

## REVIEW

# PEDOT: PSS for Implantable and Wearable Bioelectronics: From Material Engineering and Energy Storage to Clinical Translation

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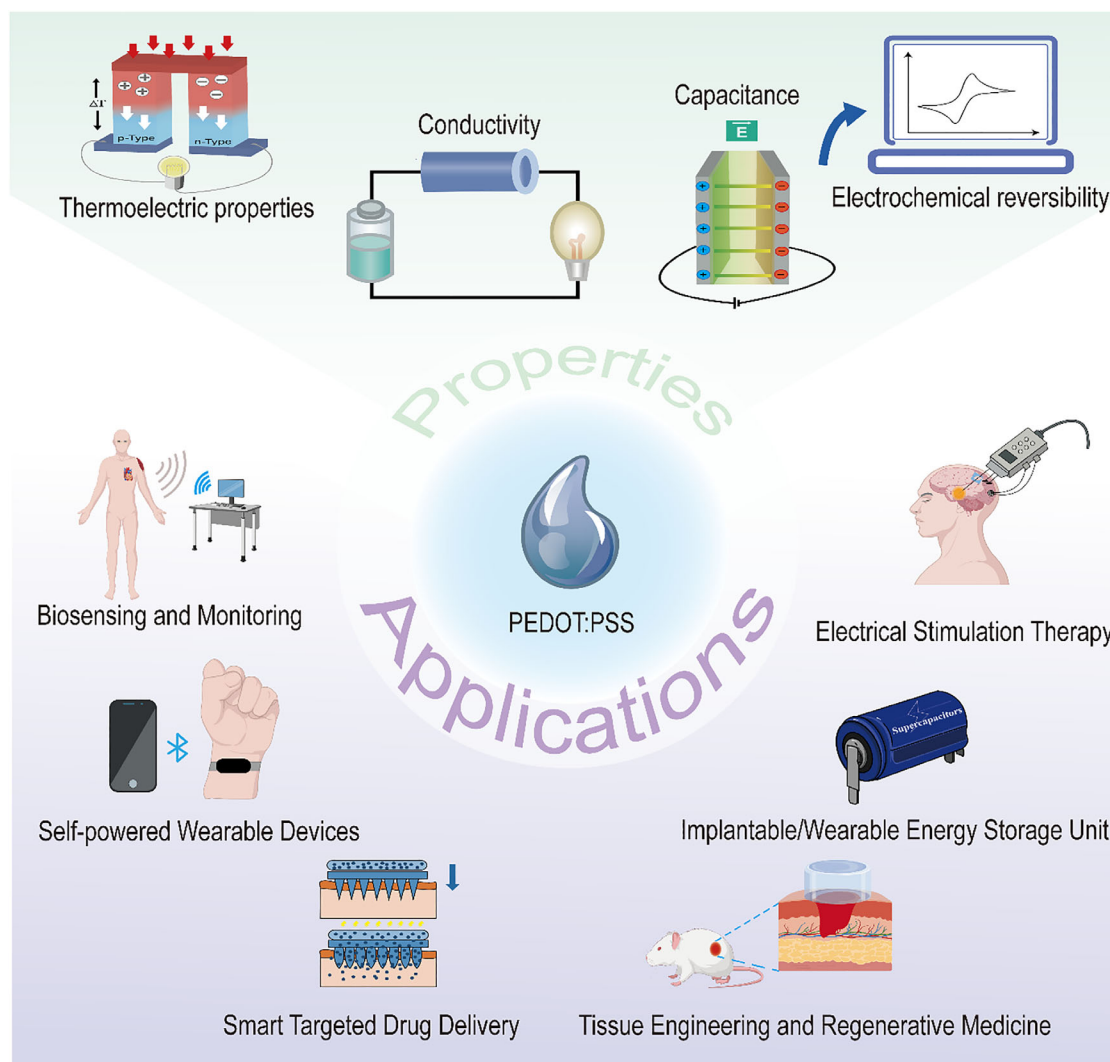
## ABSTRACT

Poly(3,4-ethylenedioxythiophene): polystyrene sulfonate (PEDOT: PSS), distinguished by its exceptional electrical conductivity, superior biocompatibility, and capacity for multifunctional integration, has emerged as a pivotal biomaterial at the nexus of biomedical engineering and flexible electronics. This review systematically elucidates the fundamental physicochemical attributes and charge transport mechanisms of PEDOT: PSS. It critically examines mainstream modification strategies—including solvent doping, surfactant engineering, nanocomposite formulation, and plasma treatment—providing deep insights into how these approaches govern the material's microstructure and macroscopic performance. Building on this foundation, we detail recent breakthroughs in frontier applications such as biosensing and real-time monitoring, electroceuticals, tissue engineering and regenerative medicine, smart targeted drug delivery, and self-powered wearable devices. Special emphasis is placed on the synergistic interplay among performance optimization, modification strategies, and clinical translation. Furthermore, the article offers a critical analysis of persistent challenges hindering clinical adoption, including long-term stability, biosafety, and batch-to-batch consistency. Finally, we outline future trajectories, such as counterion substitution, biomimetic interface functionalization, and intelligent closed-loop systems. This work aims to establish a robust theoretical and technical framework to accelerate the advanced research and broad deployment of PEDOT: PSS in biomedical contexts.

## 1 | Introduction

Conventional medical electronic materials have predominantly relied on metals (e.g., platinum, gold, titanium) or inorganic compounds (e.g., indium tin oxide, ITO). However, these materials face significant challenges in biomedical applications, including suboptimal biocompatibility, excessive electrochemical impedance, mechanical mismatch with soft biological tissues, and a high propensity to induce inflammatory and fibrotic

responses [1]. With the rapid advancement of biomedical engineering, there is an increasingly urgent demand for novel materials capable of meeting the stringent requirements of clinical diagnosis and therapy. In this context, PEDOT: PSS, a water-soluble conductive polymer, has emerged as one of the most prominent conductive polymers in current research and applications, owing to its exceptional electrical conductivity, intrinsic flexibility, extraordinary mechanical robustness, and superior chemical and electrochemical stability [2–5].

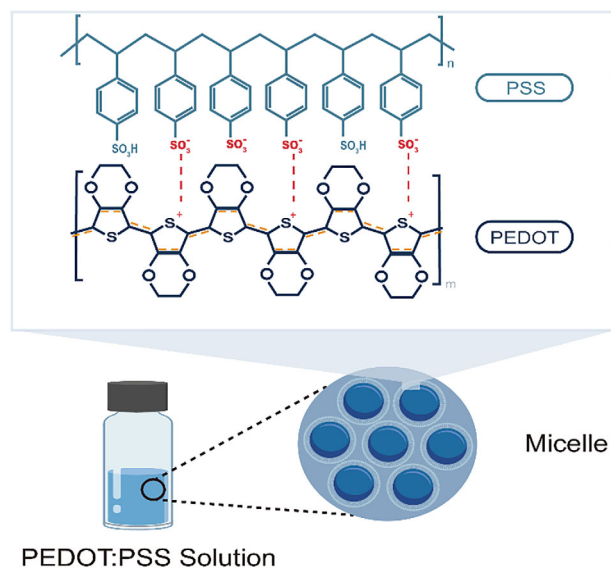


**FIGURE 1** | Key Properties of PEDOT: PSS and Its Applications in the Biomedical Field. (Partly created with BioGDP.com).

The distinctive advantages of PEDOT: PSS have unlocked substantial potential across multiple frontier domains, as illustrated in Figure 1. In flexible electronics, it effectively overcomes the inherent brittleness and mechanical failure of traditional ITO electrodes under bending, serving as an ideal substitute for flexible optoelectronic devices. Furthermore, PEDOT: PSS resolves interfacial bottlenecks in two-dimensional (2D) and organic flexible transistors by establishing defect-free van der Waals contacts. Benefiting from its unique ion–electron coupled conduction mechanism, it has established itself as a core material platform for flexible bioelectronics, wearable physiological sensors, and implantable brain–computer interfaces. In the realm of energy storage, PEDOT: PSS functions as a tri-functional component integrating active material, conductive agent, and binder. This integration not only addresses the limitations of conventional electrodes associated with high ratios of inactive components and limited energy density but also leverages its intrinsic flexibility to mitigate volume strain during cycling. By combining pseudocapacitance and electrical double-layer capacitance mechanisms, PEDOT: PSS achieves an optimal synergy of high specific capacity and long-term cycling stability. Moreover, in biosensing and monitoring, PEDOT: PSS significantly enhances the signal-to-noise ratio, enabling the precise

capture of faint biological signals for high-fidelity recording and stimulation, thereby offering new avenues for the development of highly sensitive optical sensors [6, 7]. Crucially, characterized by a low inflammatory profile and favorable biocompatibility [8], PEDOT: PSS-based smart wound dressings can accelerate healing by remodeling endogenous electric fields via electrical stimulation, potentially acting synergistically with other therapeutic modalities [9–11].

Beyond these applications, PEDOT: PSS has pioneered new paradigms in disease treatment and device power supply. Through voltage or photothermal stimulation, it facilitates switch-like, on-demand targeted drug delivery, providing an innovative strategy for precision therapy [12]. Simultaneously, leveraging its self-powered characteristics such as thermoelectricity and triboelectricity, PEDOT: PSS enables the fabrication of advanced sensing devices like smart textiles and flexible patches, opening new pathways for the development of self-powered wearable systems [13–15]. Given these multifaceted capabilities, this review aims to systematically elucidate the material properties and mechanisms of action of PEDOT: PSS, highlighting its distinct advantages over conventional counterparts. It critically analyzes modification strategies and underlying principles



**FIGURE 2** | Schematic diagram of the core-shell micelle structure and chemical structure of PEDOT:PSS. (Partly created with BioGDP.com).

for optimizing PEDOT:PSS in biomedical applications. Finally, it synthesizes the latest preclinical research advances while discussing current challenges and outlining future developmental directions.

## 2 | Properties and Modifications of PEDOT:PSS

PEDOT:PSS is characterized by a distinctive core-shell micelle structure, featuring a conductive, hydrophobic core surrounded by a hydrophilic, dispersing shell.

As shown in Figure 2, A key feature of this structure is the ethylene oxide substituent ( $-\text{O}-\text{CH}_2-\text{CH}_2-\text{O}-$ ) at the 3,4-positions of the thiophene ring. Acting as an electron donor, this group lowers the oxidation potential of the ring, facilitating the formation of a positively charged main chain. In contrast, the PSS component consists of an amorphous polystyrene backbone with sodium sulfonate groups ( $-\text{SO}_3^-\text{Na}^+$ ) attached at the para-positions of the benzene rings. Within the composite, PSS serves as both a dopant and a dispersant. Its molecular weight, typically much higher than that of PEDOT, provides the spatial framework necessary to stabilize the core-shell structure. Together, PEDOT and PSS form a stable ion-pair complex that retains the conductivity of PEDOT while leveraging the water solubility of PSS to enable solution processing [16].

### 2.1 | Conductivity and Modification Strategies

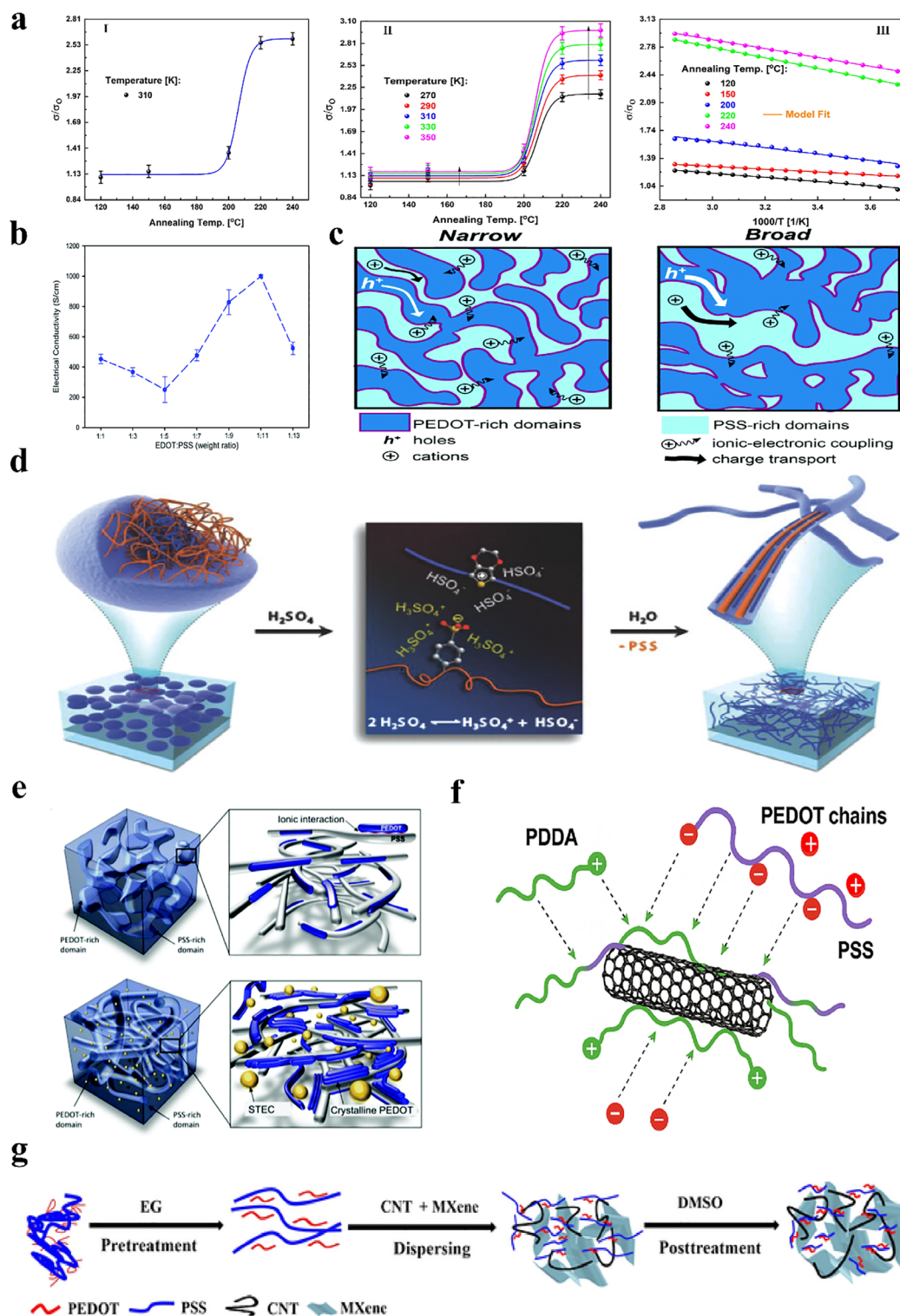
In the PEDOT:PSS complex, PEDOT serves as the conductive conjugated backbone. Charge carriers migrate along PEDOT chains and traverse inter-chain gaps via a hopping mechanism, establishing percolation pathways that act as “highways” for charge transport [17]. This unique architecture endows PEDOT:

PSS with mixed ionic-electronic conductivity, enabling the simultaneous transport of electrons and ions [18, 19].

The electrical conductivity of PEDOT:PSS is governed by several critical factors: the oxidation level of PEDOT, the PSS-to-PEDOT mass ratio and molecular weight, and the degree of crystallinity. The oxidation state of PEDOT can be effectively modulated via thermal annealing or UV-ozone treatment. Yigzaw et al. [20] identified  $200^\circ\text{C}$ – $220^\circ\text{C}$  as the optimal thermal annealing range, reporting a 121% enhancement in conductivity compared to samples treated at  $150^\circ\text{C}$  (Figure 3a). Similarly, UV-ozone treatment generates reactive oxygen species (e.g.,  $\cdot\text{OH}$ ,  $\text{O}_3^+$ ) that directly oxidize the PEDOT backbone while concurrently reducing the  $\text{Na}^+$  content and promoting PSS protonation. This optimization of the ionic equilibrium between PEDOT and PSS leads to a substantial increase in conductivity.

Conversely, an excessive PSS mass ratio impedes charge transport by insulating the conductive PEDOT domains (Figure 3b). Commercially available PEDOT:PSS dispersions typically exhibit PSS: PEDOT mass ratios ranging from 1:4 to 1:8 (often denoted as high-conductivity grades), yielding conductivities between 100 and 1000 S/cm, which represents an optimal balance of performance [21]. Regarding molecular weight, high-MW PSS improves dispersion stability, while a narrow polydispersity index ( $\text{PDI} < 1.6$ ) facilitates a more ordered molecular arrangement [22] (Figure 3c). Studies indicate that a PSS molecular weight of approximately 30 kDa offers the best compromise between maintaining network integrity and ensuring efficient PEDOT connectivity [23].

Furthermore, enhancing crystallinity is a potent strategy for boosting conductivity. This process often involves a conformational transition of the PEDOT chain from a coiled benzenoid structure to a linear quinoid structure, which extends conjugation length and enhances carrier mobility. The quinoid conformation promotes tighter  $\pi$ - $\pi$  stacking and reduces the energy barrier for electronic transitions. Seong-Kim et al. [24] demonstrated this by comparing films prepared via three distinct methods: pristine films (Pr-P) via direct spin-coating and annealing; ethylene glycol-treated films (EG-P); and highly crystalline films (Crys-P) prepared via solvent-assisted crystallization using concentrated sulfuric acid, which induces structural rearrangement and partial PSS removal. The Crys-P films exhibited a remarkable conductivity of 4100 S/cm—representing a 2412-fold increase over Pr-P and a 6.9-fold improvement over EG-P. This superior performance is attributed to an “edge-on” stacking orientation, where PEDOT chains align preferentially along the in-plane direction. This alignment minimizes the  $\pi$ - $\pi$  stacking distance ( $d \sim 0.34$  nm), thereby facilitating efficient intra-chain and inter-chain charge transport. Doshi et al. [25] proposed replacing conventional 3-Glycidyloxypropyltrimethoxysilane (GPTMS) chemical cross-linking with high-temperature, short-duration heat treatment to remove the insulating PSS and enhance the crystallinity of PEDOT:PSS. The resulting films exhibit water stability comparable to that of GPTMS-cross-linked films, with conductivity and volume capacitance increased threefold; the process is compatible with a variety of substrates, including glass, elastomers, and textiles.



**FIGURE 3** | PEDOT:PSS conductivity and influencing factors. (a-I) The curve of normalized conductivity with respect to annealing temperature at a fixed test temperature of 310 K. (a-II) The variation of normalized conductivity with annealing temperature at different in situ test temperatures. (a-III) Normalized Arrhenius fitting conductivity curves under different annealing temperatures. Reproduced with permission. Copyright 2025, Springer Nature. (b) The electrical conductivity of PEDOT:PSS varies with different mass ratios of EDOT and PSS. Reproduced with permission. Copyright 2019, Royal Society of Chemistry. (c) Effect of Different PSS Particle Size Distributions on Electrical Conductivity. Reproduced with permission. Copyright 2022, Royal Society of Chemistry. (d) Diagram of the structural rearrangement of PEDOT:PSS. Reproduced with permission. Copyright 2015, John Wiley and Sons. (e) Schematic diagram representing the morphology of PEDOT:PSS with a stretchable transparent electronic conductor enhancer. Reproduced with permission. Copyright 2020, Royal Society of Chemistry. (f) Schematic of electrostatic interaction mechanism between PDDA, SWCNT, and PEDOT:PSS. Reproduced with permission. Copyright 2025, Royal Society of Chemistry. (g) Mechanisms to enhance the properties of PEDOT/SWCNT/MXene composite films. Reproduced with permission. Copyright 2025, Shilong Zhang et al.



