

Advances in Conducting Polymers for Healthcare Monitoring

Subjects: Polymer Science

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Conducting polymers (CPs) are an innovative class of materials recognized for their high flexibility and biocompatibility, making them an ideal choice for health monitoring applications that require flexibility. They are active in their design. Advances in fabrication technology allow the incorporation of CPs at various levels, by combining diverse CPs monomers with metal particles, 2D materials, carbon nanomaterials, and copolymers through the process of polymerization and mixing. This method produces materials with unique physicochemical properties and is highly customizable. In particular, the development of CPs with expanded surface area and high conductivity has significantly improved the performance of the sensors, providing high sensitivity and flexibility and expanding the range of available options. However, due to the morphological diversity of new materials and thus the variety of characteristics that can be synthesized by combining CPs and other types of functionalities, choosing the right combination for a sensor application is difficult but becomes important.

Keywords: conducting polymers ; sensor technology ; human health monitoring

1. Overview of the Use of CP in Sensor Design

1.1. CP Characterization

Researchers are drawn to CPs because of their controllable wide range of electrical conductivity and flexible mechanical properties. The alternating single-bond and double-bond structure (π -conjugated backbone) and the controllability of the type and level of doping are particularly advantageous. **Figure 1** shows the conduction mechanism of PAc, which was the first synthesized CP based on π -conjugated backbone extension, allowing electron movement within the conjugated polymer chain ^[1]. Achieving high conductivity in CPs requires a structure with overlapping p-molecular orbitals and a high degree of π -bond conjugation. CPs feature an extensive π -conjugated system characterized by a network of irregular single and double bonds along the polymer chain. In their neutral state, highly conjugated CPs function as insulators. However, conductivity is achieved only when a p-bond electron is extracted from the π -conjugated polymer backbone, which creates a positively charged defect known as a polaron. The electrical conductivity of the CP-conjugated chain is affected by the type of doping and CPs electronic transitions that occur because of the presence of impurities, which alter the amount of charge within the band gap. The doping process in CPs differs considerably from that in inorganic semiconductors such as silicon and germanium in terms of the doping concentration and charge transformation of the conduction band energy. Doping in CPs involves the partial oxidation or reduction of the polymer, in which reactive ions are introduced to maintain electrical neutrality. This can be achieved either chemically or electrochemically by introducing cations or anions to balance the charge of the conjugated polymer through oxidation (p-doping) or reduction (n-doping) ^[2]. The degree of doping in CPs is significantly higher than that in traditional semiconductors, with approximately one-third to two-thirds of the monomer units being doped, which corresponds to doping concentrations falling within the range of 10^{18} to 10^{22} cm^{-3} . The doping level is the main difference between CPs and other semiconductor materials. CPs exhibit distinct electronic properties that distinguish them from inorganic crystalline semiconductors in two critical aspects: their long-range order and molecular nature. The movement of charge carriers is the primary mechanism of electrical conduction in doped CPs. During the doping process, charges are either added to or removed from the polymer, resulting in the generation of mobile charge carriers capable of moving along the conjugated polymer chains because of the rearrangement of double and single bonds in the conjugated system ^[3]. This process transforms the insulating polymer into a conductive material. The extraction of p-bond electrons induces the delocalization of the remaining electrons within the p-orbitals along the length of the π -conjugated backbone, enabling the unrestricted movement of charge along the chain. Doping alters the bandgap energy of the polymer, leading to the increased conductivity of CPs ^{[4][5]}.

