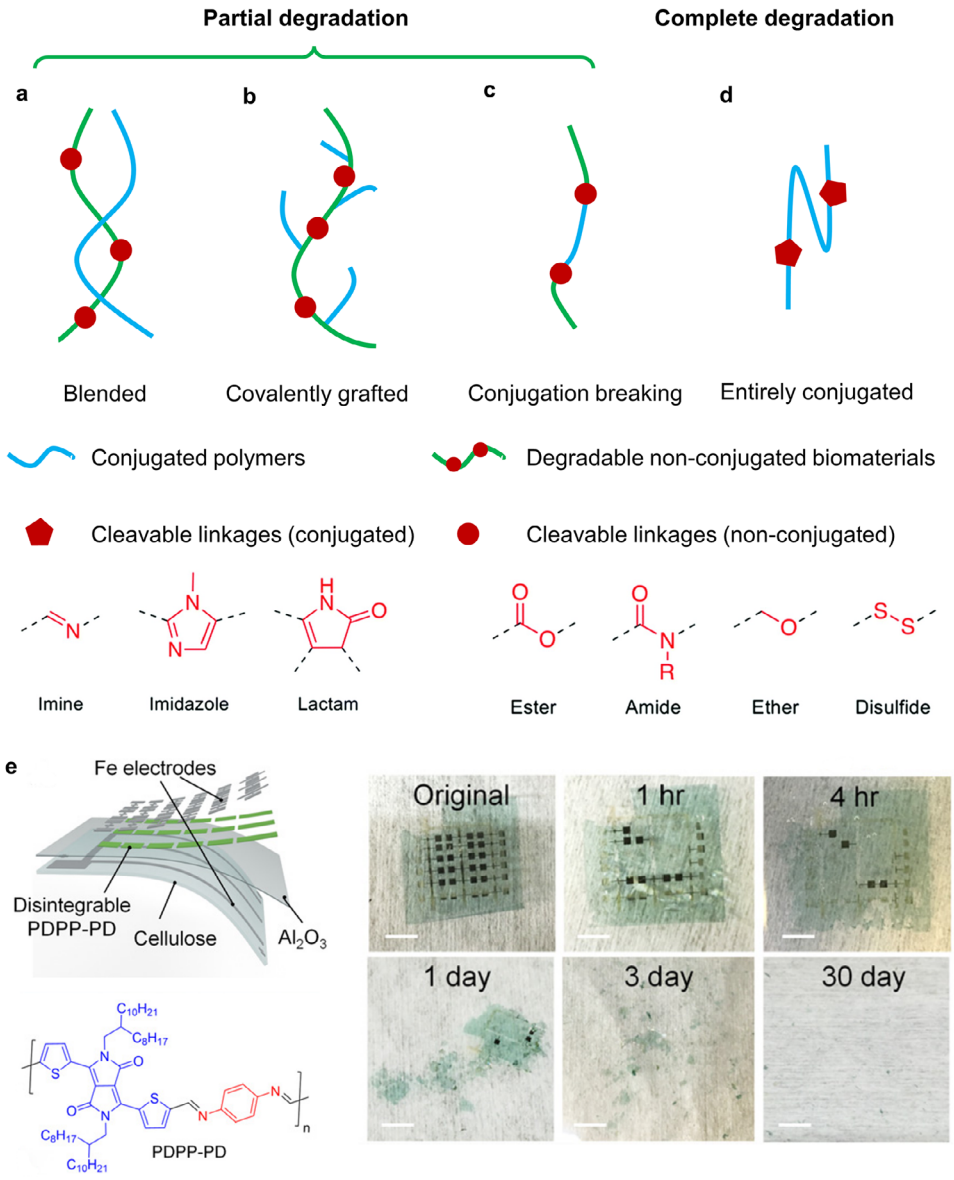

FIGURE 7 | Strategies for achieving degradable CPs and their applications. (a) Blending CPs with biodegradable polymers. (b) Incorporating CP oligomers into the backbone of biodegradable materials through cleavable linkages. (c) Connecting CP segments with biodegradable polymers. (d) Entirely degradable CPs containing reversible conjugated connectors. Blue lines represent non-degradable CPs such as polythiophene (PTh) and PEDOT. Green lines represent degradable but non-conjugated biomaterials such as poly(glycolide-L-(-)-lactide) (PGLA). Pentagons and circles denote degradable conjugated and non-conjugated linkers, respectively. Redrawn according to ref. [129]. (e) Schematic of the materials and device structure used for totally disintegrable electronics, and photographs of a device at various stages of disintegration [41]. (Scale bars: 5 mm.) Copyright 2017, National Academy of Sciences.

molecular designs are still limited. Achieving a balance among electrical performance, biocompatibility, and degradability in CPs demands continued research efforts.