### 2.1.1 | Solvent-Doped Modification

Solvent doping has emerged as the most prevalent and effective strategy due to its simplicity and high efficiency. High-dielectric-constant solvents attenuate the electrostatic attraction between PEDOT<sup>+</sup> and PSS<sup>-</sup> through dielectric screening. Solvent dipoles surround the PSS<sup>-</sup> chains, forming a shielding layer that weakens the Coulombic binding forces, thereby facilitating the unfolding of the PEDOT backbone [26]. Concurrently, specific solvent-polymer interactions disrupt the hydrogen bonding and ionic cross-linking between PEDOT and PSS, further promoting chain extension [27]. This process drives a critical conformational transition: PEDOT transforms from a low-conductivity, coiled benzoid structure to a highly conductive, linear/extended quinoid structure. As shown in Figure 3d, adoption of the quinoid conformation extends the effective conjugation length, expands the  $\pi\pi$ -electron delocalization range, and reduces the carrier effective mass. Accompanying this transition is a narrowing of the bandgap, which significantly enhances both carrier concentration and mobility [28]. Furthermore, solvent treatment induces the reorganization of PEDOT chains into a more compact  $\pi$ - $\pi$  stacked arrangement, increasing crystallite size and crystallinity to establish a long-range ordered morphology [29].

The incorporation of additives such as inorganic acids, organic solvents, or ionic liquids can synergistically enhance conductivity through multiple mechanisms. A universal effect is the promotion of grain growth; larger PEDOT crystallites reduce the density of grain boundaries, thereby lowering the barrier for inter-grain hopping. Simultaneously, these solvents induce microphase separation between PEDOT and PSS, optimize chain conformation, and boost carrier density, collectively accelerating charge transfer kinetics [30]. Among these, organic solvent treatment remains the most widely adopted approach [31]. Table 1 summarizes mainstream solvent modification strategies and their corresponding performance enhancements. Notably, solvent doping is frequently combined with other modification techniques to achieve synergistic effects, yielding conductivity improvements far exceeding those of single-method approaches.

### 2.1.2 | Surfactant Modification

Surfactants, leveraging their unique amphiphilic architecture, serve as precise regulators of the PEDOT: PSS microstructure. Their hydrophobic tails intercalate at the interface between the hydrophobic conjugated PEDOT core and the hydrophilic PSS shell, effectively disrupting the electrostatic Coulombic interactions between the two components. This disruption drives a critical conformational transition: PEDOT chains evolve from a tightly coiled benzoid structure to a linearly extended quinoid conformation. This structural reorganization markedly enhances intermolecular  $\pi$ - $\pi$  stacking, shortens the carrier hopping distance, and substantially boosts carrier mobility [54]. Furthermore, surfactants form robust associations with the sulfonate groups of PSS via hydrogen bonding or electrostatic interactions, inducing macroscopic phase separation between the conductive PEDOT-rich domains and the insulating PSS-rich matrix, as illustrated in Figure 3e. During post-processing, excess insulating PSS and residual surfactants can be selectively

eluted. This purification not only minimizes carrier scattering by insulating barriers but also facilitates the formation of a continuous, three-dimensional (3D) percolation network.

Distinct classes of surfactants operate via specific mechanisms:

**Anionic Surfactants:** Their anionic headgroups competitively displace PSS from binding sites on the PEDOT backbone, triggering pronounced phase separation [55]. Hossain et al. [56] demonstrated that sodium dodecylbenzene sulfonate yields optimal results; adding merely 0.94 wt.% sodium dodecylbenzene sulfonate surged film conductivity from 0.48 to 480.45 S/cm.

**Non-ionic Surfactants:** Lacking free ions, these agents introduce no ionic impurities while offering superior dispersion stability, biocompatibility, and processability. Park et al. [57] utilized Triton X-100 to fabricate a protective layer (7.5 wt.% loading) on graphene oxide (GO)-AgNW electrodes. This modification reduced the sheet resistance to 1.61  $\Omega$ /sq—a 49.73% decrease compared to pristine GO-AgNW electrodes—significantly enhancing electrical performance.

**Cationic Surfactants:** The cationic headgroups form strong electrostatic complexes with PSS sulfonate groups, enabling highly efficient PEDOT chain release even at trace concentrations. Fang et al. [58] employed cetyltrimethylammonium bromide to reduce series resistance and enhance hole transport. Under optimal conditions (0.15 wt.% cetyltrimethylammonium bromide, annealed at 175°C for 8 min), devices achieved a power conversion efficiency of 4.4%, a 50% improvement over the 3% power conversion efficiency of control devices based on pure PEDOT: PSS.

**Fluorocarbon Surfactants:** Benefiting from exceptional hydrophobicity and oleophobicity, fluorocarbon chains exhibit phase separation efficiency and conformational control superior to conventional hydrocarbon surfactants, while simultaneously optimizing film planarity. Mahato et al. [59] synergistically combined 5% DMSO with 0.1% Capstone FS-3 fluorocarbon surfactant, yielding a modified film with a sheet resistance as low as 122  $\Omega$ /sq, rivaling commercial ITO.

### 2.1.3 | Modification of Composite Nanomaterials

The fundamental rationale for incorporating nanomaterials lies in introducing a highly conductive secondary phase to construct synergistic hybrid networks. The surface charge effects of these nanofillers effectively attenuate the Coulombic interactions between PEDOT<sup>+</sup> and PSS<sup>-</sup>, facilitating phase separation and the formation of continuous conductive domains [60]. The physical intercalation of nanoparticles at the PEDOT: PSS interface not only promotes the removal of insulating PSS and enhances the packing density of PEDOT chains but also induces a conformational transition of PEDOT from a coiled benzoid to an extended quinoid structure. This structural reorganization significantly reduces the  $\pi\pi$ - $\pi\pi$  stacking distance, thereby boosting carrier mobility by one to two orders of magnitude. Concurrently, strong interfacial interactions between the nanomaterials and PEDOT: PSS mitigate the insulating encapsulation effect of the PSS shell, further enhancing charge transport efficiency [61, 62]

**TABLE 1** | Representative solvent-doped modification properties.

| Solvent                              | Modification conditions                                                                                                                                    | electrical conductivity (S/cm) | Efficiency (fold)     | Refs. |
|--------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------|-----------------------|-------|
| H <sub>2</sub> SO <sub>4</sub>       | 95% sulfuric acid                                                                                                                                          | 3200                           | 6400                  | [32]  |
| CH <sub>3</sub> CH <sub>2</sub> COOH | Propionic acid, 8 mol/L (120°C–160°C)                                                                                                                      | 197                            | 985                   | [33]  |
| HNO <sub>3</sub>                     | 70% HNO <sub>3</sub> drop-casting treatment, annealing at 140°C                                                                                            | 2250                           | 2250                  | [34]  |
| EG                                   | 7 wt.% solution spin-coated at 6000 rpm, annealed on a hot plate at 110°C for 10 min                                                                       | 4800                           | 7.3 × 10 <sup>4</sup> | [35]  |
| EG                                   | Heat and stir, spin-coat at 1000 rpm, anneal at 160°C                                                                                                      | 1228.4                         | 3000                  | [36]  |
| PEG                                  | PEG 200–400 at 2% concentration                                                                                                                            | 805                            | 2680                  | [37]  |
| Glycerol                             | 55 wt.% glycerol, humidity 40%–45%, temperature 22°C                                                                                                       | —                              | 5                     | [38]  |
| DMF                                  | DMF synergizes with AgNO <sub>3</sub> , ZnCl <sub>2</sub> , CuCl <sub>2</sub> , and InCl <sub>3</sub>                                                      | 0.022                          | 2200                  | [39]  |
| Sorbitol                             | 6 wt.% concentration, stirred for 12 h, filtered and annealed                                                                                              | 722.06                         | 471                   | [40]  |
| ACN                                  | ACN to water volume ratio 1:1, 180°C                                                                                                                       | 103                            | 100                   | [41]  |
| DMSO                                 | 5% DMSO, suspension stirred for 20 min, sonicated for 15 min                                                                                               | 1033                           | 2000                  | [42]  |
| MeOH                                 | Add a few drops first, then soak                                                                                                                           | 1362                           | 4540                  | [43]  |
| DMSO/Na <sub>2</sub> SO <sub>3</sub> | Films were prepared by spin-coating, followed by post-treatment in a DMSO/Na <sub>2</sub> SO <sub>3</sub> mixture, rinsed with deionized water, and dried. | ~800                           | 800                   | [44]  |
| DMSO/MeOH                            | Spin-coating at 500 rpm for 60 s, followed by annealing in a nitrogen atmosphere at 140°C for 10 min, then post-processing.                                | 1105                           | 3683                  | [45]  |
| TFMS/MeOH                            | Add 200 µL of the mixture to a hot plate at 130°C. After drying, wash three times with methanol and dry at 130°C for 2 min.                                | 2980                           | 4257                  | [46]  |
| MAI/TFA                              | Spin-coat 120 µL of a 3 wt.% MAI/TFA mixed solution in one step                                                                                            | 1508                           | 15 080                | [47]  |
| DPM                                  | 6 wt.% DPM, stirred at 300 rpm at room temperature for 10 h                                                                                                | 746.27                         | 49 751                | [48]  |
| PPH                                  | 1.5 wt.% PPH, stirred at 300 rpm at room temperature for 10 h                                                                                              | 710.21                         | 47 347                | [48]  |
| EG/ MeOH                             | 16 wt.% mixed co-solvent, stirred thoroughly at room temperature                                                                                           | 780                            | 780                   | [49]  |
| DBSA                                 | Spin coating at 500 rpm for 10 s, spin coating at 1500 rpm for 45 s                                                                                        | 500                            | 500                   | [50]  |
| DMSO/EG/DMF                          | Stir for 12 h, followed by solvent post-treatment.                                                                                                         | 858.1                          | 1430                  | [51]  |
| IPA                                  | 0.48 g Na <sub>2</sub> S <sub>2</sub> O <sub>8</sub> , 40 mg Fe <sub>2</sub> (SO <sub>4</sub> ) <sub>3</sub> , 0°C to room temperature, 3.5 h              | 0.0609                         | 1.2                   | [52]  |
| LiBF <sub>4</sub> /CuCl <sub>2</sub> | Dispense volume: 10 µL; electrode spacing: 2.5 mm; vacuum drying temperature: 25°C                                                                         | 0.67                           | 23                    | [53]  |

(Figure 3f). Moreover, nanofillers act as effective fillers for pores and defects within the film, minimizing charge scattering sites and substantially lowering overall resistivity.

**2.1.3.1 | Carbon-Based Nanomaterials.** Owing to their exceptional electrical conductivity and mechanical robustness, carbon-based nanomaterials have emerged as ideal fillers for

PEDOT: PSS composites [63]. Prominent examples include carbon nanotubes (CNTs) and GO/rGO [64].

**Graphene Hybrids:** Zhang et al. [65] developed a PEDOT: PSS/rGO composite electrocatalyst where strong  $\pi\pi$ – $\pi\pi$  interactions induce a benzoid-to-quinoid transition in PEDOT chains, accompanied by electron transfer from rGO to PEDOT. Consequently, the composite exhibits a superior electron transfer

number of 3.3–3.8 in the oxygen reduction reaction, significantly outperforming pure PEDOT: PSS (2–2.2) and pristine rGO (2.3–2.8).

**Shear-Induced Assembly:** Zhang et al. [66] proposed a novel high-speed non-solvent turbulent secondary doping strategy. By introducing intense shear forces, single-walled carbon nanotubes (SWCNTs) trigger the morphological reconfiguration of PEDOT: PSS colloids from spherical to elongated or multi-branched filamentous structures. These structures subsequently co-assemble with SWCNTs to form a robust conductive network. This architecture not only aggregates PEDOT domains into continuous pathways but also enables SWCNTs to tightly wrap around PEDOT: PSS filaments, creating a layered stacking motif that overcomes the discontinuity limitations of pure PEDOT: PSS. At a loading of 40 wt.% SWCNTs, the film achieved an ultrahigh conductivity of  $4717.8 \pm 41.5$  S/cm.

**Microfluidic Synthesis for Flow Electrodes:** Rauer et al. [67] pioneered the use of PEDOT: PSS conductive hydrogel microspheres as alternatives to traditional carbon-based flow electrodes. Utilizing a high-throughput 8-nozzle microfluidic system, they synthesized porous PEDOT: PSS/CNT composite particles with controlled morphology. Incorporating 5–10 wt.% CNTs increased the particle conductivity from 20 S/cm (pristine PEDOT: PSS) to 32 S/cm. This work challenges conventional activated carbon-based designs, offering a novel material platform to resolve the critical trade-off between the percolation threshold and pumpability in flow capacitive deionization systems.

**2.1.3.2 | Metallic Nanomaterials.** Metallic nanomaterials act as highly conductive fillers that create continuous, low-resistance pathways within the PEDOT: PSS matrix. Zero-dimensional nanoparticles function as “conductive bridges,” connecting nearby PEDOT domains and filling the insulating gaps between grains [68]. Das et al. [69] studied hybrid films made of covalently encapsulated gold nanoparticles and polyvinyl alcohol (PVA), finding that these nanoparticles naturally form clusters with excellent internal connectivity. This creates a hierarchical network where resistance within clusters is much lower than between them, allowing the films to achieve an extremely low resistivity of about  $4.42 \times 10^{-5}$   $\Omega$ /m. Moving to one-dimensional structures, nanowires can form long-range, interconnected networks that significantly lower the threshold needed for conductivity (percolation threshold) and provide fast paths for charges. For example, Seimela et al. [70] used copper nanorods doped into PEDOT: PSS as a hole transport layer in solar cells, increasing device efficiency by 42% thanks to this combined effect of better charge transport and improved interfacial contact. Additionally, liquid metals offer a unique solution by seamlessly filling voids inside the film, adapting to surface shapes, and removing rigid boundaries between grains [71, 72]. Zhao et al. [73] created a conductive hydrogel using liquid metal nanoparticles stabilized by PEDOT: PSS, achieving a conductivity of 0.0485 S/cm. In this system, PEDOT: PSS prevents the liquid metal particles from clumping together while its own conductive chains build bridges between them, creating a continuous network without the negative effects of traditional insulating stabilizers.

### 2.1.3.3 | Non-Metallic Oxide Nanomaterials.

Non-metallic oxide nanofillers leverage their surface oxygen-containing functional groups (e.g., hydroxyl, carboxyl, and epoxy) to form robust hydrogen bonds or electrostatic interactions with the sulfonate moieties of PSS chains. This interaction effectively attenuates the Coulombic attraction between PEDOT<sup>+</sup> and PSS<sup>−</sup>, triggering a critical conformational transition in the PEDOT backbone from a coiled, low-conductivity benzoid structure to a linearly extended, highly conductive quinoid conformation. This structural reorganization significantly enhances  $\pi$ – $\pi$  conjugation and intra-chain charge transport. Concurrently, these interfacial interactions induce macroscopic microphase separation between PEDOT-rich and PSS-rich domains, substantially mitigating the insulating barrier effect of PSS and thereby boosting inter-chain carrier mobility. Vázquez-López et al. [74] fabricated layered hybrid composites using high-purity, high-crystallinity SnO nanoparticles synthesized via hydrolysis. This architecture optimizes charge transport pathways by reconstructing the polymer chain configuration, which not only elevates carrier mobility but also amplifies carrier concentration through interfacial charge transfer. This synergistic enhancement resulted in a dramatic four-order-of-magnitude increase in conductivity, rising from  $1.82 \times 10^{-2}$  S/cm for pristine PEDOT: PSS to  $6.33 \times 10^2$  S/cm for the SnO/PEDOT: PSS composite.

**2.1.3.4 | MXene Nanomaterials.** MXenes, typically exemplified by  $\text{Ti}_3\text{C}_2\text{T}_x$ , represent a burgeoning class of 2D transition metal carbides/nitrides. Owing to their ability to establish robust interfacial interactions with PEDOT: PSS, they have emerged as ideal dopants for surmounting the intrinsic conductivity bottlenecks of conductive polymers [75]. First synthesized by Naguib et al. [76] in 2011 via room-temperature hydrofluoric acid etching of  $\text{Ti}_3\text{AlC}_2$ , MXenes consist of few-layered  $\text{Ti}_3\text{C}_2$  nanocrystals exhibiting intrinsic metallic conductivity. When dispersed within a PEDOT: PSS matrix, these 2D nanosheets act as highly efficient “conductive bridges,” effectively disrupting the insulating core–shell architecture of PEDOT: PSS colloids. This disruption induces vertical phase segregation, driving the insulating PSS phase toward the film surface while enriching the conductive PEDOT domains at the interface, as illustrated in Figure 3g. Consequently, this structural reorganization constructs a continuous conductive framework that bridges inter-chain gaps, establishing a synergistic percolation network characterized by coupled “MXene ballistic pathways/PEDOT hopping transport”. Furthermore, the surface terminal groups (–OH, –O, –F) on MXenes foster strong interfacial coupling with PEDOT chains, enhancing compatibility while significantly mitigating charge scattering and contact resistance at the heterojunctions. Notably, Zhang et al. [77] demonstrated a triple-mechanism enhancement strategy via tartaric acid treatment of  $\text{Ti}_3\text{C}_2\text{T}_x$ /PEDOT: PSS composites. This post-treatment serves three critical functions: (i) it passivates the MXene surface against oxidative degradation into insulating  $\text{TiO}_2$ ; (ii) it selectively etches away the hydrophilic, insulating PSS component; and (iii) it optimizes interfacial packing. This synergistic approach reduced charge transport barriers and elevated the composite conductivity from 552 to 2240 S/cm, representing a fourfold enhancement.

### 2.1.4 | Plasma Modification

Plasma modification represents a solvent-free, dry physico-chemical synergistic strategy. Its core mechanism relies on the bombardment of active plasma species—comprising high-energy electrons, ions, and free radicals—onto the surface and subsurface regions of PEDOT: PSS films. This interaction induces selective ablation of the insulating PSS phase, promotes PEDOT chain alignment, and optimizes the aggregate morphology, collectively minimizing charge transport resistance and substantially boosting conductivity. Vaagensmith et al. [78] pioneered an eco-friendly, strong-acid-free protocol for PEDOT: PSS transparent electrodes by integrating additive blending, solvent post-treatment, and mild oxygen plasma exposure. This collaborative approach yielded breakthrough optoelectronic performance, achieving a minimum sheet resistance of 15  $\Omega/\text{sq}$  and a maximum conductivity of 5012 S/cm. Furthermore, the plasma treatment drastically reduced the water contact angle from 32° to 14°, signifying a marked enhancement in surface wettability. This improvement effectively mitigated wetting defects during the sequential spin-coating of multilayer structures, thereby reinforcing interlayer adhesion. Crucially, the controlled surface oxidation optimized the interfacial energetics for subsequent perovskite layer deposition without compromising the highly conductive, fibrous morphology of the underlying PEDOT network.

## 2.2 | Thermoelectric and Modification Strategies

PEDOT: PSS is currently recognized as the leading p-type flexible organic thermoelectric material, offering the most favorable balance of properties. Its success stems from tunable carrier transport within its conjugated system, inherently low lattice thermal conductivity, and the ability to independently optimize key thermoelectric parameters through multi-scale regulation [79–82]. The performance of thermoelectric materials is defined by the dimensionless figure of merit,  $ZT = S^2\sigma T/\kappa ZT = S^2\sigma T/\kappa$ . Here, the Seebeck coefficient and electrical conductivity form the power factor, which determines the material's ability to generate electricity [83].