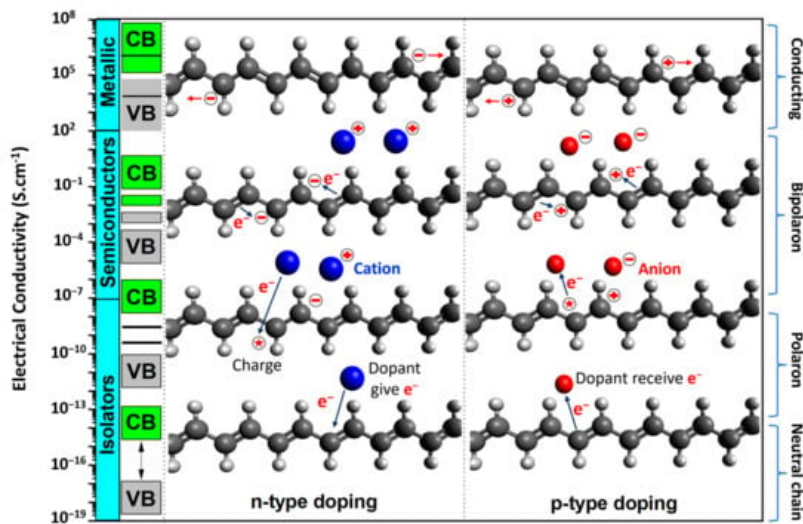


Figure 1. Conduction mechanism of PAC, a typical of CPs. (Referenced from Ref. [3] Copyright (2018), with permission from MDPI Publisher).

The simplest CP structure comprises a backbone series of π -conjugated polymers belonging to polyenes such as PAC and PIP. The more complex structures are π -conjugated polymers belonging to polyaromatics such as PANi, PPy, PTh, PPP, and PPV classes, and they have been extensively studied. Another type of CP is a copolymer of a CP and another polymer, such as PEDOT:PSS [6], PANi:poly(methyl methacrylate) (PMMA) [7], PPy:poly(dimethyl siloxane) (PDMS) [8], PPy:poly(*N*-vinylcarbazole) [9], and P3HT:poly(ethylene glycol) [10]. Polymers featuring amino groups ($-\text{NH}_2$) and carboxyl groups ($-\text{COOH}$) along the CP backbone readily facilitate bioconjugation with essential biorecognition molecules, such as enzymes, antibodies, proteins, and DNA [11]. Thiolate bio molecules, particularly mRNA, can autonomously assemble on CPs decorated with silver and gold nanoparticles. The fusion of CPs with water-swollen hydrogels yields porous CP hydrogels that provide a plethora of advantageous characteristics for biosensing platforms. These porous CP hydrogels exhibit exceptional electrical conductivity, robust mechanical properties, a sophisticated hierarchical structure, and the ability to absorb and release substances because of the inherent swelling capability of the polymer chain [12].

1.2. CP Processing

Achieving the required sensitivity of a sensor requires adjusting its properties before its use. The precursor material and manufacturing method determine most of the sensor's properties. For CP materials and the synthesis environment, three main methods are employed: chemical oxidate polymerization, vapor-phase polymerization, and electrochemical polymerization, which lead to the formation of structures containing π -conjugates [13]. An alternative chemical method called vapor-phase polymerization has gained significant attention because of its ability to produce CP films with different thicknesses, uniformities, and densities. Typically, a CP is synthesized directly on a substrate surface through a two-step process. In the first step, an oxidizer, such as iron thiocyanate, is applied to the surface through a solvent coating process. Subsequently, the surface is exposed to CP monomer vapor to induce the polymerization reaction [14]. This method is commonly employed to synthesize PEDOT and PANi for their application in electrodes. The three main CP polymerization methods are shown in Figure 2.

1.2.1. Chemical Oxidate Polymerization

Chemical oxidation polymerization is commonly used to synthesize PPy, PANi, PTh, and PIN. This method is based on redox principles and stimuli such as optical, physical, and biological stimuli [15]. The monomers used in this method exhibit electron-donating properties and a high tendency to undergo oxidation. Monomer oxidation is achieved using different oxidizing agents that generate cationic radical sites in the monomer [16]. Chemical polymerization can involve two mechanisms: polycondensation and chain growth. Polycondensation involves the recombination of cation radical oxidation sites, whereas chain growth is characterized by electrophilic substitution. The chemical oxidative method for CP polymerization has several advantages: it is suitable for producing large high-quality polymers, it allows the use of inexpensive and diverse oxidizing agents, and the resulting polymers exhibit stability with significant conductivity. A conductivity of 9.1 S/cm and an 80% increase in conductivity were achieved for PTh prepared by chemical oxidation with FeCl_3 as the oxidant. The conductivity increased up to an oxidant–monomer molar ratio of 1:6, but further increasing the molar ratio to 1:7 caused a sharp decrease in conductivity (4.46×10^{-1} S/cm), although the performance increased by 92% [17]. CPs can undergo reversible redox reactions to switch between conductive and insulating states. This property is important for biosensors because it allows the detection of analytes on the basis of changes in electrical conductivity.