5 | Conclusion

CPs, owing to their unique electronic structures and van der Waals intermolecular interactions, combine favorable electrical properties with biocompatibility, exhibiting distinct advantages for bioelectronic applications. These characteristics not only enable efficient charge transport and energy-level modulation at the molecular scale, thereby meeting the requirements of diverse devices for conductivity and switching behavior, but also allow the mechanical properties of the interface to be tailored for better matching with biological tissues. As core functional materials, CPs have been widely employed in passive bioelectrode devices to achieve highly sensitive and low-noise electrical signal acquisition and transmission [136]. They also play important roles in advanced systems such as OFETs and OECTs. Moreover, CPs possess high processability and structural tunability, allowing them to be combined with hydrogels, biomass-derived materials, and other polymeric matrices to form multifunctional composites with flexibility, adhesion, anti-inflammation, and degradability. These strategies significantly broaden the application scope of CPs, enabling the construction of robust device–tissue interfaces

with long-term stability and superior biocompatibility under complex physiological conditions. As a result, CPs not only excel in in situ chemical sensing and bioelectrical signal recording but also hold great promise for neuromorphic computing and implantable bioelectronic devices.

Although CP-based bioelectronic materials have achieved rapid progress in recent years, several challenges remain:

1. Although CP conductors represented by PEDOT:PSS have been relatively well developed, and the performance of p-type, n-type, and ambipolar CP semiconductors has advanced rapidly in recent years, their long-term stability under physiological conditions still needs to be improved, particularly for n-type and ambipolar materials.
2. Implantable CP-based bioelectronic devices (e.g., OECTs) still exhibit relatively low levels of integration, with limited in situ signal-processing capability, and slow response speeds, making it difficult to handle high-frequency bioelectrical signals effectively.
3. Although CP-hydrogel composites have demonstrated good biocompatibility, studies specifically focused on the intrinsic biocompatibility of CPs themselves remain scarce, highlighting the need for more targeted molecular design.
4. Fully degradable CP-based electronic devices remain scarce, and the overall sustainability of such bioelectronic systems still falls short of practical requirements.

To address these issues, a balance must be struck between the material's performance and its biocompatibility. Material design should not only focus on further improving the chemical and morphological stability of CPs during doping/dedoping processes [12], but also place greater emphasis on their stability under exposure to electrolytes, enzymatic activity, and mechanical stress. Incorporating bioactive units into CPs could enhance their biocompatibility, while introducing additional dynamic cleavable units may improve their degradability. From a device-design perspective, it is necessary to optimize material composition and circuit architecture in accordance with practical application scenarios, thereby enhancing in situ signal acquisition and processing capabilities. In addition, current biocompatibility assessments are largely limited to short-term in vitro and in vivo studies, whereas chronic implantable devices require long-term, physiologically relevant investigations to evaluate immune responses, degradation byproducts, and tissue remodeling. A deeper understanding of the fundamental interactions between CPs and living cells—particularly at the molecular level—will be essential for guiding the development of next-generation materials with improved functionality and safety.

To achieve long-term stable and high-performance bioelectronic devices, research should move beyond the concept of "passive biocompatibility", which merely minimizes adverse tissue responses, and instead focus on developing dynamic materials capable of actively adapting to environmental changes [137]. Such materials can enhance device stability, promote tissue regeneration and immune modulation, and ultimately enable closed-loop therapeutic interventions. Integrating CPs with soft and stretchable substrates, bioactive molecules, and advanced fabrication technologies (e.g., 3D printing, roll-to-roll processing, micro- and nanofabrication), while improving their compatibility with flexible materials, will facilitate the development of scalable and customizable bioelectronic platforms [136]. This approach can bridge the gap between laboratory studies and clinical applications, while deepening our understanding of bioelectronic–biological interactions [102].

Acknowledgements

This work is supported by Beijing Natural Science Foundation (2262050 [Zhang], QY25018 [Gao]) and National Natural Science Foundation of China (52403219 [Zhang], T2425010 [Lei], T2521001 [Lei]). The authors thank Mr. Chengwen Wu, Mr. Zhiyuan Xiong, and Mr. Xun Lei for their assistance in the literature survey and helpful discussions.

Funding

Beijing Natural Science Foundation (2262050 [Zhang], QY25018 [Gao]) and National Natural Science Foundation of China (52403219 [Zhang], T2425010 [Lei], T2521001 [Lei])

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The authors have nothing to report.

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