As a typical p-type organic semiconductor, PEDOT: PSS uses holes as its majority carriers. When subjected to a temperature gradient, holes at the high-temperature end gain higher kinetic energy and diffuse faster toward the low-temperature end. This net migration creates a positive thermoelectric potential, resulting in a positive Seebeck coefficient [84]. Crucially, the material's thermal conductivity is exceptionally low ( $\sim 0.17$  W/m/K), significantly less than that of traditional inorganic materials like  $\text{Bi}_2\text{Te}_3$  ( $\sim 1.5$  W/m/K) [85, 86]. This intrinsic low thermal conductivity helps minimize heat loss, maintaining a stable temperature gradient essential for efficient conversion. This advantage partially compensates for the generally lower Seebeck coefficients of organic materials compared to inorganic ones, making it a key factor in achieving high  $ZT$ -values [84]. Therefore, PEDOT: PSS shows great potential for low-grade waste heat recovery and self-powered flexible devices [87, 88].

The thermoelectric properties of PEDOT: PSS are highly dependent on temperature [84, 89]. As shown in Figure 4a, at low tem-

peratures ( $<350$  K), conductivity increases with rising temperature, following the variable-range hopping mechanism, while the Seebeck coefficient rises steadily. In the mid-temperature range (350–450 K), conductivity reaches its peak while the Seebeck coefficient continues to grow; the combination of these factors leads to a maximum power factor in this interval. However, above 450 K, the PSS component begins to thermally decompose. This disrupts the conductive PEDOT network, causing a rapid decline in conductivity. Although the Seebeck coefficient increases sharply due to a drop in carrier concentration, the overall power factor decreases significantly.

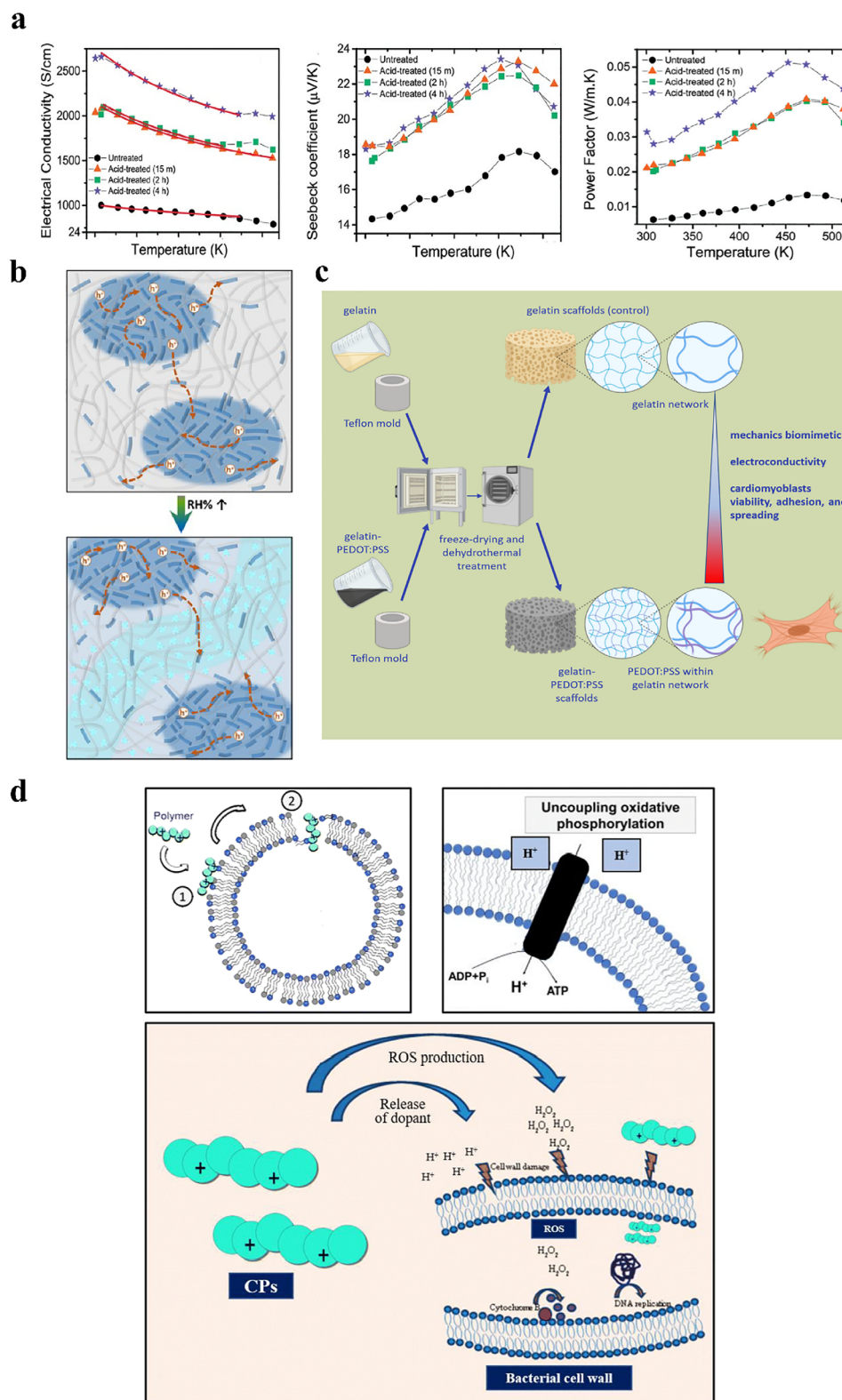
Additionally, the strong hydrophilicity of PSS poses a challenge. In humid environments, PEDOT: PSS films absorb water, causing the conductive network to swell and increasing carrier scattering, which severely reduces conductivity (Figure 4b). Moreover, moisture promotes the de-doping of PEDOT chains, leading to long-term degradation of thermoelectric performance [90].

Charge transport in conjugated polymers is predominantly governed by a variable-range hopping mechanism, wherein carriers exhibit heightened sensitivity to thermal gradients when traversing inter-chain or inter-aggregate barriers. At the hot junction, elevated carrier energies facilitate these hopping transitions, generating a substantial electrochemical potential gradient that manifests as a high Seebeck coefficient. While pristine PEDOT: PSS inherently possesses a favorable  $S$  (typically 40–60  $\mu\text{V/K}$ ), optimizing the power factor requires a delicate balance between  $S$  and electrical conductivity. Strategic regulation of carrier concentration is essential to decouple these interdependent parameters, preventing the characteristic degradation of  $S$  at high  $\sigma$  levels [91]. Concurrently, minimizing lattice thermal conductivity is critical to suppress parasitic heat conduction. PEDOT: PSS excels in this regard, exhibiting an intrinsically low thermal conductivity significantly below that of conventional inorganic thermoelectrics, thereby approaching the ideal “phonon-glass electron-crystal” paradigm. Advanced modification strategies, such as engineering porous architectures and incorporating nanocomposites, further intensify phonon scattering at interfaces and grain boundaries, drastically reducing thermal conductivity and consequently boosting the dimensionless figure of merit [92]. These exceptional attributes enable PEDOT: PSS composites to efficiently harvest energy from low-grade thermal sources, particularly by exploiting the minute temperature differential between human body heat and ambient environments. This capability underscores their immense potential as self-powered supplies for next-generation wearable medical electronics. Table 2 provides a comprehensive summary of mainstream thermoelectric modification strategies, detailing material systems, dopants, processing protocols, and key performance metrics.

## 2.3 | Biocompatibility and Modification Strategies

PEDOT: PSS is considered a promising bioelectronic interface material due to its low cytotoxicity, mild inflammatory response, and excellent blood compatibility [122, 123]. Its good biocompatibility is partly due to the chemical stability of the PEDOT backbone and the moderate hydrophilicity provided by the sulfonic acid groups on PSS, which help prevent non-specific protein adsorption. However, a significant challenge





**FIGURE 4** | (a) TE properties of  $\text{H}_2\text{SO}_4$ -treated PEDOT: PSS films as a function of temperature. (a-I) Electrical Conductivity. (a-II) Seebeck coefficient, and d-III) power factor. Reproduced with permission. Copyright 2019, John Wiley and Sons. (b) Schematic Diagram of the Effect of Humidity Rise on Carrier Transport in PEDOT: PSS. Reproduced with permission. Copyright 2023, American Chemical Society. (c) Schematic representation of gelatin-PEDOT-PSS-based scaffold preparation. Reproduced with permission. Copyright 2023, Elsevier. (d) Schematic diagram of the mechanism of PEDOT: PSS damaging the film structure. Reproduced with permission. Copyright 2021, Springer Nature.

TABLE 2 | Summary of Thermoelectric Modification of PEDOT: PSS.

| Materials                                                         | Treatment method                                                                              | T (K) | $\Sigma$ (S/cm) | S ( $\mu$ V/K) | PF ( $\mu$ W/m/K <sup>2</sup> ) | K (W/m/K) | ZT        | Refs. |
|-------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|-------|-----------------|----------------|---------------------------------|-----------|-----------|-------|
| PEDOT: PSS                                                        | Post-treatment for H <sub>2</sub> SO <sub>4</sub> and NaOH                                    | 300   | 2170            | 39.2           | 334                             | 0.2–0.34  | 0.29–0.49 | [93]  |
| PEDOT: PSS                                                        | 0.1 mol MAI in 80% DMF solvent                                                                | 300   | 1831            | 28             | 144                             | 0.29      | 0.11      | [94]  |
| PEDOT: PSS sulphate                                               | None                                                                                          | 300   | ~2500           | 20.6           | 107                             | 0.27–0.64 | —         | [95]  |
| PEDOT: PSS                                                        | ILs treatment                                                                                 | 300   | 520             | 17             | 15                              | —         | —         | [96]  |
| PEDOT: PSS                                                        | Treatment with benzenesulfonic acid + DMSO and hydrazine                                      | 300   | 1119            | 42.6           | 203.1                           | —         | —         | [97]  |
| PEDOT: PSS                                                        | IL and acid treatment followed by alkaline treatment                                          | 300   | 1594.8          | 63.3           | 754                             | 0.2–0.5   | 0.75      | [98]  |
| PEDOT: PSS                                                        | Triple post-treatment: CH <sub>3</sub> NO, H <sub>2</sub> SO <sub>4</sub> , NaBH <sub>4</sub> | 298   | 1786            | 28.1           | 141                             | —         | —         | [99]  |
| PEDOT: PSS                                                        | ILs processing and addition of L-ascorbic acid                                                | 423   | 1100            | 31.9           | 117                             | —         | —         | [100] |
| SFS-F-PEDOT: PSS                                                  | Post-treatment using formamide and sodium formaldehyde                                        | 300   | 693             | 51.8           | 185.8                           | 0.41–0.87 | 0.07–0.14 | [101] |
| PEDOT: PSS/SWCNTs                                                 | None                                                                                          | 300   | ~900            | ~30.5          | 83.9                            | —         | —         | [102] |
| PEDOT: PSS/TeNWs                                                  | None                                                                                          | 300   | 100             | 53             | 28.5                            | —         | —         | [103] |
| Bi <sub>2</sub> Te <sub>3</sub> NWs/PEDOT: PSS                    | 3% SDS and 10% EG treatment                                                                   | 300   | 123.72          | 24.5           | 7.45                            | 0.047     | 0.048     | [104] |
| PEDOT: PSS/BP                                                     | None                                                                                          | 300   | 1446            | ~15.8          | 36.2                            | —         | —         | [105] |
| PEDOT: PSS/SnS                                                    | DMF treatment                                                                                 | 300   | 697.5           | 19.1           | 27.8                            | —         | —         | [106] |
| PEDOT: PSS/ce-MoS <sub>2</sub>                                    | None                                                                                          | 300   | 867             | 21.9           | 41.6                            | —         | —         | [107] |
| PEDOT: PSS/Te-NWs                                                 | DMSO vapor annealing                                                                          | 300   | —               | —              | 11.3                            | —         | 0.02      | [108] |
| PEDOT: PSS/Bi <sub>0.5</sub> Sb <sub>1.5</sub> Te <sub>3</sub>    | DMSO treatment                                                                                | 343   | ~180            | ~22            | 8.3                             | —         | —         | [109] |
| Te/PEDOT: PSS/Cu <sub>7</sub> Te <sub>4</sub>                     | None                                                                                          | 300   | 39              | 129            | 65.3                            | 0.198     | 0.1       | [110] |
| SWCNT/PEDOT: PSS-coated Te nanorods                               | H <sub>2</sub> SO <sub>4</sub> treatment                                                      | 300   | 332             | 56             | 104                             | —         | —         | [111] |
| PPy/PEDOT: PSS/SWCNT                                              | DMSO treatment                                                                                | 300   | 907.17          | —              | 45.3                            | —         | —         | [112] |
| n-Bi <sub>2</sub> Te <sub>3</sub> (proton irradiation)/PEDOT: PSS | None                                                                                          | 300   | 1350            | 49             | 324                             | 0.3       | 0.28      | [113] |
| Bi-Tebasedalloynanosheet/PEDOT                                    | None                                                                                          | 300   | 1223.8          | 20.7           | 52.3                            | 0.2–0.4   | 0.04–0.08 | [114] |
| PEDOT: PSS/Bi <sub>2</sub> Te <sub>3</sub> NWs                    | Polar solvent vapor annealing                                                                 | 300   | 1000            | 45             | 205                             | 0.29      | ~0.2      | [115] |
| PEDOT: PSS/Cu <sub>x</sub> Se <sub>y</sub> NW                     | None                                                                                          | 300   | 1047.1          | 50.8           | 270.3                           | 0.25–0.3  | ~0.3      | [116] |
| PEDOT: PSS/Bi <sub>0.5</sub> Sb <sub>1.5</sub> Te <sub>3</sub>    | None                                                                                          | 300   | 1285            | 49             | 308                             | 0.2       | 0.484     | [117] |
| PEDOT: PSS/LDH                                                    | None                                                                                          | 300   | 511.9           | 11.02          | 6.19                            | —         | —         | [118] |
| MXene/PEDOT: PSS                                                  | None                                                                                          | 300   | 656             | 48.6           | 155                             | 0.35      | 0.12      | [119] |
| PEDOT: PSS/CNTs                                                   | DMSO treatment                                                                                | 300   | 1043.5          | 70.1           | 512.8                           | —         | —         | [120] |
| PEDOT: PSS/Bi <sub>0.5</sub> Sb <sub>1.5</sub> Te <sub>3</sub>    | Copper-tellurium layer coating                                                                | 300   | 2270            | 37.1           | 312                             | —         | —         | [121] |

arises when PEDOT undergoes over-oxidation. This irreversible reaction can occur under high electrical potentials, prolonged exposure to oxygen-rich environments, or within inflammatory sites. Over-oxidation breaks down the conjugated structure of PEDOT and generates harmful free radicals and reactive oxygen species, which disrupt normal cell functions. Importantly, even without external electrical stimulation, dissolved oxygen in body fluids and reactive oxygen species from inflammatory cells can gradually over-oxidize PEDOT, posing a risk for long-term implants.

Another critical factor is the potential release of PSS. In physiological conditions, ions such as  $\text{Na}^+$  and  $\text{Ca}^{2+}$  can replace the bonding between PEDOT and PSS, causing the complex to break apart and release PSS chains into the surrounding tissue. Free PSS is a strongly negatively charged polyanion that can cause various biocompatibility issues, including direct cell toxicity, chronic local inflammation, and potential systemic reactions. Therefore, preventing PSS leaching is crucial for ensuring the long-term safety of PEDOT: PSS in vivo.

Despite the inherent biocompatibility of PEDOT: PSS, its translation into practical biomedical applications is hindered by critical limitations, including suboptimal cell adhesion and proliferation, as well as poor tissue integration. The lack of specific biorecognition motifs on the pristine surface often triggers a foreign body response, leading to immune activation and subsequent fibrotic encapsulation. These biological barriers severely compromise the long-term stability and functional lifespan of implanted PEDOT: PSS devices. Consequently, strategies that enhance biocompatibility while preserving the material's superior electro-mechanical properties are paramount for expanding its clinical utility. Current research predominantly focuses on three synergistic approaches: polymer blending [124–126], surface functionalization [127, 128], and the incorporation of biocompatible nanofillers [129], all aimed at optimizing the surface chemistry to concurrently boost biocompatibility, conductivity, and mechanical robustness.

Polymer blending has emerged as a versatile strategy for both scalable manufacturing and laboratory investigation due to its procedural simplicity and efficacy. Solazzo et al. [124] engineered PEDOT: PSS/PEGDE composite films by leveraging the bio-inert nature of polyethylene glycol (PEG) segments. In this system, the epoxy groups of PEGDE undergo covalent crosslinking with the sulfonic acid groups of PSS, while the pendant PEG chains significantly mitigate protein fouling and enhance cytocompatibility. In vitro assays using C3H/10T1/2 mouse embryonic fibroblasts demonstrated that cell viability in all PEGDE-crosslinked groups exceeded 85%, statistically indistinguishable from the tissue culture plastic control, thereby confirming the non-cytotoxic profile of the modified matrix. Alternatively, blending with natural biopolymers can further impart intrinsic bioactivity via in situ polymerization or composite formation. For instance, gelatin and chitosan have been shown to substantially elevate the bioactivity of PEDOT: PSS scaffolds [125, 126] (Figure 4c).

Surface functionalization offers precise spatiotemporal control over biological interactions, enabling biomimetic engineering through the grafting of specific ligands or surface group

modulation. This approach is particularly critical for high-performance implantable devices. For example, the immobilization of heparin, a potent natural anticoagulant, has successfully enhanced the hemocompatibility of PEDOT-based cardiovascular stents [127]. Furthermore, the covalent co-grafting of the cell-adhesive peptide RGD and the neural-specific peptide YIGSR onto the composite surface created a multifunctional neural interface coating [128]. This bioactive modification significantly improved cellular integration and ensured long-term implantation safety, effectively bridging the gap between synthetic electronics and biological tissues.

## 2.4 | Antimicrobial and Modification Strategies

With the rise of antibiotic resistance, there is an urgent need for alternative antimicrobial therapies. While pure PEDOT: PSS usually shows weak antibacterial activity, its properties can be significantly enhanced through photothermal activation, electrochemical stimulation, or by forming composites with other materials [123]. PEDOT: PSS kills bacteria through four main mechanisms: charge transfer, photothermal sterilization, reactive oxygen species generation, and physical damage.

First, PEDOT: PSS binds to bacterial cell membranes via electrostatic interactions, disrupting the membrane potential and damaging its structure, which sets the stage for further antibacterial action [130], as illustrated in Figure 4d. In composite systems, this effect provides broad-spectrum activity, effectively breaking down the cell walls of bacteria like *Staphylococcus aureus* (*S. aureus*) [131]. Second, PEDOT: PSS has excellent near-infrared photothermal conversion capabilities. Under 808 nm laser light, it can rapidly heat up to 50°C–60°C, causing thermal damage to bacterial proteins and DNA and destroying membrane integrity. This thermal effect works together with membrane damage to kill bacteria efficiently, achieving over 97% elimination of drug-resistant strains like MRSA [132].

Third, under an electric field, PEDOT: PSS generates reactive oxygen species that oxidize bacterial components, stop replication, and lead to cell death [133]. Last, nanostructures like PEDOT: PSS nanotubes or nanofibers can physically pierce bacterial membranes, causing leakage of cell contents. Special microstructures, such as honeycomb patterns, can also trap bacteria and rupture their cell walls through mechanical force [123]. Together, these mechanisms make PEDOT: PSS a powerful tool against bacterial infections.