Drawing on the chemical oxide polymerization mechanism, advanced manufacturing techniques like electrospinning, coating, and 3D printing have been explored for the production of electrodes from CPs [18]. While these methods above involving melting and thermoforming, and photocatalysis provide the benefit of increased productivity, they may introduce numerous additives into the final product, posing a noteworthy concern for manufacturing, especially probes from CPs [14] [19].

1.2.2. Electrochemical Polymerization

Electrochemical polymerization involves the introduction of three electrodes—a reference electrode, a counter electrode, and a working electrode—into a solution containing either reactants or monomers. Applying a voltage to these electrodes triggers a redox reaction that results in the formation of the polymer. Electrochemical polymerization can be further categorized into the following methods. The electrochemical synthesis of CPs can be carried out both at a controlled current and at a controlled potential of the working electrode. Also, using the method of cyclic voltammetry, CPs can be synthesized already at a potential (voltage) that changes during cycling. The primary advantage of electro(co)polymerization is the production of high-purity products. However, it is noteworthy that this method can produce only a small number of products simultaneously. Electrochemical polymerization is a cost-effective and environmentally friendly method for transforming monomers into CPs. The initiation of monomer polymerization is facilitated by the application of an oxidizing agent to the working electrode, which can be made of materials such as carbon [20], metal [21], and conductive glass. Notably, this polymerization method does not involve toxic chemicals, and it not only yields high-purity CP materials with outstanding electrical and electronic properties, but has a high level of reproducibility. Electrochemical polymerization comprises three steps. The first is the dissolution of the oligomer in the diffusion solution following the oxidation of the monomer, and the second is the deposition nucleation process. Finally, growth and chain propagation occur through polymerization. With the exception of the initial oxidation stage, the synthesis mechanism of each polymer is well understood because the process is governed by the synthesis parameters [22]. In the case of electrochemical polymerization, an understanding of the nucleation process and growth kinetics can facilitate the customization of polymer characteristics, including crystallinity, structure, morphology, and density, according to requirements. CPs feature a carboxyl or amino group that serves as an immobilization matrix for the covalent attachment of recognition molecules [23].

The polymerization process can occur through two potential pathways: the interaction between neighboring radical cations or the reaction between a neutral monomer and a radical cation. Various methods that induce charges from interactions are employed for the electrochemical polymerization of monomers and their derivatives. Several factors, such as the type of monomer, dopant, pH environment, electrolyte type, applied potential and potential window, initial scanning mode, solvent effects, and temperature, regulate the conductive properties of the resulting polymer film. The conductive properties, in turn, determine the applications for which the produced polymer film can be employed. The electrochemical polymerization method offers a unique advantage: the seamless integration of fabrication and modification in a single process. This versatile technique allows for precise control over the thickness of the polymer film and facilitates the production of monolayer or multilayer structures. Films with conductive or insulating properties can be prepared depending on the desired application. Notably, electroactive and conductive films produced using this method can be directly characterized without the need for additional purification. Furthermore, these CPs maintain their mechanical integrity while exhibiting metallic and semiconductor properties [24]. A significant advantage of this technique lies in the precise regulation of the initiation and termination processes by adjusting the oxidation potential applied during polymerization [25]. Additionally, the control of the electrode potential facilitates processes such as doping, rapid fabrication, the maintenance of film thickness, and deposition control, apart from helping achieve high cleanliness.

1.2.3. Vapor-Phase Polymerization

In this method, polymerization occurs when the vapor-phase monomer is deposited onto an oxidant-coated substrate [26]. Polymerization reactions can be either chemical or electrochemical in nature, but they occur when the monomer is in the vapor phase. This method has several advantages over other techniques: it eliminates the need for solvents, minimizes the risk of agglomeration because the monomer is in vapor form, and enables the production of CPs with high electrical conductivity. Because of the homogeneity of the monomer, it can easily combine with volatile substances and coat uneven surfaces with a porous structure and interwoven fibers [27].