While pristine PEDOT: PSS exhibits limited intrinsic antimicrobial activity mediated by electrostatic interactions, oxidative stress, and membrane disruption, its clinical utility necessitates robust enhancement strategies. To address this, researchers have engineered multifunctional PEDOT: PSS composites by incorporating potent antimicrobial agents, ranging from inorganic nanomaterials to natural macromolecules. A prominent approach involves the synergistic integration of GO and silver nanoparticles, which amplifies bactericidal efficacy while minimizing the reliance on conventional antibiotics [134]. Furthermore, hybrid nanostructures such as  $\text{Fe}_3\text{O}_4$ @C-PVPS: PEDOT have demonstrated potent photothermal antibacterial activity, effectively eradicating *S. aureus* and *Escherichia coli* (*E. coli*) under

near-infrared irradiation [135]. Alternatively, the incorporation of natural polyphenols offers a green, multifunctional route; for instance, carboxymethyl cellulose (CMC)/tannic acid (TA)/PEDOT: PSS composite films achieved a 76% inhibition rate against *E. coli*, presenting a sustainable strategy for next-generation flexible wearable sensors [136].

Beyond physical blending, molecular engineering of the EDOT monomer enables the direct synthesis of functionalized PEDOT via oxidative polymerization, followed by blending with PSS. This strategy allows for precise control over the density of antimicrobial moieties, imparting bioactivity while preserving intrinsic electrical conductivity. For example, Khan et al. [137] developed PEDOT: PSS/chitosan/PVA biohybrid films. The antimicrobial mechanism is driven by the protonation of chitosan's amino groups ( $-\text{NH}_2$ ) to form cationic  $-\text{NH}_3^+$  species. These cations engage in strong electrostatic interactions with the anionic components (e.g., teichoic acids in Gram-positive peptidoglycan and lipopolysaccharides in Gram-negative outer membranes) of bacterial cell walls. This interaction disrupts the membrane potential, induces structural disorganization, and increases permeability, ultimately leading to metabolic arrest and cell death.

In a groundbreaking advance, Reynoso et al. [138] designed a bifunctional monomer, EDOT-C60, covalently linking EDOT with fullerene C60. The resulting electropolymerized coating retains the exceptional photochemical properties of C60, functioning as a highly efficient photosensitizer. It generates reactive oxygen species via dual mechanisms: Type I (superoxide anion radicals) and Type II (singlet oxygen). Notably, this system exhibits superior photostability compared to traditional porphyrin-based sensitizers. Under visible light irradiation, the coating achieves >99.9% bactericidal efficiency against planktonic cells, surface-adhered bacteria, and mature *S. aureus* biofilms. This work establishes a novel paradigm for developing self-disinfecting surfaces and broad-spectrum antimicrobial coatings for medical devices, offering a stable and potent solution for combating hospital-acquired infections.

## 2.5 | Electrochemical Reversibility and Capacitive Modification Strategies

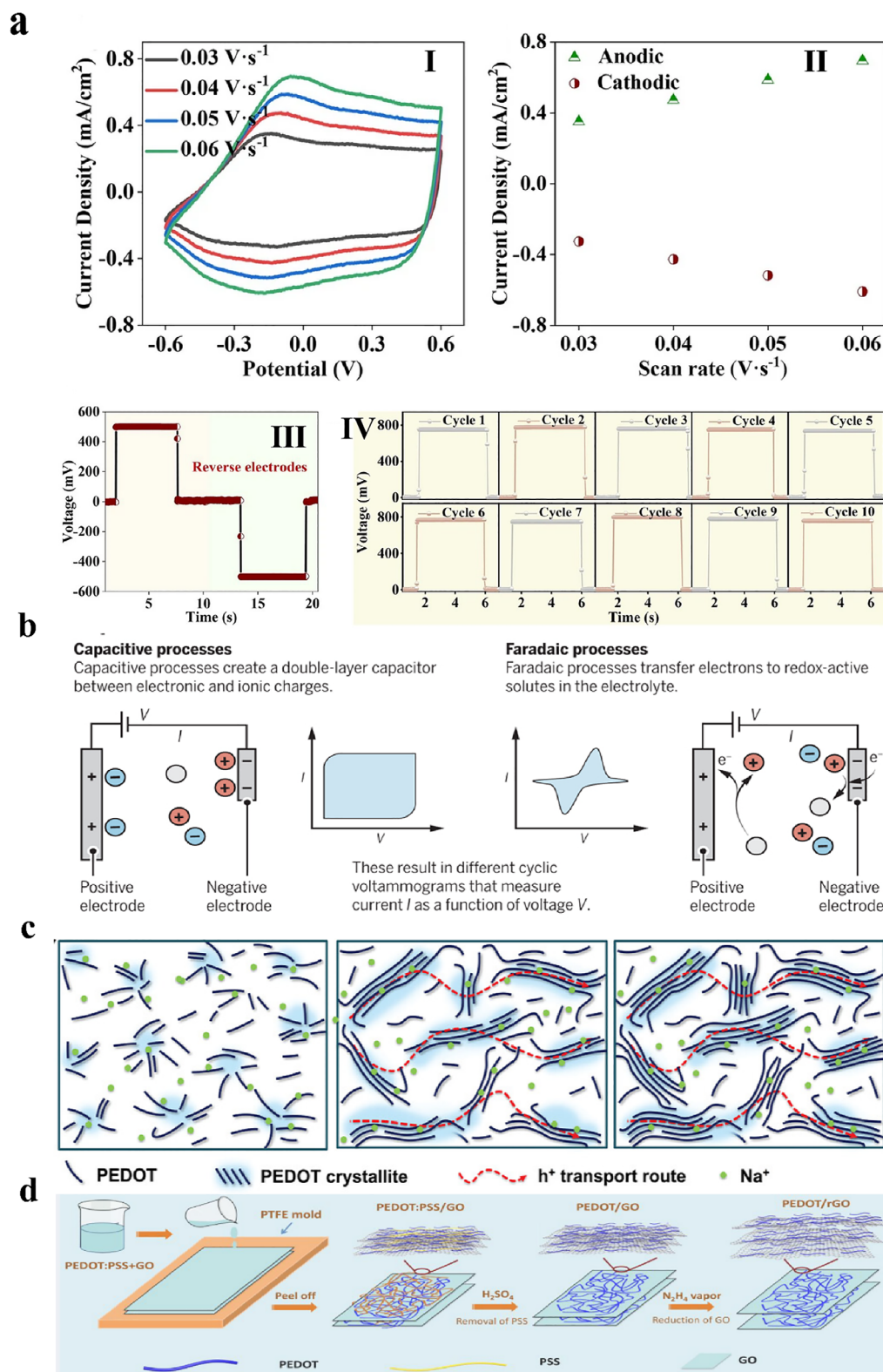
The electrochemical reversibility of PEDOT: PSS refers to its ability to maintain electrochemical activity, charge storage capacity, conductivity, structural integrity, and functionality over repeated oxidation–reduction (doping/dedoping) cycles [139]. This phenomenon is fundamentally driven by the reversible switching of the PEDOT chain's oxidation state, coupled with the concomitant insertion and extraction of counter-ions to ensure charge neutrality (Figure 5a). During oxidation (doping), a positive potential drives the conversion of neutral PEDOT segments into polarons (radical cations) and subsequently into bipolarons (dications). To balance the positive charges on the backbone and the fixed negative charges of  $\text{PSS}^-$ , anions from the electrolyte (e.g.,  $\text{Cl}^-$ ,  $\text{PF}_6^-$ ) ingress into the film. This doped state is characterized by high conductivity and a deep blue/blue-black coloration. Conversely, reduction (dedoping) is induced by a negative potential, reversing the process:

bipolarons revert to polarons and finally to the neutral state. This is accompanied by the intercalation of cations (e.g.,  $\text{Na}^+$ ,  $\text{Li}^+$ ) or the expulsion of anions, resulting in a pale blue or transparent appearance with significantly reduced conductivity. The  $\text{PSS}^-$  matrix provides a fixed negative charge background, facilitating ion migration within its hydrophilic domains while electrons traverse the conjugated PEDOT chains. This decoupled transport enables mixed ionic-electronic conductivity with robust reversible switching. Reversibility is typically assessed via cyclic voltammetry; symmetrical redox peaks with minimal peak potential separation indicate rapid electron transfer kinetics and negligible hysteresis. Such reversibility is paramount for the long-term stability of PEDOT: PSS in supercapacitors, organic electrochemical transistors, electrochromic devices, and biosensors [140].

As the most commercially mature water-soluble conductive polymer, PEDOT: PSS exhibits hybrid charge storage mechanisms dominated by electric double-layer capacitance and supplemented by Faradaic pseudocapacitance [141], as illustrated in Figure 5b. The electrochemical capacitor component arises from the porous morphology and high specific surface area of PEDOT: PSS films, where charge separation occurs at the electrode/electrolyte interface without electron transfer. This mechanism enables rapid charge/discharge rates, extended cycle life, and near-100% coulombic efficiency [142]. In contrast, Faradaic pseudocapacitance, contributing approximately 20%–50% of the total capacitance, originates from reversible redox reactions within the PEDOT conjugated backbone and bulk ion insertion/extraction processes [143]. Upon electrification, holes are injected into the highest occupied molecular orbital of PEDOT from the electrode. These holes delocalize along the polymer chains while counter-ions migrate from the electrolyte into the polymer matrix to achieve electrostatic compensation. By combining high specific capacitance, exceptional cycling stability, and mechanical flexibility, PEDOT: PSS has emerged as a cornerstone electrode material for flexible supercapacitors and integrated sensing-energy storage systems.

Electrochemical reversibility in PEDOT: PSS is governed by a complex interplay of factors, including the cyclic leaching of excess insulating PSS, irreversible oxidative degradation of the PEDOT backbone, steric blockage of ion transport channels, structural collapse induced by volumetric expansion/contraction during doping/dedoping, and parasitic side reactions at the electrode/electrolyte interface. To fundamentally mitigate these degradation pathways, strategies must target the molecular-level optimization of the intrinsic structure and doping equilibrium. Counterion and dopant engineering represents a pivotal approach, wherein conventional PSS counterions are partially replaced or synergistically combined with highly stable, reversibly bound dopants. This strategy effectively suppresses counterion depletion and excessive PEDOT aggregation during cycling while preserving high doping efficiency. For instance, 1-ethyl-3-methylimidazolium based ionic liquids have been employed to systematically tailor the molecular packing and nanomorphology of PEDOT: PSS, as illustrated in Figure 5c. Specifically, modification with 1-ethyl-3-methylimidazolium trifluoromethanesulfonate induces the formation of compact, fibrous PEDOT-rich domains with a loosely packed architecture, achieving an optimal balance between electronic conductivity





**FIGURE 5** | (a-I) Cyclic voltammetry curves of PEDOT: PSS recorded at different scan rates. (a-II) Peak currents extracted from the cyclic voltammetry curves at different scan rates. (a-III) Potential difference measured between PEDOT: PSS(−) and PEDOT: PSS(+), followed by inverse polarization of these two electrodes. (a-IV) Potential differences measured between PEDOT: PSS(−) and PEDOT: PSS(+) during repeated polarization, depolarization, and repolarization processes for 10 cycles. Reproduced with permission. Copyright 2024, Springer Nature. (b) Storing or transferring charge. Reproduced with permission. Copyright 2019, The American Association for the Advancement of Science. (c) Schematics that represent molecular packing of PEDOT: PSS with and without Ionic liquids modification. Reproduced with permission. Copyright 2021, John Wiley and Sons. (d) Illustration of the Fabrication Procedure for PEDOT/rGO Films. Reproduced with permission. Copyright 2022, American Chemical Society.

and ionic mobility [144]. Similarly, ProDOT-functionalized polyhedral oligomeric silsesquioxane serves as a multifunctional crosslinker for EDOT copolymerization [145]. This approach remarkably enhances long-term cycling stability without compromising the conjugated backbone continuity or charge transport properties.

Furthermore, constructing a robust 3D network via covalent or physical crosslinking solidifies the film microstructure, effectively restraining PSS leaching and preventing structural failure caused by repeated swelling/shrinkage cycles in aqueous electrolytes. Notably, Tang et al. [146] demonstrated that crosslinking PEDOT: PSS with GPTMS significantly mitigated drain current decay and enhanced device robustness, enabling tolerance to higher turn-off pulse voltages under pulsed gate bias conditions. Since electrochemical reversibility is the cornerstone of capacitive performance, the practical utility of supercapacitors depends not merely on initial specific capacitance but critically on capacitance retention over prolonged cycling. Degradation in reversibility is the primary driver of capacitance fade. The charge storage mechanism in PEDOT: PSS involves a combination of electric double-layer capacitance and Faradaic pseudocapacitance arising from redox transitions within the PEDOT backbone. Consequently, mainstream modification strategies focus on three core objectives: maximizing electrical conductivity [147], expanding the electrochemically active surface area to improve ion accessibility [148], and introducing additional pseudocapacitive active sites.

The incorporation of high-boiling-point polar solvents induces a conformational transition in PEDOT chains from coiled to linear/benzoid structures, thereby boosting conductivity and minimizing charge transfer resistance. Liu et al. [147] employed DMSO post-treatment to remove excess insulating PSS and synergistically integrated the high conductivity of PEDOT with the substantial pseudocapacitance of polyaniline. The resulting symmetric fiber-shaped supercapacitor delivered a remarkable energy density of 42.4 Wh/kg at a power density of 302.3 W/kg. Moreover, given that free PSS contributes negligibly to capacitance and impedes ion transport, Su et al. [149] utilized a hydrothermal treatment with  $\text{H}_2\text{SO}_4$  to purify free-standing PEDOT: PSS films. This process effectively removed undoped PSS under high temperature and pressure, yielding a film with a high volumetric capacitance of 110 F/cm<sup>3</sup> across a broad current density range (0.1–100 A/cm<sup>2</sup>). The derived flexible supercapacitor exhibited exceptional cycling stability, retaining 95% of its capacitance after 10 000 cycles. Finally, engineering a 3D interconnected porous network significantly enhances the electrochemically active surface area, shortens ion diffusion pathways, and maximizes the exposure of redox-active sites, thereby overcoming the kinetic limitations of dense PEDOT: PSS films. As shown in Figure 5d, Zhu et al. [150] fabricated a “graphene/PEDOT/graphene” sandwich architecture by infiltrating PEDOT nanofibers between graphene sheets via a casting–dissolution method. This composite electrode achieved a specific capacitance of 210 F/g (at 1 A/g), an energy density of 89 Wh/kg, and a superior power density of 12 kW/kg—representing a fivefold enhancement over pristine PEDOT: PSS. Further optimization using hydrazine vapor-reduced porous rGO foam exposed additional active sites, substantially boosting both specific capacitance and rate capability.

## 2.6 | Broadband Transparency

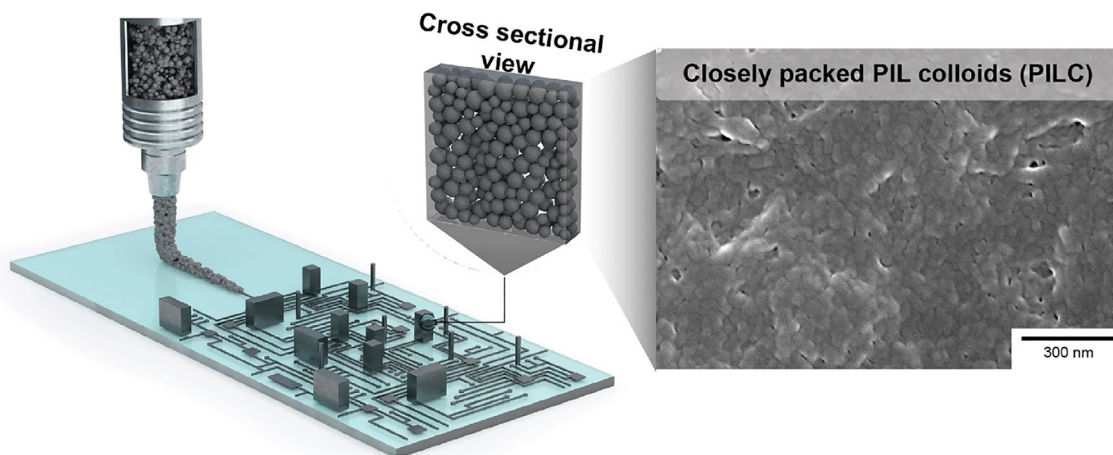
Owing to its exceptional broadband transparency, PEDOT: PSS enables the synergistic integration of electrical conductivity and optical functionality in biomedical applications. It effectively overcomes the opacity bottleneck inherent to traditional conductive materials (e.g., metals), serving as a core functional substrate for multimodal bioelectronic devices [50]. Its primary value lies in scenarios requiring simultaneous electrical signal modulation/detection and compatibility with optical imaging, photostimulation, or photodetection. Structurally, the  $\pi$ – $\pi^*$  interband transition energy gap of the PEDOT conjugated backbone primarily resides in the near-ultraviolet and regions. Consequently, photon absorption in the visible spectrum (400–700 nm) is minimal, yielding high optical transmittance [151]. Furthermore, the material exhibits favorable transmission properties in the terahertz regime [152].

Song et al. [153] optically characterized a highly conductive, flexible transparent electrode (S-PH1000) derived from commercial Heraeus Clevis PH1000 using UV–vis–NIR spectrophotometry. Their results demonstrated a transmittance exceeding 85% at the critical wavelength of 550 nm. Even when configured in a typical electrode–electrolyte–electrode sandwich architecture, the device maintained an overall transmittance above 60%. In stark contrast, traditional metallic electrodes (e.g., Ag/AgCl, Cu) are completely opaque. When placed over optical sensing sites (such as fingertip or wrist pulse oximetry areas), they obstruct incident and reflected light paths, rendering optical sensing ineffective. Conversely, PEDOT: PSS transparent electrodes can serve directly as the conductive layer for optical detection windows. They allow light signals to pass through with negligible attenuation to interact with underlying tissue while simultaneously acquiring high-fidelity electrophysiological signals. This capability achieves a seamless electro-optical dual-modality integration within a single interface.

## 2.7 | Solution Processability

PEDOT: PSS does not exist as a true molecular solution in aqueous media but rather forms a polyelectrolyte complex colloidal dispersion. This intrinsic colloidal nature underpins its exceptional solution processability. In this system, the hydrophobic and rigid conjugated PEDOT backbones spontaneously aggregate via  $\pi$ – $\pi$  stacking and hydrophobic interactions to form a conductive core. Concurrently, PSS chains partially wrap around the positively charged PEDOT core through strong electrostatic anchoring, while the remaining unbound PSS segments extend into the aqueous phase, creating a sulfonate-rich hydrophilic shell. This arrangement yields core–shell structured colloidal particles with typical diameters ranging from 20 to 200 nm [154, 155]. The hydrophilic shell stabilizes the dispersion kinetically and thermodynamically by preventing irreversible aggregation through a dual mechanism of electrostatic repulsion and steric hindrance.

Rheologically, PEDOT: PSS dispersions exhibit pronounced shear-thinning behavior. At low shear rates, colloidal particles assemble into a reversible 3D network via weak inter-particle interactions, resulting in high viscosity



**FIGURE 6** | Schematic illustration (left) and SEM image (right) of the PILC ink enabling 3D printed structures with high structural integrity through the dense packing of colloidal particles. Reproduced with permission. Copyright 2024, Springer Nature.

that ensures storage stability. Conversely, under high shear conditions encountered during spin-coating, inkjet printing, or extrusion molding, this network rapidly dissociates, allowing particles to align along the flow direction [156]. This dynamic rheological response is pivotal: it maintains structural integrity during storage while facilitating optimal flow and film-forming characteristics during processing, thereby enabling compatibility with a diverse array of solution-based fabrication techniques [157], as illustrated in Figure 6.

## 2.8 | Mechanical Flexibility

The PEDOT: PSS composite system embodies a unique synergy of rigidity and flexibility: the conjugated PEDOT backbone provides structural stiffness, whereas the long, flexible PSS chains impart segmental mobility and interchain slip capability. This synergistic interaction enables the resulting films to withstand bending and tensile deformation without brittle fracture. Mechanical compliance can be further enhanced by moderately weakening the electrostatic coupling between PEDOT and PSS or by incorporating flexible polymer matrices [158]. Furthermore, composite engineering with nanofillers facilitates the construction of synergistic percolation networks [159]. These nanofillers act as crack bridges, effectively suppressing crack propagation and reconstructing conductive pathways upon deformation. Consequently, such composites exhibit significantly improved stability under cyclic bending and stretching, maintaining both mechanical robustness and electrical conductivity.

## 2.9 | Stability

PEDOT: PSS demonstrates exceptional chemical and thermal stability, attributed to the inherent robustness of its molecular architecture and microphase-separated configuration. The high bond energy of the conjugated PEDOT backbone, combined with the strong electrostatic interactions between PEDOT and the sulfonate groups of PSS, creates a stable “self-doped” complex. This robust interaction effectively suppresses structural degradation or dedoping during operation, ensuring long-term

performance fidelity [155]. Thermally, the intimate PEDOT: PSS association enhances the material’s resistance to thermal decomposition, supporting reliability under elevated temperatures or prolonged service conditions [160]. Owing to its stable conjugated framework, robust inter-component interactions, and unique phase-separated morphology, PEDOT: PSS exhibits outstanding durability against electrochemical cycling, thermal stress, and long-term operational wear. These attributes provide a critical foundation for its deployment in high-performance bioelectronics and flexible devices.

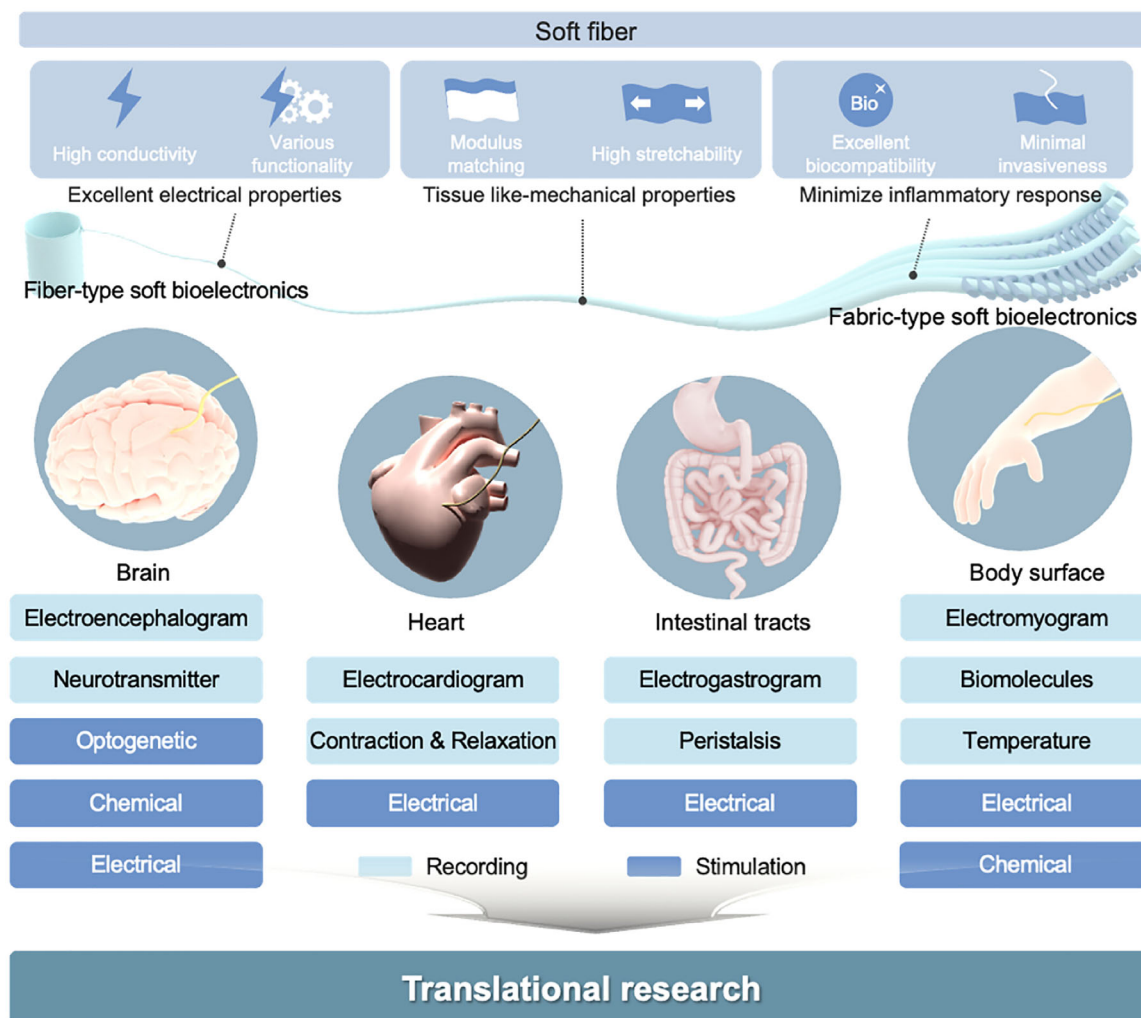
## 3 | Applications of PEDOT: PSS in Biomedicine

Leveraging its unique synergistic electrical, mechanical, and biological properties, PEDOT: PSS is catalyzing a paradigm shift in medical devices—transitioning from traditional rigid metallic instruments to flexible, intelligent, and bio-integrated systems [71, 161] (Figure 7). Despite persistent challenges in long-term stability and clinical translation, continuous breakthroughs in material engineering and manufacturing protocols suggest that PEDOT: PSS-based innovations are poised for widespread adoption across neuroscience, tissue engineering, and precision medicine. These advancements promise safer, more effective, and personalized therapeutic solutions for patients [162, 163].

### 3.1 | Biosensing and Monitoring

Biosensing and biomonitoring represent a convergent frontier of biomedical engineering, analytical chemistry, and materials science. The fundamental mechanism entails the specific recognition of biological targets, such as molecules, ions, cells, or electrophysiological signals, by biorecognition elements, followed by transduction into detectable physical or chemical signals, including electrical, optical, or piezoelectric responses. This enables qualitative and quantitative analysis as well as real-time dynamic monitoring of biological systems [164], spanning applications from in vitro diagnostics and wearable physiology tracking to implantable in vivo monitoring. As one of the most commercially viable domains for conductive polymers [165],





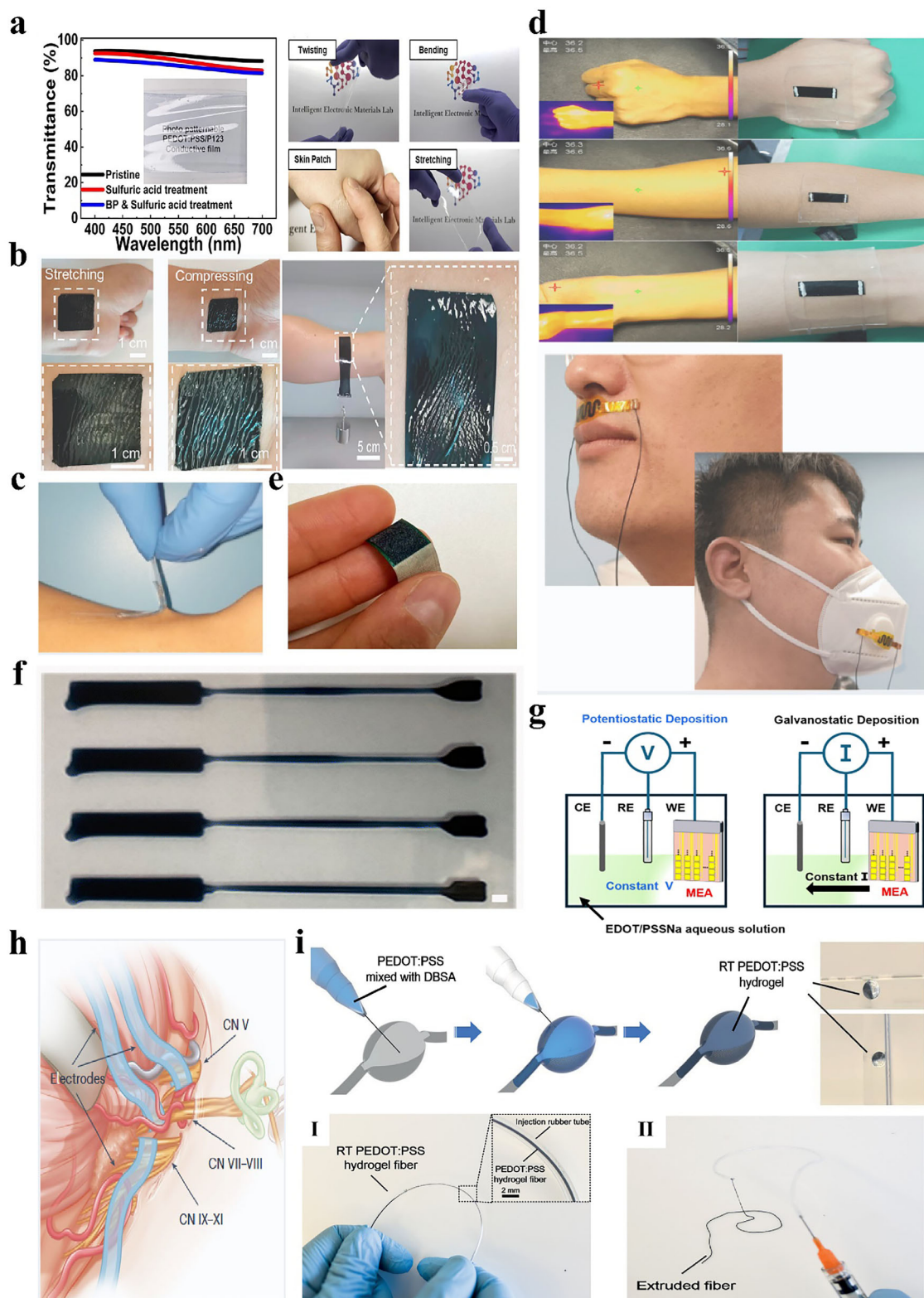
**FIGURE 7** | Schematic illustration of the evolution of fiber-type soft bioelectronics for translational research in health monitoring and therapeutic interventions. Reproduced with permission. Copyright 2025, John Wiley & Sons Australia.

bioelectric sensors stand out as the most clinically mature branch. They provide real-time, non-invasive, and objective quantification of organ function by capturing endogenous bioelectric signals from excitable tissues, serving as a cornerstone for the entire diagnostic and therapeutic workflow.

In the realm of advanced fabrication and wearable interfaces, Yoon et al. [166] developed an eco-friendly, water-based direct photolithography technique for PEDOT: PSS using a P123/BP system. The resulting composite films exhibit high optical transparency (94% at 575 nm) and exceptional mechanical durability, with resistance fluctuations of  $\leq 5\%$  after 1000 cycles at 30% strain (Figure 8a). These films have been successfully deployed in tactile sensors and electrophysiological monitors for electrooculography (EOG), electrocardiography (ECG), and electromyography (EMG), featuring a baseline capacitance of 1.02 pF and non-contact detection capabilities ranging from 1 to 5 cm. Similarly, Cao et al. [167] engineered a composite organic dry electrode characterized by high conductivity, stretchability, self-adhesion to wet and dry skin, and sweat resistance (Figure 8b). This sensor achieves low RMS noise levels (11.8  $\mu\text{V}$  on dry skin; 12.2  $\mu\text{V}$  on wet skin) with clearly resolved PQRST waveforms, outperforming commercial Ag/AgCl gel electrodes in contact impedance and

offering stable, irritation-free monitoring during both rest and activity. Electro-bioadhesive interfaces serve as the critical interface between bioelectronic devices and tissue, and are used for monitoring electrophysiological signals such as EMG and ECG. Existing PEDOT: PSS hydrogel-based electro-bioadhesive interfaces are predominantly single-use products, lacking the ability to re-adhere and self-heal. Wan et al. [168] developed a reusable, self-healing, biocompatible electro-bioadhesive interface using polyacrylamide as the hydrogel matrix, incorporating polydopamine and PEDOT: PSS. This electro-bioadhesive interface exhibits excellent properties, including high electrical conductivity of  $5.57 \times 10^{-3} \text{ S/cm}$ , a tissue-like Young's modulus of 2700 Pa, low interfacial impedance of 1 k $\Omega$ , an adhesion strength to porcine skin of 46 450 Pa, and a self-healing efficiency of 94.11%. The repeatable EMG monitoring patch fabricated from this material achieves a signal-to-noise ratio of 30.05 dB for electromyographic monitoring, maintaining an SNR of 21.82 dB even after 200 adhesion-peel cycles. This significantly outperforms commercial electrodes, enabling high-resolution electromyographic signal monitoring and time-frequency analysis. Similarly, Wan et al. [169] developed a PEDOT: PSS-PVAF composite 3D printing ink and used direct-writing 3D printing technology to fabricate a highly conductive, strongly adhesive and electrochemically





**FIGURE 8** | (a) Transmittance of the PEDOT: PSS film on SEBS for the wavelength in the visible range (left). Images of PEDOT: PSS films on the SEBS substrate that show transparency and stretchability (right). Reproduced with permission. Copyright 2024, Springer Nature. (b) Attachment of a fully organic PPT composite film (PEDOT: PSS/PVA/tannic acid) to the hand of a volunteer. The attachment is not affected by the hand movement (left). PPT film attached on wet skin lifting a load of 100 g. The contact area between the PPT film and skin was 2.5 cm × 3 cm, and the shining spots were artificial sweat on the skin (right). Reproduced with permission. Copyright 2022, American Chemical Society. (c) The iontronic skin with sticky PDMS mounted on skin. Copyright 2019, American Chemical Society. (d) Comparison photographs of temperature measurements of different body parts using an infrared thermometer and a flexible temperature sensor (left). Test photos of the sensor attached under the nose and to the outside of the breathing valve (right). Reproduced with permission. Copyright 2024, American Chemical Society. (e) Bending of a textile one-component organic electrochemical transistor

stable conductive hydrogel bioelectronic interface; the hydrogel exhibited a conductivity exceeding 1 S/cm and an adhesion to porcine skin of 31 440 Pa, with a charge storage capacity of 18.80 mC/cm<sup>2</sup> and a charge injection capacity of 13.72 mC/cm<sup>2</sup>. The EMG skin electrodes fabricated using this material exhibited a signal-to-noise ratio of >10 dB, with signal stability superior to that of commercial electrodes, making them suitable for health monitoring and the field of epidermal bioelectronics.

Regarding stretchable electronics and multifunctional sensing, Hong et al. [170] fabricated intrinsically stretchable PEDOT: PSS/g-Polydimethylsiloxane (PDMS) electrodes by grafting Poly(methacrylic acid) onto PDMS to enhance interfacial adhesion via hydrogen bonding (Figure 8c). Combined with a biaxial pre-stretching strategy to induce a pleated morphology, these electrodes achieve a low surface resistance of 90  $\Omega$  that remains stable under 100% strain, showing no fatigue after 10 000 cycles. When integrated into ionic electronic skins, they deliver high pressure sensitivity ( $7 \times 10^{-6}$  Pa) and an ultra-low detection limit (0.3 Pa), capable of detecting masses less than 1 mg while simultaneously responding to pressure and strain. In another multifunctional approach, Smith et al. [170] constructed a wearable pH-responsive and antimicrobial sensor using Polyaniline (PANI)/PEDOT: PSS fibers. DMSO treatment induced a conformational transition in PEDOT chains from coiled benzoid to linear quinoid structures, boosting conductivity from approximately 122 to 802 S/cm. This enhancement improved pH sensitivity to −56 mV/pH compared to −49 mV/pH for untreated fibers. Furthermore, the cationic nitrogen sites in the PANI coating disrupt bacterial membrane integrity, significantly reducing *E. coli* fluorescence intensity and enhancing antibacterial efficacy. Addressing the need for thermal monitoring, Zhu et al. [171] developed a PEDOT: PSS/SWCNTs/rGO composite temperature sensor with high sensitivity, excellent linearity (0.98), and rapid response and recovery times of 4.8 and 5.8 s, respectively. Its 4 × 4 array configuration enables precise temperature mapping and subcutaneous vascular detection, matching infrared thermography performance (Figure 8d).

Advancements in hydrogels and non-invasive metabolite detection have also been significant. Li et al. [172] reviewed PEDOT: PSS-based conductive hydrogels, highlighting three gelation strategies involving cross-linking, ion induction, and light induction that yield networks with high conductivity, tissue compatibility, and mechanical adaptability. These hydrogels exhibit a charge storage capacity one million times higher than gold electrodes and a sixfold increase in charge injection capacity, alongside freeze resistance and self-healing properties. For non-invasive glucose monitoring, Roshanbinfar et al. [173] developed a textile-compatible sensor utilizing porous PEDOT: PSS source-drain

electrodes and a glucose oxidase-modified electrolyte (Figure 8e). This device distinguishes diabetic from healthy states by detecting sweat glucose concentrations between 10  $\mu$ M and 1 mM with high specificity, although batch consistency and long-term durability require further optimization.

In the context of 3D cell culture and neural interfaces, Yang et al. [174] developed AuNP-modified PEDOT: PSS hydrogel electrodes to bridge the gap between in vitro models and in vivo physiology (Figure 8f). These electrodes exhibit exceptional conductivity ranging from 11.76 to 32.65 S/cm and high sensitivity toward dopamine. In neuroelectronics, Microelectrode Arrays modified with PEDOT: PSS are critical for spatiotemporal neural recording. Addressing uniformity issues in constant-current plating, Shin et al. [175] proposed a constant-potential deposition method (Figure 8g), achieving 100% yield and superior uniformity with an impedance standard deviation of only  $6.39 \times 10^{-3} \Omega$  across more than 100 channels with cellular-scale dimensions. For continuous intraoperative neurophysiological monitoring, Zhou et al. [176] fabricated ultra-thin, rail-shaped PEDOT: PSS electrodes blended with a supramolecular crosslinker. These low-impedance ( $\sim 2.25 \times 10^{-3} \Omega$ ) and low-modulus electrodes conform tightly to nerves, recording close-net action potentials with amplitudes approximately 50-fold higher than far-field signals, significantly improving postoperative neurological outcomes in animal models (Figure 8h).

Finally, in cancer detection and brain–computer interfaces, Song et al. [177] developed an Organic Electrochemical Transistor array with anti-EpCAM-functionalized PEDOT: PSS channels for label-free cancer cell detection. Electrostatic interactions upon circulating tumor cell capture shift the transfer curve, enabling high-throughput detection within one hour. Zhang et al. [178] introduced a room-temperature-formable PEDOT: PSS hydrogel using DBSA, featuring injectability, self-healing, and tunable modulus, which supports minimally invasive therapies like nerve regeneration (Figure 8i). In the field of brain–computer interfaces, Sun et al. [179] advanced flexible neural microelectrodes by developing a spin-coating fabrication process modified with ethylene glycol and DBSA. These electrodes offer superior mechanical stability without delamination after ultrasonication and achieve significantly higher signal-to-noise ratios (approximately 32.5 dB) compared to electroplated counterparts, facilitating robust single-neuron recording for next-generation brain–machine communication and the treatment of neurological disorders.