Vapor-phase polymerization has been used to synthesize PPy-coated filter paper for ammonia-sensing applications. Doping enhanced the conductivity of the filter paper from 1.78×10^{-5} to 3.34×10^{-5} S/cm. Consequently, the limit of detection (LOD) of ammonia vapor was 13 parts per million (ppm). Vapor-phase doping with HCl increased dopant localization along the PPy structure to create more active sites, which improved the LOD to 5.2 ppm [28]. A bacterial nanocellulose/PEDOT material was also prepared through vapor-phase polymerization. Environmentally friendly bacterial

nanocellulose was used as a flexible substrate, and the highly conductive PEDOT polymer was introduced on the substrate to obtain composites with a sheet resistance 10 times lower (18 Ω /square) than those produced through polymerization in solution (188 Ω /square). The resulting material could be improved 100 times and rolled completely without significant loss of electronic performance. Furthermore, a bent bacterial nanocellulose/PEDOT film could be used as a green-light-emitting diode., indicating the high applicability of the conductive bacterial nanocellulose/PEDOT film [29]. The vapor-phase technique has been used to fabricate PANi nanotubes with high conductivity by combining aniline monomer and oxidant Mn_3O_4 nanofibers [30]. Furthermore, a PEDOT/graphene composite-based polymer film with high mechanical strength and electrical conductivity (310 ± 20 S/cm) was synthesized via vapor-phase polymerization on a Ta_2O_5 porous dielectric surface using FeTos/graphene [31]. Thiophene polymerization can be achieved through the vapor-phase polymerization of p-toluene sulfonic acid and other sulfonic acids that act as oxidants to polymerize PTh. The high electrical conductivities of the two types of PTh were observed to be 2.91×10^4 and 3.75×10^4 S/cm, respectively [32]. **Table 1** lists the advantages and disadvantages of the main polymerization methods for CP synthesis, as well as the morphologies of the synthesized polymers [33][34][35].

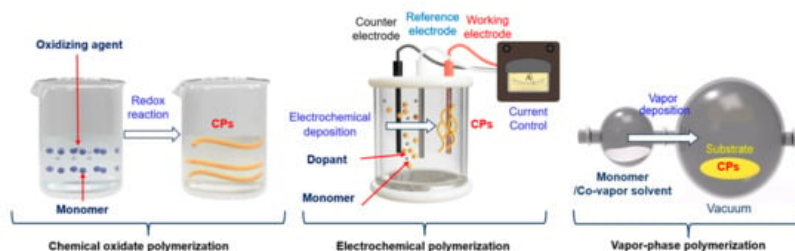


Figure 2. CPs polymerization methods. (Reprint from Ref. [34] Copyright (2015), with permission from Springer Nature Publisher).

Table 1. Comparison of different CP polymerization methods.

Method	Advantages	Disadvantages
Chemical	Scalable production, easy to functionalize, involves chemical doping, straightforward and efficient route, yields a composite material, easy to control the morphology	Time-consuming, only thick films and powders can be synthesized, CPs may impurify, heterogeneity optimization, indirect approach
Electrochemical	No oxidizing agent is required, requires less time, produced CPs have high electrical conductivity, thin films can be produced with dimensional control. Eco-friendly, solventless, efficient, requires a small amount of chemical	Large-scale production is not possible, it is difficult to remove the grown film from the electrode surface, larger reactors are required
Vapor-phase polymerization	Covers many surfaces, monomer easily combines with volatile substances, no solvent required, few impurities	Long duration, low yield, hard to control synthesis, CPs heterogeneity

2. Role and Advantages of CPs in Enhancing Sensor Performance

For tracking human health, the main function of a sensor is to effectively identify or respond to analytes or external stimuli such as chemicals, force, pH, temperature, humidity, and voltage selectively, with good sensitivity and linear response. Subsequently, the sensor should connect and transmit signals to other processing units. Most sensors used for monitoring the human body are passive and incorporate an analog signal receiver. An effective sensor design for human applications should feature a probe with a high sensitivity, good selectivity, fast response time, an appropriate operating range, reproducibility, and compatibility. In general, biosensors comprise three elements: a receptor biological recognition element, which is highly specific toward biological material analytes, integrated with or connected to a physicochemical transducer; a transducer part for converting the signal received from the biological target into an electrical signal; and an amplification and detection part for generating a discrete or continuous digital electronic signal that is proportional to the amount of a specific analyte or a combination of similar analytes [36]. Consequently, the transducer is the most crucial component that determines the effectiveness of the sensor because it directly determines the nature of the stimulating event with the stimulus and determines the operating principle of the sensor. In this component, CPs play a significant role, leveraging their unique electrical and chemical properties to convert recognition stimulation signals into electrical signals. **Figure 3** shows some notable properties of CPs in comparison with other materials, highlighting their ability to achieve tunable conductivity across various applications. Most polymers fall within the semiconducting region (10^{-7} to 10^2), which is inherently advantageous for electrochemical surfaces [4].