### 3.2 | Self-Powered Wearable Devices

PEDOT: PSS, distinguished by its exceptional thermoelectric, triboelectric, and hydroelectric properties, serves as a versatile

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between fingers. (f) Patterned electrodes fabricated with printable PEDOT: PSS hydrogels, scale bar, 1 mm. Reproduced with permission. Copyright 2023, Royal Society of Chemistry. (g) Illustration of PEDOT: PSS electroplating in a 3-electrode system. Reproduced with permission. Copyright 2024, Springer Nature. Elsevier. (h) Schematics showing the soft PEDOT electrodes wrapped around the trigeminal nerve (CN V), the facial–acoustic nerve complex (CN VII, CN VIII), and lower cranial nerves (CN IX–XI) for nerve identification. Reproduced with permission. Copyright 2023, Springer Nature. (i) Schematic of injectable RT-PEDOT: PSS hydrogels: Puncturing the soft tissue with a syringe; Syringe-injecting PEDOT: PSS suspension (4 v/v% DBSA) into the cavity; and RT-PEDOT: PSS hydrogel formed spontaneously within 10 min. (i-I) Formation of the RT-PEDOT: PSS hydrogel in a plastic tube via syringe injection. Inset: enlarged view of the RT-PEDOT: PSS hydrogel in the tube. (i-II) Extruded RT-PEDOT: PSS hydrogel fibers with a syringe.

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platform for harvesting thermal, mechanical, and biochemical energy from the human body and the environment. The generated electrical energy can directly power flexible wearable systems or be stored in micro-supercapacitors and thin-film batteries, enabling sustained autonomous operation [180, 181].

In the domain of thermoelectric energy harvesting, researchers have addressed the limitations of conventional rigid temperature monitors by developing flexible, high-efficiency alternatives. Luo et al. [182] utilized a wet-spinning process to fabricate continuous PEDOT: PSS/SWCNT composite fibers, which were subsequently optimized via sulfuric acid post-treatment and polyurethane encapsulation. A thermoelectric textile constructed from 32 p-type fibers achieved a power density of  $60.1 \mu\text{W}/\text{cm}^2$  under a 50 K temperature gradient. Its integrated intelligent monitoring system demonstrated rapid thermal response ( $<5$  s) and excellent cyclic stability (3–4.3 s over 50 cycles), enabling real-time detection of febrile states with remote alert capabilities when worn on the forehead or wrist (Figure 9a). Similarly, Fan et al. [183] employed full 3D printing to fabricate stretchable thermoelectric devices based on PEDOT: PSS/thermoplastic polyurethane. These devices delivered an open-circuit voltage of 3.18 mV and a power density of  $6.78 \text{ nW}/\text{cm}^2$  at a 40 K temperature difference, retaining over 90% of their performance after 2000 stretching cycles. They successfully powered low-energy electronics, including LEDs and vital sign sensors, by scavenging body heat (Figure 9b). Advancing the fundamental thermoelectric performance, Chen et al. [184] proposed a strategy combining surface-initiated polymerization with wet spinning to create PEDOT: PSS/eutectic gallium–indium (EGaIn) liquid metal composite fibers. By leveraging the energy filtering effect at the EGaIn–PEDOT: PSS interface and interfacial phonon scattering, they achieved a decoupling of thermoelectric parameters (Figure 9c). The optimized 0.20% EGaIn–PP fiber, following sulfuric acid treatment, exhibited a Seebeck coefficient of  $118.7 \mu\text{V}/\text{K}$  (a 13-fold enhancement), a power factor of  $2289.6 \mu\text{W}/\text{m}/\text{K}^2$ , and a reduced thermal conductivity of  $0.6 \text{ W}/\text{m}/\text{K}$ , yielding a figure of merit (ZT) of 1.21. This fiber maintained stable performance under bending, washing, and thermal cycling with a strain tolerance of 30.9%, demonstrating significant potential for self-powered sensing.

Regarding triboelectric nanogenerators (TENGs) for mechanical energy harvesting, Liu et al. [185] developed a flexible organic semiconductor textile TENG activated by hydrogen bond modulation. Comprising a PEDOT: PSS/PVA core, conductive textiles, and an aluminum slider, the device was activated by 95% ethanol, which dissolved the PVA and formed hydrogen bonds with PSS<sup>−</sup>, thereby releasing more active PEDOT<sup>+</sup> charge carriers (Figure 9d). This mechanism elevated the current density to  $8.75 \text{ A}/\text{m}^2$  and achieved a peak power density of  $1074.5 \text{ mW}/\text{m}^2$ —representing 438-fold and 170-fold improvements over solvent-free controls, respectively. Notably, its centimeter-scale current density surpassed existing TENGs by a factor of 3.43, enabling the direct driving of LEDs, electronic clocks, and Bluetooth alarms, as well as charging mobile phones. Drawing inspiration from nature, Li et al. [186] designed a biomimetic TENG based on Ecoflex/PEDOT: PSS featuring a microcolumn structure modeled after cicada wings. This architecture enhanced the specific surface area, while PEDOT: PSS improved charge retention and MXene electrodes optimized conductivity (Figure 9e). The

resulting device enabled dual-mode sensing (contact and non-contact) with a non-contact range of 80 mm, an open-circuit voltage of 124 V, and a power density of  $75.3 \text{ mW}/\text{m}^2$ . Integrated into gesture recognition and game control systems, the EP-TENG array overcame single-mode limitations, offering robust solutions for human–machine interaction in complex environments.

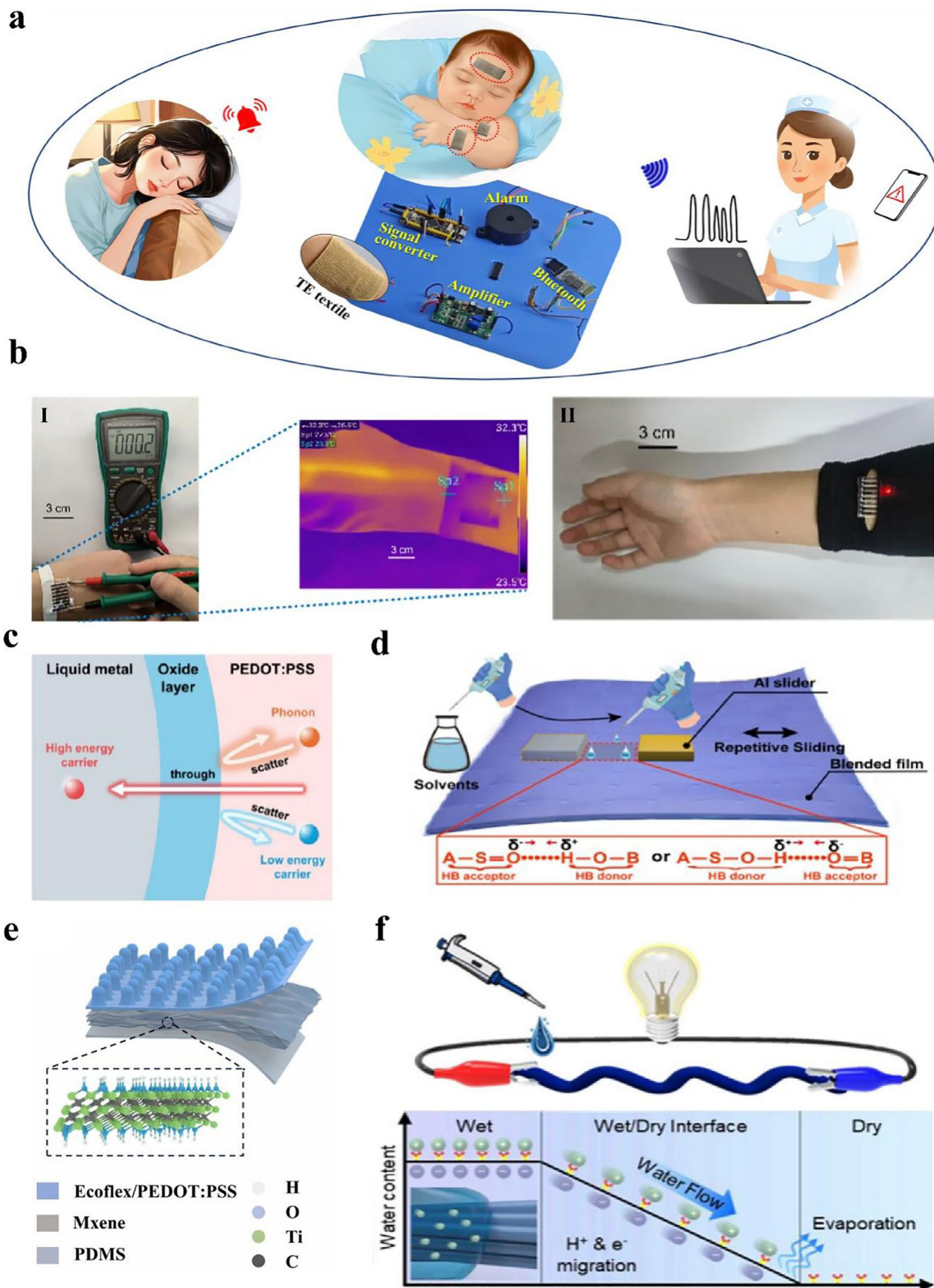
Furthermore, hydroelectric technologies capable of converting perspiration and ambient humidity into electricity have emerged as a critical research frontier. Yoon et al. [187] engineered a transpiration-driven electro-kinetic generator using PEDOT: PSS-coated silk yarns cross-linked with divinyl sulfone (Figure 9f). This design utilized silk as a hydrophilic substrate while addressing the water instability of PEDOT: PSS through covalent cross-linking, simultaneously preserving the ion selectivity of PSS. In artificial sweat, the device achieved a maximum volumetric power density of  $112 \mu\text{W}/\text{cm}^3$ . Remarkably, it retained 54.8% of its voltage and 47.7% of its current after five washing cycles, significantly outperforming pure PEDOT: PSS counterparts (0.51% and 0.87%, respectively). By assembling 25 units in a series-parallel configuration on waterproof fabric, the system charged a 1000  $\mu\text{F}$  capacitor to 0.35 V within 330 s, validating its efficacy for sweat-based energy harvesting in wearable applications.

### 3.3 | Tissue Engineering and Regenerative Medicine

Biomedical materials serve as the foundational scaffolds for tissue engineering and regenerative medicine, designed to mimic the extracellular matrix, construct 3D microenvironments, and deliver cells and bioactive factors to facilitate tissue repair and regeneration. Among these, PEDOT: PSS has emerged as a transformative biomaterial, demonstrating exceptional efficacy in bone, cardiac, and cutaneous regeneration. Its unique advantage lies in its ability to deliver electrical stimulation (ES), a potent physical cue that modulates cellular behavior, activates regenerative signaling pathways, and accelerates tissue healing.

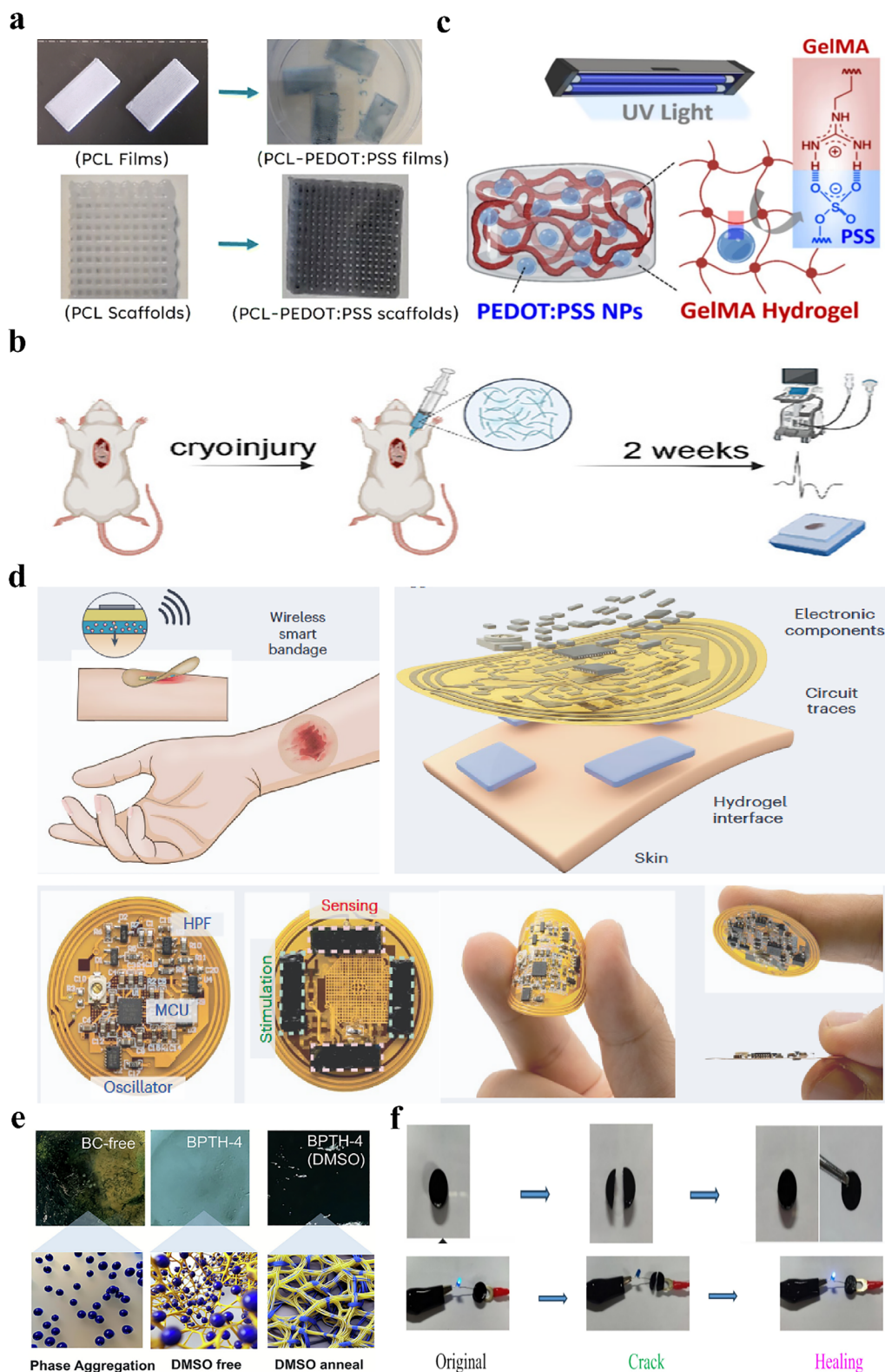
In the realm of bone tissue engineering, electrical stimulation acts as a critical physicochemical regulator that accelerates osteogenesis by modulating osteoblast–osteoclast homeostasis and optimizing the local regenerative microenvironment. This approach holds significant clinical promise for refractory conditions such as non-union fractures and critical-sized bone defects. Barbosa et al. [188] fabricated polyacrylonitrile/PEDOT: PSS nanofibrous scaffolds via electrospinning, followed by sulfuric acid annealing to impart bone-mimetic conductivity and subsequent mineralization to form a hydroxyapatite coating. These scaffolds, featuring collagen-like fiber diameters, exhibited high hydrophilicity and biocompatibility, significantly promoting the proliferation of MG-63 osteoblasts and human bone marrow-derived mesenchymal stem cells (hBM-MSCs) while upregulating key osteogenic markers (OPN, COLI). Similarly, Silva et al. [189] utilized 3D extrusion printing to create polycaprolactone scaffolds coated with a PEDOT: PSS conductive layer, anchored via crosslinkers such as GPTMS or DVS and functionalized with gelatin (Figure 10a). Exhibiting high conductivity ( $11.3\text{--}20.1 \text{ S}/\text{cm}$ ) and stability in physiological saline for 21 days, these scaffolds enhanced in vitro mineralization. When subjected to daily AC electrical stimulation (1.2 V, 1 h), they induced a synergistic





**FIGURE 9** | (a) Schematic diagram of wearable TE fabric for intelligent monitoring and warning of children's body temperature. Reproduced with permission. Copyright 2025, John Wiley and Sons. (b-I) The fully 3D-printed PEDOT: PSS-based fabric stretchable thermoelectric devices worn on the wrist convert human body heat energy into electrical energy. (b-II) The device lights up the LEDs. Reproduced with permission. Copyright 2025, American Chemical Society. (c) Schematic of thermal and electrical transport at the interface. Reproduced with permission. Copyright 2025, American Chemical Society. (d) 3D schematic diagram of the flexible organic textile tribovoltaic generator. Reproduced with permission. Copyright 2025, American Chemical Society. (e) Structure diagram of the EP-TENG; the enlarged part is the MXene structure. Reproduced with permission. Copyright 2025, Elsevier. (f) Schematic of the operating method of the yarn-type transpiration-driven electro-kinetic generator system and the pseudo-streaming current generation mechanism. Reproduced with permission. Copyright 2025, John Wiley and Sons.





**FIGURE 10** | (a) Physical image of Polycaprolactone /PEDOT: PSS scaffolds. Reproduced with permission. Copyright 2024, Royal Society of Chemistry. (b) Collagen-PEDOT: PSS protects the heart against ventricular tachycardia. Reproduced with permission. Copyright 2024, John Wiley and Sons. (c) Schematic illustrating the preparation of GelMA–PEDOT: PSS conductive hydrogel through UV photo-crosslinking polymerization, electrostatic interactions, and hydrogen bonding. Reproduced with permission. Copyright 2025, Elsevier. (d) Overall design of the wireless smart bandage for chronic wound management. Reproduced with permission. Copyright 2022, Springer Nature. (e) Hydrogel physical diagram and internal structure diagram. Reproduced with permission. Copyright 2025, Elsevier. (f) Schematic diagram of the self-repair process and electrical conductivity of SCPPC hydrogel. Reproduced with permission. Copyright 2025, Elsevier.

osteogenic response in hBM-MSCs, increasing calcium deposition by 2.29-fold and significantly upregulating osteogenic genes (COL1, OC, CACNA1C).

For cardiac repair, conductive hydrogels offer a strategic solution to restore electrical continuity following myocardial infarction (MI), which often leads to cardiomyocyte death, electrical dyssynchrony, and fatal arrhythmias. Roshanbinfar et al. [190] developed an injectable collagen/PEDOT: PSS conductive hydrogel that self-assembles via electrostatic interactions into a fibrous network resembling the native cardiac ECM, achieving a conductivity of  $65.32 \pm 4.76$  S/cm. In vitro, this matrix promoted the maturation of human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs), enhancing calcium handling and electromechanical coupling. In vivo, intracardiac injection in MI mice reduced the incidence of ventricular tachycardia from 85% to 25% (comparable to healthy controls) and, when combined with hiPSC-CM transplantation, improved left ventricular ejection fraction (LVEF) from 45.3% to 56.3% (Figure 10b). Addressing ischemia-reperfusion (IR) injury, Chou et al. [191] engineered a UV-curable GelMA-PEDOT: PSS hydrogel via microwave-assisted synthesis (Figure 10c). The optimized formulation (G15P0.3) featured tunable porosity, swelling, and degradation rates while maintaining excellent electrochemical performance. In a rabbit IR injury model, this hydrogel significantly enhanced cardiac conduction velocity, suppressed ventricular arrhythmias, and improved LVEF, demonstrating robust therapeutic potential.