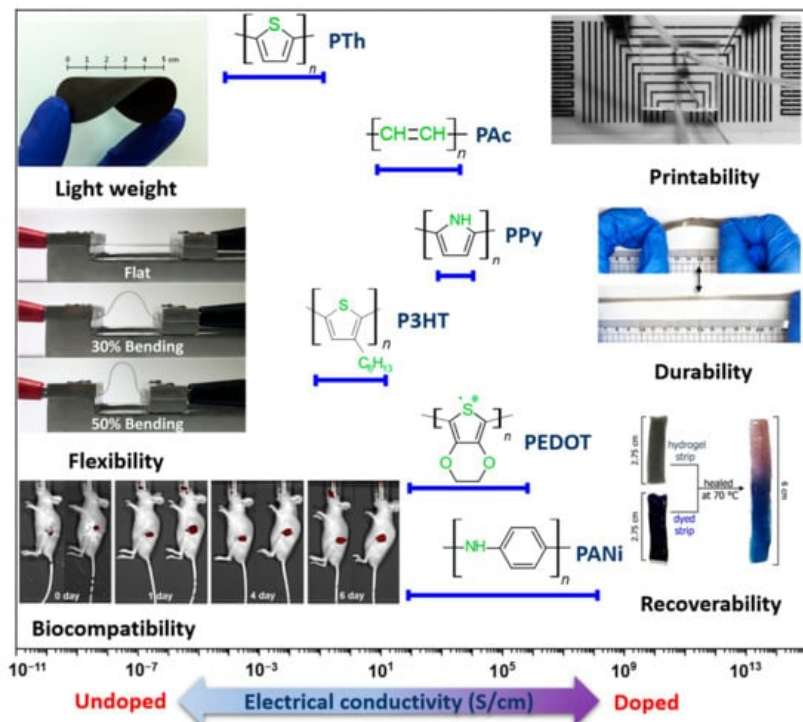


Figure 3. Advantages of using CPs for biosensors (Reprint from Ref. [37] Copyright (2018), with permission from Elsevier Publisher). (Reprint from Ref. [38] Copyright (2015), with permission from Springer Nature Publisher). (Reprint from Ref. [39] Copyright (2020), with permission from ACS Publisher). (Reprint from Ref. [40] Copyright (2020), with permission from MDPI Publisher).

With advances in manufacturing techniques, the development of CPs for biosensors is based on fundamental principles surrounding polymer chain structure, morphology, combination ability, and signal reception mechanism signals and electrical conductivity. The π -conjugated system of CPs with electrons is localized along the polymer backbone. This delocalization allows them to conduct electricity when doped by chemical or electrochemical methods. By doping or dedoping, the conductivity of CPs can be controlled [41]. For applications in human health tracking, additional requirements are necessary for CP development. Currently, one research approach focuses on the synthesis of complicated CP structures such as poly(3, 3"-dialkylquaterthiophene) (PQT12), poly(9,9-dioctylfluorene-alt-bithiophene) (F8T2), poly[2,5-bis(3-tetradecylthiophen-2-yl)thieno[3,2-b]thiophene] (PBTTT), poly[N-9'-heptadecanyl-2,7-carbazole-alt-5,5-(4',7'-di-2-thienyl-2',1',3'-benzothiadiazole)] (PCDTBT), poly(phenylacetylene) (PPA), and poly(diketopyrrolopyrrole-co-bithiophene) (DPP4T) [41]. Another approach involves modifying suitable common CPs such as PAc, PPy, PANi, PPV, PTh, PEDOT, P3HT, and their various derivatives because of their excellent biocompatibility, stability, cost-effectiveness, and exceptional electrical and electrochemical properties, making them suitable for sensor design applications [42][43]. **Table 2** shows the chemical and mechanical properties of CPs used in the field of sensor manufacturing, showcasing characteristic quantities such as conductivity and Young's modulus.