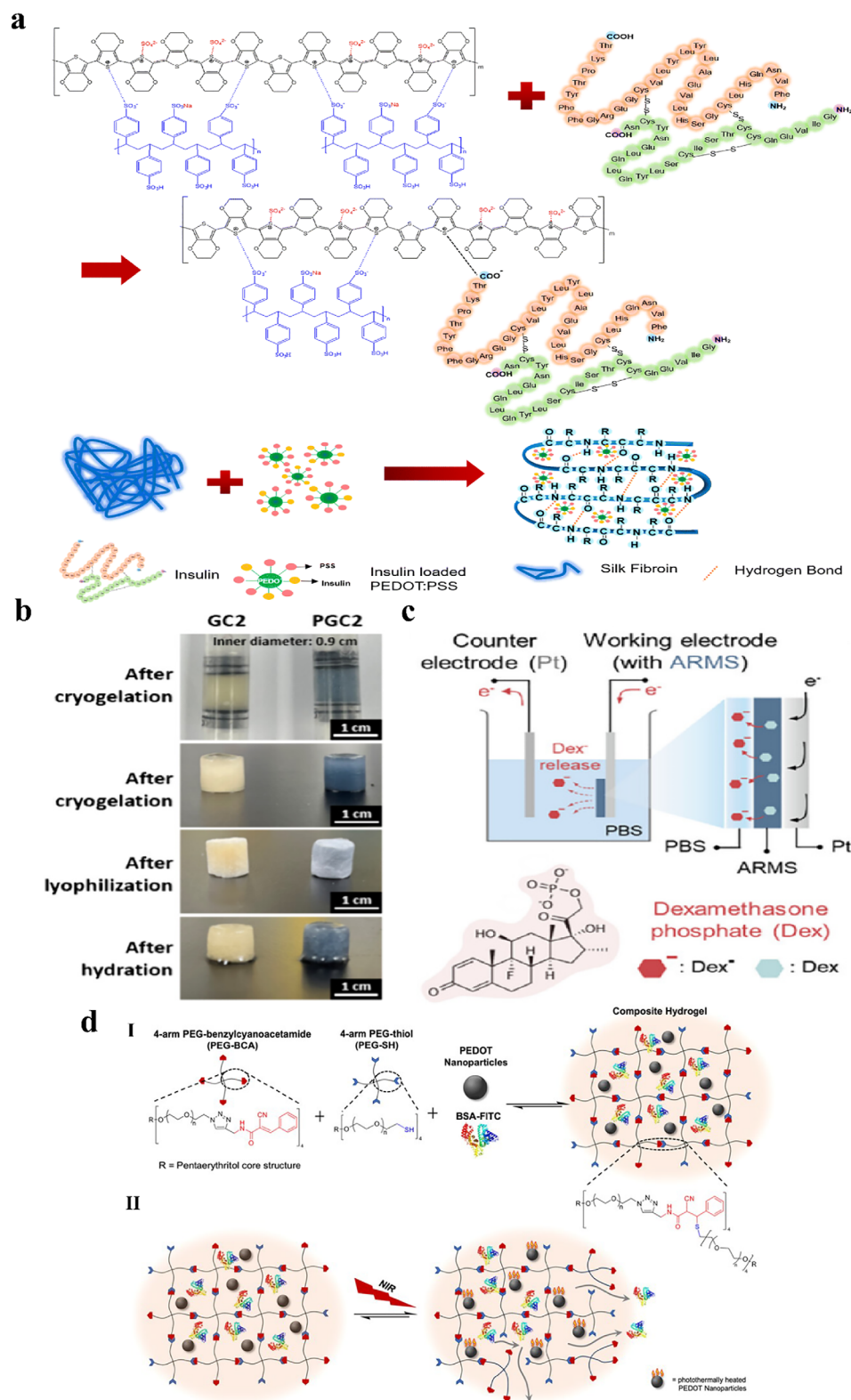
Smart wound dressings integrating sensing, therapeutic, and communication functionalities represent a paradigm shift from passive coverage to active management of the wound microenvironment. Jiang et al. [192] developed a wireless closed-loop smart bandage integrating a PEDOT: PSS conductive hydrogel electrode, a dual-mode sensor (impedance/temperature), and an ES module powered by radio-frequency wireless energy transfer (Figure 10d). Featuring thermoresponsive reversible adhesion and high toughness, this system accelerated wound healing by ~25% and enhanced dermal remodeling by 50% in murine models (including diabetic wounds). Mechanistically, it promoted M2 macrophage polarization (upregulating CD163 and MRC1) and reduced bacterial load. To address chronic wounds complicated by infection and the phase separation issues common in conventional hydrogels, Luo et al. [193] synthesized a composite hydrogel using bacterial cellulose as a template for PEDOT: PSS within a PVA/ polyacrylic acid /tannic acid matrix (Figure 10e). This design yielded ultra-high conductivity, superior mechanical properties, and broad-spectrum antimicrobial activity (inhibition zones of 29.3 mm for *S. aureus*\* and 24.6 mm for *E. coli*\*). By disrupting bacterial membrane potentials, it achieved a 74.78% closure rate in *S. aureus*\*-infected wounds within 12 days, while simultaneously enabling real-time EMG/ECG monitoring. Furthermore, for deep burn management, Liu et al. [194] created a sodium alginate/calcium/PEDOT: PSS (SCPPC) hydrogel with skin-like conductivity, self-healing capability, and injectability via dynamic ionic cross-linking (Figure 10f). In a rat deep second-degree burn model, ES combined with SCPPC achieved a 96.46% wound closure rate within 10 days (~25% faster than controls). This efficacy was attributed to the modulation of M2 macrophage polarization, a 287% increase in angiogenesis (CD31+), and enhanced collagen deposition,

offering an integrated “theranostic” solution for severe burn injuries.

### 3.4 | Smart Targeted Drug Delivery

Smart targeted drug delivery utilizes biocompatible materials as carriers, surface-modified with specific ligands (e.g., antibodies, peptides, folic acid) to achieve active recognition and accumulation at lesion sites. By leveraging the carrier’s responsiveness to endogenous or exogenous stimuli, these systems trigger structural changes that facilitate on-demand drug release. This integrated approach—combining targeted positioning, intelligent release, enhanced efficacy, and reduced toxicity—has become pivotal in the precision treatment of tumors and central nervous system disorders. Capitalizing on the exceptional electrochemical reversibility of PEDOT: PSS, researchers have developed diverse stimulus-responsive delivery platforms capable of controlled release and precise therapeutic intervention.

Electro-responsive systems represent the most prominent application of PEDOT: PSS in drug delivery. The mechanism relies on the electrochemical reversibility of the conjugated PEDOT: PSS structure, electrostatic interactions, and electric field-induced material deformation. These properties enable low-voltage triggering for reversible, quantitative, and precise drug release, making them ideal for treating localized lesions. Sakunpongpitiporn et al. [195] developed a physically crosslinked hydrogel using sericin fiber as a matrix and PEDOT: PSS as an insulin carrier for transdermal iontophoresis. In this system, insulin binds to PEDOT: PSS via electrostatic interactions (Figure 11a). Incorporation into the sericin fiber hydrogel significantly enhanced swelling, pore size, and network aperture. Under an electric field of 3–6 V at pH 7.4, the system achieved an insulin release efficiency of 81.9% and a transdermal release rate of 75.2%. The release profile followed Fickian diffusion kinetics, and the hydrogel exhibited excellent biocompatibility (cell viability  $\geq 80\%$ ), offering a controllable, low-toxicity transdermal insulin delivery solution for diabetes management. Chen et al. [196] fabricated a gelatin-based cryogel (PGC2) loaded with PEDOT: PSS via a freeze-gelation process using glutaraldehyde as a crosslinker. This macroporous material demonstrated high water absorption, moderate enzymatic degradability, reversible compressive deformation, and injectability (Figure 11b). The inclusion of PEDOT: PSS reduced the impedance of PGC2 to 17 400  $\Omega$ , significantly lower than that of pure gelatin cryogels. Under electrical stimulation, the drug release rate reached 23%, compared to only 7% in non-stimulated controls, while maintaining excellent biocompatibility (NIH-3T3 cell viability  $\geq 70\%$ ). Furthermore, Jung et al. [197] pioneered a synergistic therapeutic strategy combining a body-coupled targeted stimulation (BOOST) system with an active release muscle stimulation (ARMS) hydrogel. The battery-free BOOST system delivers wireless deep electrical stimulation via tissue capacitive charge accumulation, while the ARMS hydrogel, composed of a PVA/PEDOT: PSS matrix modified with dodecyl acrylate to prevent drying, enables electrically responsive release of dexamethasone phosphate (Figure 11c). This synergy facilitated deep drug penetration (up to 10 000  $\mu\text{m}$ ) from the skin into muscle tissue. In vitro studies confirmed significant repair of oxidative stress-damaged muscle cells, with desmin-positive cells exceeding 40% and restored expression of myogenic markers such



**FIGURE 11** | (a) The electrostatic adsorption between PEDOT: PSS and insulin, and the transition of the insulin-loaded PEDOT: PSS/ sericin fiber hydrogel from a random coil structure to a  $\beta$ -sheet crystal structure. Reproduced with permission. Copyright 2023, Royal Society of Chemistry. (b) Photos of cryogels after cryogelation in a syringe, lyophilization, and hydration. Cryogels were prepared using 3 mL syringes with an inner diameter of 0.9 cm. Reproduced with permission. Copyright 2025, Chen et al. (c) Schematic illustration of the active Dex release mechanism by the ARMS hydrogel. Reproduced with permission. Copyright 2025, John Wiley and Sons. (d-I) Schematic showing the dynamic thiol-Michael cross-linking between 4-arm PEG-BCA and 4-arm PEG-SH in the presence of PEDOT nanoparticles and BSA-FITC or DOX to give a cargo-loaded Gel/PEDOT system. (d-II) The release of BSA-FITC or DOX can then be photothermally modulated by NIR light. Reproduced with permission. Copyright 2023, American Chemical Society.



as myosin heavy chain, providing a non-invasive, personalized therapy for muscle atrophy.

Photo-responsive systems primarily target tumor therapy, leveraging PEDOT: PSS's strong NIR absorption and superior photothermal conversion efficiency. Unlike inorganic photothermal agents (e.g., gold nanorods), PEDOT: PSS offers enhanced light stability, making it ideal for constructing platforms that synergize photothermal therapy with chemotherapy for solid tumor treatment [198]. Thapa et al. [199] developed a PEG/PEDOT composite hydrogel (Gel/PEDOT) based on dynamic thiol/Michael addition crosslinking. The embedded PEDOT nanoparticles, synthesized via oxidative emulsion polymerization, exhibited potent near-infrared absorption and photothermal capabilities (Figure 11d). Upon stimulation with an 808 nm laser, the hydrogel underwent a reversible gel-sol phase transition. This platform combined injectability, self-healing properties, and excellent biocompatibility (cell viability  $\geq 70\%$ ) to enable on-demand pulsed release of model proteins (BSA-FITC) and the chemotherapeutic agent doxorubicin (DOX). At a laser power density of  $2 \text{ W/cm}^2$ , the release rates reached 27% for BSA-FITC and 75% for DOX. Crucially, the released DOX retained its anticancer activity, establishing an efficient photothermal-responsive smart platform for precise cancer therapy.

### 3.5 | Electrical Stimulation Therapy

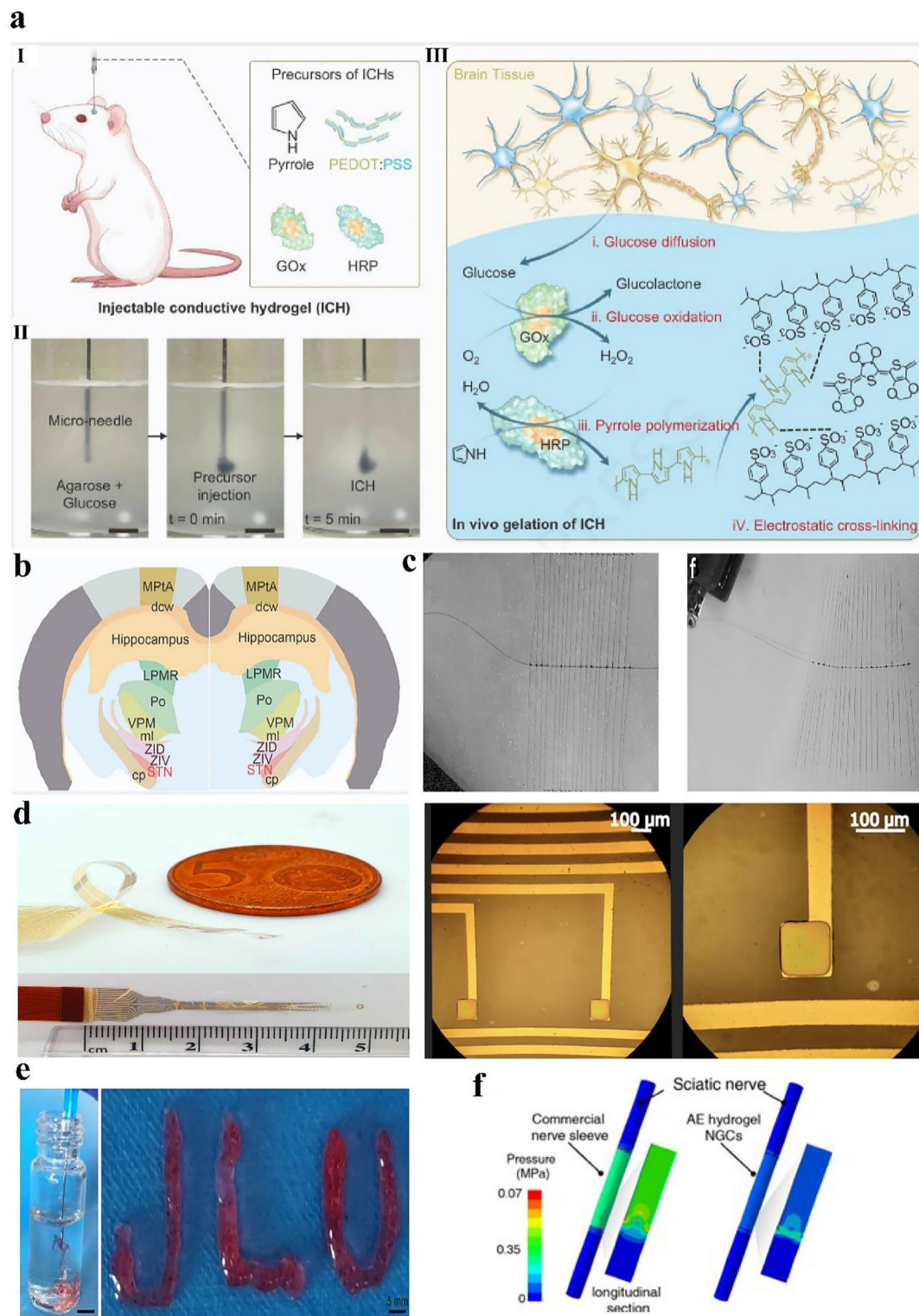
Electrical stimulation therapy is a physical treatment modality grounded in bioelectrophysiological principles, utilizing controlled electrical pulses delivered via external or implanted devices to modulate cell membrane potentials and regulate the excitability of neurons or muscle cells. This approach effectively restores physiological functions, alleviates symptoms, and promotes recovery, establishing itself as a cornerstone in rehabilitation, pain management, and neural regulation [200]. PEDOT: PSS, as a prototypical mixed ion/electron conductor, significantly enhances ES efficacy by reducing tissue-electrode interface impedance, minimizing energy loss, and enabling precise low-voltage stimulation. Its 3D porous architecture provides abundant active sites for high charge injection capacity, while its electrochemical reversibility—often termed the “sponge effect”—facilitates charge transfer without the release of toxic metal ions. These attributes substantially mitigate inflammatory responses associated with chronic stimulation, making PEDOT: PSS ideal for implantable devices. Furthermore, its soft mechanical properties closely match those of biological tissues, offering significant potential for wearable patches and compliant neural interfaces [201].

Neurostimulation represents the most extensive application domain for PEDOT: PSS, addressing critical limitations of traditional metallic electrodes such as poor adhesion, high impedance, and long-term instability. In Deep Brain Stimulation, often referred to as a “brain pacemaker,” high-frequency pulses are delivered to specific nuclei to correct abnormal circuit activity in movement and psychiatric disorders. Yang et al. [202] developed an injectable conductive hydrogel capable of *in situ* gelation. Through glucose-triggered GOx-HRP cascade biocatalytic polymerization and electrostatic self-assembly, the hydrogel forms a conductive network composed of PEDOT: PSS and PPy within

brain tissue (Figure 12a). Possessing mechanical properties compatible with brain tissue (Young's modulus  $\sim 495.07 \text{ Pa}$ ), high electrical conductivity ( $\sim 0.3 \text{ S/cm}$ ), excellent biocompatibility, and long-term stability. It enables minimally invasive, wireless electrical stimulation of deep brain regions. In a rat model of Parkinson's disease (PD), this system significantly improved the motor behavior of the model animals and protected dopaminergic neurons in the substantia nigra pars compacta. Furthermore, it possesses excellent MRI compatibility, allowing for simultaneous neuromodulation and whole-brain functional/structural imaging, providing a novel technological platform for the minimally invasive, wireless neurostimulation treatment of neurological and psychiatric disorders. Addressing the challenge of precisely locating the small and deep subthalamic nucleus (STN) in Parkinson's disease (PD), Jing et al. [203] developed a 16-channel MEMS-based microelectrode array (MEA) modified with MWCNT/PEDOT: PSS nanocomposites. With detection sites distributed at varying depths to match STN morphology, this device achieved single-cell-level signal acquisition (Figure 12b). The study identified distinct PD biomarkers, including heightened spike frequency, beta-band (13–30 Hz) oscillations, and synchronous spectral shifts in delta and beta bands, enabling precise STN localization without multiple implantations and overcoming the spatial resolution limits of traditional tungsten electrodes.

Spinal Cord Stimulation has evolved from pain management to a versatile tool for motor recovery and consciousness arousal. Vara et al. [204] investigated the stability of PEDOT: PSS-co-MA coated carbon microfibers (PCMFs) for long-term neural repair (Figure 12c). In a porcine spinal cord injury (SCI) model, 6 mm PCMFs withstood 2 million biphasic pulses while maintaining voltage offsets within safe limits ( $-0.9$  to  $+0.4 \text{ V}$ ). Although minor transverse cracks appeared in the polymer coating, no significant delamination occurred, confirming their viability as electroactive scaffolds. Advancing this further, Woodington et al. [205] developed “i360,” a flexible,  $4 \mu\text{m}$ -thick annular bioelectronic device featuring 32 interleaved PEDOT: PSS electrodes on a Parylene-C film. Capable of 360-degree circumferential wrapping around the spinal cord, i360 enabled multidimensional recording and stimulation (Figure 12d). In an acute complete transection model, a dual-device closed-loop bypass system reduced neural conduction delay to  $0.083 \text{ ms}$ —surpassing normal conduction speeds—and successfully restored hindlimb motor function in rats. Six-week chronic implants showed no adverse effects on spinal morphology or function, with successful validation in human cadavers, marking a significant step toward clinical translation for SCI.