While CPs are generally regarded as easily processable materials for biosensor fabrication, achieving optimal results requires continuous research to optimize their usage conditions. Therefore, designing biosensors using CPs requires careful consideration of several key properties to ensure effectiveness and reliability, such as selecting a CP with appropriate conductivity for a specific application. In this review, material fabrication and application to devices are influenced by many factors, especially in fields requiring high sensitivity, such as health-monitoring sensors. Any proactive change in these processes may introduce desired or unforeseen deviations in the characteristics of the CPs and may affect their applicability [44]. Therefore, the next section discusses important influences such as those of the CP characteristics, combination composition, and polymerization method on sensor function. It also explores the effect of the structure and morphology of the CP on the performance of the sensor. Furthermore, an assessment of the effect of the CP dimensions and size on the performance of the sensor is provided. This detailed review of CPs, their properties, and influencing factors aims to assist readers in identifying crucial components for producing highly efficient CPs for application in industrial devices and sensors. Composites derived from CPs or their combinations with other polymers exhibit enhanced mechanical properties suitable for specific applications. Moreover, CPs such as PPy and PANi have been investigated for use as conductive additives, particularly in conjunction with natural polymers, to address the challenges associated with the processing of CPs and to enhance the conductivity of insulating polymers [45]. On the basis of their function and the degree of interaction with the body, sensors used for human health monitoring can be divided into two main categories: biosensors and wearable sensors [46]. While most biosensors are quantitative or semiquantitative

and involve biological or chemical sensing methods, wearable sensors operate on the basis of electromagnetic signals generated by the physiological activities of the body. **Figure 4** describes the main properties and roles of CPs in human tracking sensors.

Table 2. Characteristics of CPs and their role in human health sensors.

Role of CP/Analyte Detection	Polymerization Method	Conductivity	Young's Modulus	CP Advantages	CP Disadvantages
Transducer PPA/interleukin 6 sensing [47]	Vapor-phased deposition	10 to 104 S/cm	1.2 to 2.0 GPa	Easy synthesis, controllable, high electrical conductivity	Poor stability, non-thermoplastic
Transducer PPy/dopamine detection [48]	Chemical oxidative	40 to 200 S/cm [49]	430 to 800 MPa [49]	Biocompatibility, promotes cell proliferation, high conductivity, environmental friendliness, low cost, compatibility	Rigid, brittle, non-thermoplastic, nondegradable, insoluble in acetone, methanol, and ethanol solvents
Transducer PANi/pH detection [50]	Chemical oxidative	5 S/cm [51]	2.0 to 4.0 GPa [51]	Reversible doping, properties controllable by pH, wide range of conductivity, controllable conductivity, colored and transparent, various synthesis ways, stability with environment	Low processing capacity, inflexibility, lack of biodegradability, poor solubility, complex process
Transducer PTh/parathyroid hormone detection [52]	Vapor-phased deposition	10 to 100 S/cm [53]	3.0 GPa [53]	Low cost, high electrical, mechanical, and optical properties, high thermal and environmental constancy, smaller bandgap energy (2.0 eV) compared with PANi and PPy	Poor solubility with ordinary solvents, difficult to synthesize, poor chemical stability and processability, poor flexibility
Transducer P3HT/immunoglobulin G detection [54]	Chemical, 3D printing	10^{-2} , 10^{-5} to 10 S/cm [55]	28 MPa [56]	Low cost, high electrical, mechanical, and optical properties, high thermal and environmental constancy	Difficult process, poor solubility with common solvents, difficult to synthesize
Transducer PEDOT/temperature sensing [57]	Chemical oxidative	1200 S/cm [58]	1.2 to 4.0 GPa [58]	Transparent conductor, low redox potential, moderate bandgap, environmentally and electrochemically stable	Limited solubility, acidic nature, anisotropic charge injection, hygroscopicity

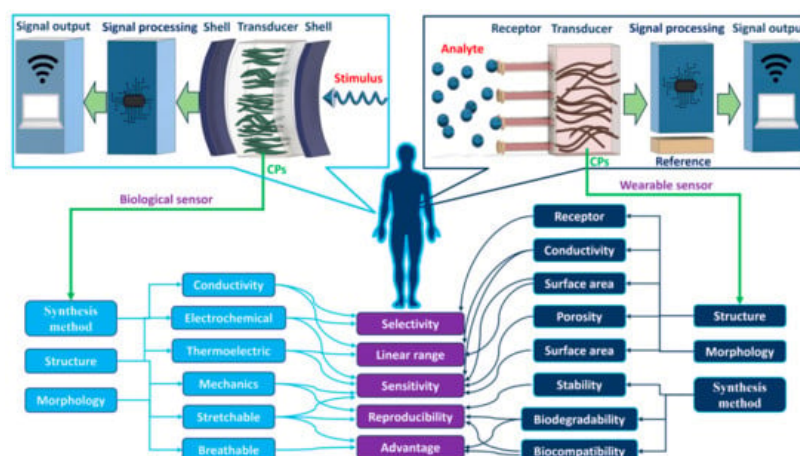


Figure 4. Main properties and roles of CPs in human health sensors [59][60][61].

2.1. The Use of PAc in the Fabrication of the Transducer

2.1.1. Effect of PAc Polymerization on Transducer Fabrication

PAc is a conducting polymer that is formed through the polymerization of acetylene monomers. The synthesis of polyacetylene involves chemical processes, typically initiated by doping with a suitable dopant or using a catalyst. PAc's pure form is susceptible to oxidation when exposed to air and is also affected by humidity, which should be prevented in its application in wearable sensors [62]. However, each hydrogen unit on a polyene unit can be substituted with one or two replacements, resulting in a monosubstituted or disubstituted polyene unit to improve PAc's stability. PAc can also be manufactured through the controlled combustion of acetylene in the presence of air to support a combination with other materials to enhance its properties. Electrodes incorporating PAc exhibit exceptional biocompatibility, high electrical conductivity, and a substantial specific surface area. Hence, PAc proves valuable in fabricating electrochemical sensors with remarkable sensitivity [63][64]. Both pristine PAc and its doped variations have been used for the detection of various substances, including glucose oxidase, colchicine, monoamine neurotransmitters, and their metabolites.

2.1.2. Effect of PAc Structure and Morphology on Transducer Fabrication

The doped PAc structure is unstable, and its conductivity gradually decreases over time, presenting a major limitation of PAc. Some derivatives of PAc with a conjugated chain in a longer unit, such as PDA, PIP, or a derivative of PAc with a conjugated ring added to the structure (such as PPA), have a more stable structure [47][65]. However, PAc has many useful properties owing to its structure, including remarkable electrical conductivity, photoconductivity, a gas-permeable nature, the ability to form supramolecular assemblies, a chiral recognition capability to transform into helical graphitic nanofibers, and its behavior as a liquid crystal. As the first developed CP, it has undergone extensive studies on its conductivity changes, which exhibit a highly customizable range. It is commonly employed for preparing carbon paste electrodes [66] and constructing biosensors [67]. In addition, two disubstituted polyacetylenes with different side group of triazole and 2-(pyridin-2-yl)-1H-benzo[d]imidazole were built as sensor platform for glyphosate, an ingredient in pesticides. The structure shows a high degree of refinement of PAc by turning off the strong emission of PAc through Cu^{2+} and turning it on again in the presence of glyphosate at concentrations as low as 8×10^{-8} M. This result demonstrates the high customization and diversity of PAc's architecture and opens a new approach for building sensing platforms based on PAc derivatives [68]. In addition, based on the change in shape of poly (phenylacetylene) with two aldehyde pendants to identify aliphatic amines and aromatic amines through visual color indicators, this research still has great potential without considering other factors. Physicochemical properties change with structure and are an open direction to develop sensing platforms for heterocyclic compounds such as amines [69].

2.2. The Use of PPy in the Fabrication of the Transducer

2.2.1. Effect of PPy Polymerization on Transducer Fabrication

Among CPs, PPy and its derivatives have been extensively used in biosensor fabrication [70]. The development, synthesis, and polymerization of PPy have been achieved through the repeated oxidation of pyrrole by ferric chloride in methanol. Flexible conducting PPy films can be fabricated through various methods, such as electrochemical or oxidative methods using iron(III) trichloride (FeCl_3). One of the advantages of the electrochemical route is the possibility of doping the polymer chains during the process, for example, with $(\text{Fe}(\text{CN})_6)^{3-}$ [36]. Another attractive method is freezing interfacial polymerization, which can be used to obtain PPy films with a high electrical conductivity of 20 S/cm. The high conductivity results from the increased ordering of the CP structure [71]. Polymerization involves film formation on the anode. PPy is biocompatible, protects electrodes from fouling, and minimally disrupts the working environment. In some cases, PPy forms perm-selective films to exclude endogenous electrochemically active interferents. PPy exhibits numerous outstanding qualities, including excellent biocompatibility both in vitro and in vivo [23]. It exhibits robust chemical stability in both water and air [72][73], and features remarkably high electrical conductivity under physiological conditions [74][75].