Peripheral Nerve Injury, affecting millions globally, often results in incomplete recovery due to slow regeneration. Liu et al. [206] addressed this by developing a multifunctional composite hydrogel (CHs/McCbl) integrating mecobalamin (McCbl), PEDOT: PSS, and hyaluronic acid (Figure 12e). Combined with exogenous ES, this system significantly improved the sciatic function index (SFI) and compound muscle action potential (CMAP) amplitude in rats, promoting myelinated axon regeneration and reducing muscle atrophy. Similarly, Lin et al. [207] engineered an injectable conductive hydrogel (ICH) based on carboxymethyl chitosan, oxidized sodium alginate, and PEDOT: PSS. By regulating membrane potential and calcium channel



**FIGURE 12** | (a-I) Schematic diagram of in situ gelation of injectable conductive hydrogel in the mouse brain. (a-II) Representative images show in situ gelation of ICHs in tissue-mimicking agarose gel over time. Scale bar, 5 mm. (a-III) Biocatalytic polymerization and electrostatic assembly mechanism of ICHs. GOx, glucose oxidase; HRP, horseradish peroxidase; PEDOT: PSS. Reproduced with permission. Copyright 2026, Springer Nature. (b) Brain mapping of MEA pathway nuclei during implantation. Reproduced with permission. Copyright 2024, Springer Nature. (c) Appearance of the assembly before and after the electrodeposition of the polymer. Reproduced with permission. Copyright 2024, MDPI. (d) The i360 device shows looped flexibility and is presented next to a ruler (left). Optical image of the device electrodes, showing the PEDOT: PSS coating (right). Reproduced with permission. Copyright 2024, Woodington et al. (e) Presentation of CHs/McChI composite hydrogel and its excellent injectability. Reproduced with permission. Copyright 2025, Elsevier. (f) Stress distribution when AE hydrogels and commercial nerve sheaths come into contact with the sciatic nerve during the nerve growth and expansion phases. Reproduced with permission. Copyright 2025, American Chemical Society.

activity, this material enhanced PC12 cell proliferation and axonal extension. In rat sciatic nerve compression models, it significantly boosted SFI, CMAP amplitude, and nerve conduction velocity, while increasing myelin thickness and axon diameter, demonstrating a minimally invasive strategy that merges biological activity with conductivity. Finally, Feng et al. [208] created an anti-fatigue conductive hydrogel nerve guide catheter using a PVA/PEDOT: PSS matrix. Through drying/stretching techniques and acetic acid treatment, they achieved a topologically aligned structure with high conductivity (5 S/cm), a fatigue threshold of 500 J/m<sup>2</sup>, and a Young's modulus of  $1 \times 10^6$  Pa. This catheter synergized topological guidance with efficient electrical signaling to promote directional axonal growth and Schwann cell activation (Figure 12f). After eight weeks, treated rats exhibited an SFI of −30 and a CMAP amplitude of 0.4 mV, indicating accelerated neurological and electrophysiological recovery.

### 3.6 | Implantable/Wearable Energy Storage Unit

Supercapacitors (electrochemical capacitors) are ideally suited for implantable medical devices, wearable electronics, and micro-sensing applications due to their high power density, rapid charge–discharge capabilities, extended cycle life, and potential for flexible, miniaturized designs. Consequently, they have become a focal point at the intersection of biomedical engineering and energy storage materials. Supercapacitors not only satisfy the stringent demands of biomedical equipment for instantaneous high-power pulses, miniaturization, and physiological compatibility but can also be integrated with lithium batteries or energy harvesting units to form hybrid systems, effectively compensating for the limitations of single energy sources. As a mainstream electrode modification material, PEDOT: PSS demonstrates significant potential in this field. Wu et al. [209] fabricated rGO/PEDOT: PSS composites via hydrothermal reaction, achieving optimal performance at a GO to PEDOT: PSS mass ratio of 10:5, with a specific capacitance of 303 F/g. When assembled into a symmetric quasi-solid-state supercapacitor, the device exhibited a 1.6-fold increase in specific capacitance and a 1.8-fold increase in energy density under low illumination (0.18 W/cm<sup>2</sup>) compared to dark conditions. Control experiments confirmed that this enhancement stemmed from the photothermal effect, which improved the conductivity of both the electrode and electrolyte (Figure 13a). Fan et al. [210] focused on enhancing the energy density of planar micro-supercapacitors (SMSCs) by fabricating hybrid electrodes composed of activated carbon and PEDOT: PSS using the Microplotter technique (Figure 13b). Leveraging the synergistic effects of AC's electric double-layer capacitance and PEDOT: PSS's pseudocapacitance, the resulting SMSCs delivered an areal capacitance of  $2.95 \times 10^{-4}$  F/cm<sup>2</sup> at 1 mA/cm<sup>2</sup>—an 87.9% improvement over pure AC-based devices ( $1.57 \times 10^{-4}$  F/cm<sup>2</sup>). The system achieved a competitive energy density of  $2.79 \times 10^{-3}$  mW/cm<sup>2</sup> (active area) and remarkable cycling stability, retaining 85% of its capacitance after 5000 cycles, offering a promising strategy for high-performance microscale energy storage. Liu et al. [211] developed a transparent, stretchable symmetric supercapacitor by spin-coating PEDOT: PSS thin films onto PDMS substrates followed by the electrochemical deposition of uniformly dispersed  $\alpha$ -MnO<sub>2</sub> nanoparticles (Figure 13c). The PEDOT: PSS/MnO<sub>2</sub> composite electrode achieved an areal capacitance of 1.14 F/cm<sup>2</sup>, representing a

178% performance enhancement compared to pure PEDOT: PSS devices.

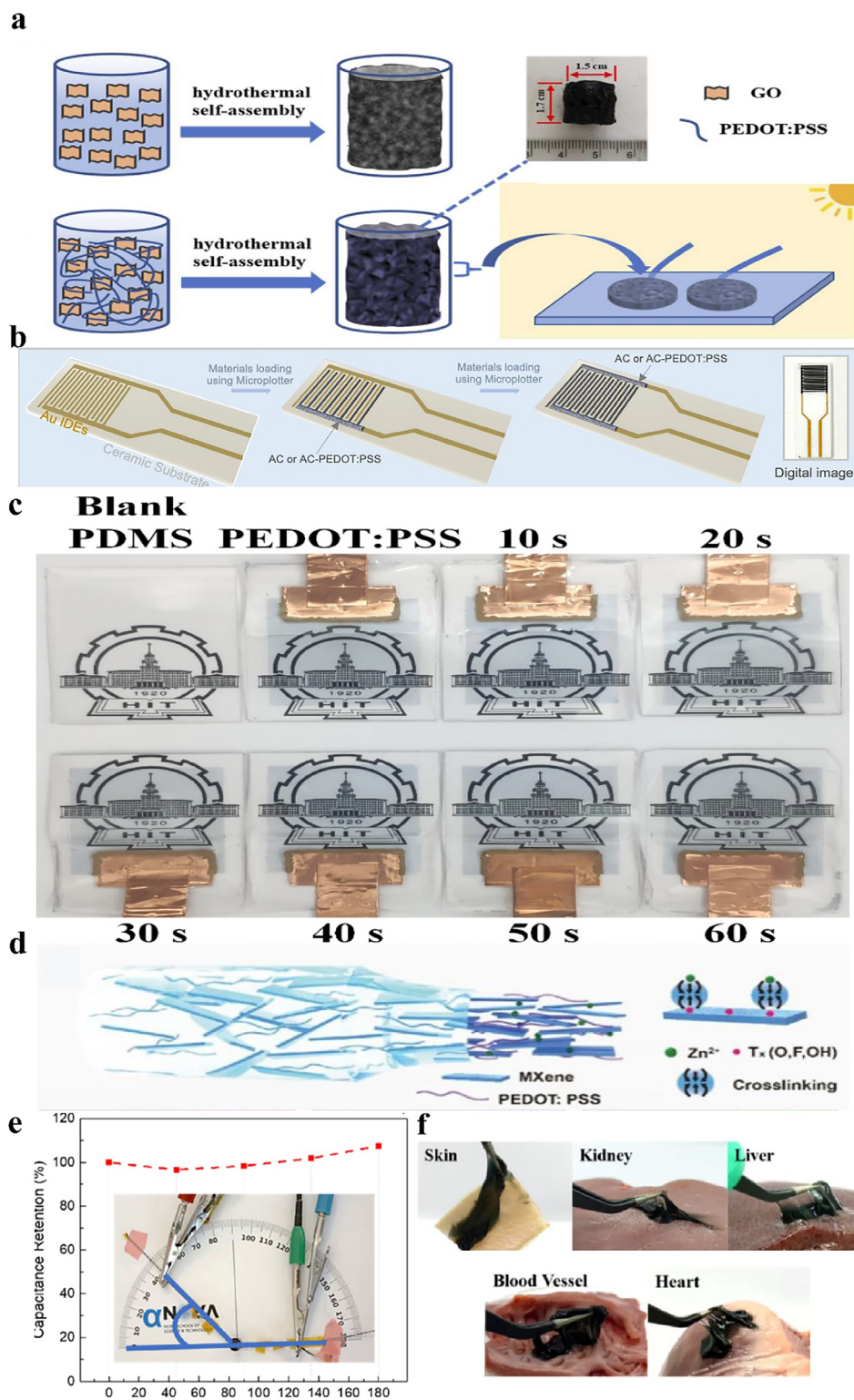
Fibrous supercapacitors have emerged as a promising platform due to their miniaturization, high flexibility, and integrability. Gao et al. [212] utilized an eco-friendly coagulation bath containing Zn<sup>2+</sup> and HCl to fabricate PEDOT: PSS/Ti<sub>3</sub>C<sub>2</sub>T<sub>x</sub> MXene composite fibers via wet-spinning (Figure 13d). The resulting M4P1-LS composite fiber, treated with *L*-ascorbic acid and concentrated sulfuric acid, served as a flexible electrode for fibrous supercapacitors, delivering a volumetric capacitance of 69.6 mWh/cm<sup>3</sup> at 0.5 A/g. At 3 A/g, the device maintained an energy density of 69.6 mWh/cm<sup>3</sup> and a power density of 3010 mW/cm<sup>3</sup>, while retaining 80.9% of its capacitance after 5000 cycles. Notably, the device preserved over 95% capacitance retention under bending and twisting and supported series-parallel connections for scalable power supply, providing a green fabrication route for high-performance micro-supercapacitors. Moniz et al. [213] employed electrospray deposition to coat PEDOT: PSS onto carbon yarn substrates, addressing the need for flexible one-dimensional energy storage in electronic textiles. This approach yielded solid-state flexible Fibrous supercapacitors free of acidic gel electrolytes. By optimizing deposition parameters, they created PEDOT: PSS/carbon yarn composite electrodes with porous spherical nanostructures, which were assembled into devices using cellulose-based gel electrolytes. These devices exhibited a specific capacitance of 0.072 F/g, retained over 85% capacitance after 1500 cycles, and maintained 100% retention even when bent to 180° (Figure 13e). Benefiting from a combined electric double-layer and pseudocapacitive charge storage mechanism, the devices could be connected in series (four units powered an LED), overcoming limitations of conventional deposition techniques such as poor adhesion and material waste.

Hydrogel-based supercapacitors represent a class of energy storage devices characterized by excellent flexibility, biocompatibility, and tissue adhesiveness. Zhou et al. [214] developed an implantable hydrogel supercapacitor based on PEDOT: PSS, optimizing its condensed-phase structure through DMSO post-treatment to form an ordered porous network within a polyacrylic acid hydrogel matrix. The device demonstrated outstanding electrochemical performance, including 97.81% capacitance retention after 10 000 cycles and a specific capacitance of  $8.7 \times 10^{-3}$  F/cm<sup>2</sup> at 0.1 mA/cm<sup>2</sup>. It also exhibited exceptional mechanical properties, strong tissue adhesion, and favorable biocompatibility, with no significant inflammatory response observed in mice 15 days post-implantation (Figure 13f). Furthermore, the incorporation of hydroxyacetylchitosan quaternary ammonium salt conferred antimicrobial activity, evidenced by a 13.3 mm inhibition zone against *Staphylococcus aureus*, thereby providing a safe and efficient energy storage solution for implantable medical devices.

### 4 | Clinical Challenges and Obstacles Associated With PEDOT: PSS

The translation of PEDOT: PSS from fundamental research to clinical applications is hindered by multiple challenges arising primarily from its intrinsic defects and processing complexities. Although PEDOT: PSS is widely regarded as biocompatible, this





**FIGURE 13** | (a) Schematic diagram of rGO and rGO/PEDOT: PSS synthesis process and diagram of photothermal enhanced supercapacitor. Reproduced with permission. Copyright 2023, Elsevier. (b) Illustration depicting the steps involved in fabricating SMSC, followed by the loading of electrode materials (AC or AC-PEDOT: PSS) onto Au IDEs using the Microplotter technique. Reproduced with permission. Copyright 2024, Elsevier. (c) Digital photos of blank PDMS, PEDOT: PSS electrode, and PEDOT: PSS/MnO<sub>2</sub> NP electrodes with various deposition times. Reproduced with permission. Copyright 2024, MDPI. (d) Interaction and forming mechanism of PEDOTPSS/MXene composite fibers. Reproduced with permission. Copyright 2025, American Chemical Society. (e) Flexible solar cells demonstrate exceptional flexibility whilst maintaining their capacitance, retaining 100% of their capacitance even when bent 180°. Reproduced with permission. Copyright 2023, Moniz et al. (f) Photographs showing the hydrogel adhering to pig liver, skin, kidneys, heart, and blood vessels demonstrate its high adhesion and good biocompatibility. Reproduced with permission. Copyright 2025, American Chemical Society.

is largely based on in vitro or short-term in vivo experiments. Following long-term implantation, the PSS component may swell, degrade, and trigger inflammatory responses (such as gliosis or fibrous encapsulation). Furthermore, in laboratories, strong acids (such as sulfuric acid) or high-boiling-point organic solvents (such as DMSO) are often used for secondary doping to enhance conductivity; the presence of such residues in clinical-grade implants is absolutely unacceptable. PEDOT: PSS is prone to delamination from flexible substrates, particularly in environments subject to long-term pulsation or tissue micro-movement in vivo. As PEDOT: PSS is non-degradable, once this phenomenon occurs, it will have irreversible consequences for the patient. Currently, most preclinical studies cover implantation periods of no more than six months, whereas chronic implantable devices require animal testing data spanning at least three years. Laboratories, in their pursuit of optimal performance metrics (such as ultra-high conductivity and drug-loading capacity), typically conduct short-term testing under idealized conditions, permit the use of toxic post-processing solvents, and exhibit a high tolerance for inter-batch variability. In contrast, clinical applications prioritize safety, long-term stability and reproducibility. Clinical requirements stipulate that target materials or devices must comply with GMP manufacturing standards, be free from sterile and cytotoxic residues, and maintain functionality for months or even years within complex in vivo microenvironments.

There is currently a lack of standardized clinical protocols for the sterilization of PEDOT: PSS materials, and medical devices made from different formulations of PEDOT: PSS require different sterilization conditions. The FDA's current classification criteria for biomaterials do not apply to polymers with electroactivity and ionic conductivity, and there is a lack of specific risk assessment frameworks and performance testing standards for conductive polymers.

## 5 | Future Outlook

In the future, the applications of PEDOT: PSS will be divided into two main categories: wearable devices (external) and implantable devices (internal). PEDOT: PSS requires different modifications to meet the specific requirements of various clinical application environments. For wearable devices, the focus is more on textiles, with an emphasis on physical and chemical stability and performance characteristics, such as wash resistance, corrosion resistance, and the device's ability to conform to the skin. Other considerations include breathability during wear, minimizing the risk of skin allergies, and low manufacturing complexity. Physiological signal monitoring is the most established application of PEDOT: PSS in wearable devices. Scalco De Vasconcelos et al. [215] reported a technique for direct micro-jet printing of personalized electroencephalogram (EEG) electronic tattoos onto the scalp, using the conductive polymer PEDOT: PSS as a substrate. This ink offers high breathability, sweat resistance (resistance change < 25% after vigorous exercise), and ease of removal, thereby addressing the issues of bulky traditional EEG devices, the short shelf life of wet gels, and interference from hair.

With regard to implantable devices, we will place greater emphasis on their safety and stability, ensuring they operate efficiently without causing serious side effects. This includes

long-term electrochemical stability and mechanical compatibility with neural or cardiac muscle tissue. Development of a PEDOT: PSS hydrogelation technique to reduce the modulus. Xie et al. [216] proposed a novel liquid–liquid 3D printing strategy that utilizes the electrostatic self-assembly of PEDOT: PSS colloidal particles and PDMS surfactants at the oil–water interface to form elastic films. Following post-processing, the PEDOT: PSS dual-interpenetrating network hydrogel achieves a conductivity of up to 3.01 S/cm, with a modulus range covering both soft and hard tissues. This hydrogel can be used in electrochemical microfluidic devices, implantable NFC biochips, and flexible neural interfaces. To avoid the cytotoxicity issues associated with secondary dopants such as DMSO, Rahman et al. [217] selected d-sorbitol as an additive for PEDOT: PSS hydrogels. d-sorbitol is completely non-toxic and exhibits excellent biocompatibility, making it suitable for long-term in vivo implantation; furthermore, its conductivity can reach up to 91 S/cm in PBS buffer. This approach brings PEDOT: PSS hydrogels a step closer to clinical application and resolves the issue of toxic dopants. Among current implantable devices, neural electrodes and brain–computer interfaces are attracting the most attention, and PEDOT: PSS plays a key role in this field. When deposited onto the surface of conventional metal electrodes via electrochemical deposition or spin-coating, PEDOT: PSS can significantly reduce impedance and markedly improve the signal-to-noise ratio; its higher charge injection capacity makes electrical stimulation safer and more effective. Fully transparent, metal-free PEDOT: PSS electrode arrays enable ‘electrophysiology + imaging’ multimodal brain–computer interfaces. High signal-to-noise ratio recording and closed-loop stimulation have already been achieved in scenarios such as ECoG (electroencephalography of the cortex), intracranial microelectrodes, intraoperative monitoring, and wearable EEG–BCI systems, with some work having progressed to the stage of intraoperative monitoring in humans and early clinical validation [218].

Transcending the traditional bioelectronic paradigm, future opportunities lie in the deep integration of conductive polymers with synthetic biology and intelligent adaptive systems. For instance, flexible electrophysiological interfaces can leverage the tunable conductivity and low interfacial impedance of PEDOT: PSS to convert minute electrical inputs into localized bioelectric signals. This capability enables the regulation of voltage-gated ion channels within excitable cells without the need for genetic modification, thereby establishing an efficient bridge between non-biological electronic components and living tissue. Concurrently, integrating modified biodegradable PEDOT: PSS with AI-driven biosensors to create closed-loop biohybrid systems holds significant promise for achieving adaptive tissue regeneration. In such systems, conductive scaffolds could dynamically adjust electrical stimulation intensity and mechanical stiffness in response to real-time physiological feedback, such as neural impulse activity or myocardial contraction signals.

In summary, functionalized PEDOT: PSS occupies a pivotal position at the intersection of flexible bioelectronics, regenerative medicine, and intelligent biomaterials. To fully realize its potential, there is an urgent need for in-depth interdisciplinary collaboration encompassing advanced polymer synthesis, computational modeling of bioelectronic interfaces, and high-end medical device manufacturing technologies. By integrating sophisticated modification strategies for PEDOT: PSS with deeper

insights into in vivo bioelectrical signaling pathways, this field is poised to deliver personalized electrical stimulation therapies that restore the body's inherent electrical homeostasis. Such advancements could revolutionize treatment paradigms for neurological disorders, cardiac dysfunction, and chronic injuries, driving transformative progress across the associated medical device industry.

## Author Contributions

Zekun Ma: writing – original draft, visualization, and investigation. Ying Zhang: conceptualization. Zhou Li: project administration and data curation. Zhaoxu Meng: writing – review and editing and funding acquisition. He Lian: writing – review and editing, funding acquisition, and supervision.

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## Conflicts of Interest

The authors declare no conflicts of interest.

## Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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