The synthesis of PPy is straightforward and versatile, and it can be performed at room temperature in various solvents, including water. Furthermore, this material can be engineered to have a substantial surface area and adjustable porosity, which makes it highly adaptable for a wide range of internal and external sensing applications involving active biological molecules [76][77]. PPy exhibits responsiveness to external stimuli, allowing its properties to be controlled through the application of a voltage [78]. However, it is important to note that PPy presents certain challenges. Its molecular composition makes it intricate to manipulate because it tends to be resistant to high temperatures, mechanically rigid, and does not dissolve in solvents [79]. Various materials have been incorporated into PPy to enhance its flexibility, and its biocompatible properties have been leveraged to construct cell-based sensor systems that emulate the innate mechanisms of the body. These materials include muscle cells, fibronectin, titanium, bovine leukemia virus, protein, poly(ethylene terephthalate) (PET), tosylate, alginate ion, biotin, silk fibroin, and heparin conjugated with chlorpromazine

[80][81][82][83]. Haung et al. conducted a notable investigation on the growth of PC-12 cells on PPY, which yielded intriguing results. PPY sheets subjected to electrical stimulation exhibited a cell growth rate approximately twice that of PPY sheets without electrical stimulation. This discovery underscores the potential of PPY in constructing neural conduits and suggests the possible use of electrical stimulation for enhancing nerve signal reception [84].

2.2.2. Effect of PPY Structure and Morphology on Transducer Fabrication

The PPY structure with only one aromatic ring in the monomer unit of PPY exhibits high post-synthetic stability. Similar to PAc, functional groups with long carbon chains are added to the polymerization unit to enhance flexibility and free space in the overall polymer structure [85]. The synthesis of PPY involves blending it with various polymers. Studies have demonstrated that polylactide and poly(vinyl alcohol) (PVA) can be combined with PPY to obtain nanosized PPY composites. However, the PPY/PVA nanocomposites may exhibit reduced strength when exposed to water. To address this issue, certain solvents can be employed to uniformly disperse PPY in polylactide solution, resulting in uniformity and a low permeation threshold [86]. PPY nanocomposites have garnered attention because of their exceptional physicochemical properties related to nanoscale effects, and they show high stability and dispersibility even in highly viscous polymers [87][88]. Significant enhancements in PPY processability and functionality were achieved through copolymerization with other monomers possessing self-stabilizing functional groups. One research group discovered that electrochemical synthesis led to the formation of nanosized PPY sheets on electrodes. Although the size and morphology of these sheets can be controlled, the electrochemical polymerization process is not suitable for large-scale production. Therefore, an efficient method to synthesize nanostructured PPY without external surfactants or stabilizers is required.

One way to compensate for the shortcomings of a CP is to combine it with another polymer, thereby creating a composite with the positive qualities of both materials. PPY, known for its brittleness, has been deposited onto PET fabrics [89] and polyester [90] to enhance its flexibility. PPY-coated polyester fabrics demonstrate cytocompatibility and support cell growth after an initial period of low adhesion [91]. However, the conventional deposition method does not adhere well to PPY, resulting in the eventual release of the coating from the surface. This issue can be addressed using an alternative approach that involves covalently merging polyester fabrics with N-modified PPY, which exhibits significantly high resistance to delamination [90]. Combining poly(D,L-lactide) (PDLLA) and PPY, either deposited onto the surface of PDLLA as a film or incorporated into the PDLLA matrix as nanoparticles, yields a flexible, biocompatible, and biodegradable composite with improved conductivity compared with PPY-coated polyester fabrics. PPY/PDLLA maintains its electroactivity for up to 1000 h, and it supports the growth of fibroblasts [92][93]. Jang et al. produced PPY nanoparticles with sizes ranging from 2 to 8 nm through microemulsion polymerization, which was achieved by regulating the surfactant quantity [94]. In addition to surfactants, water-soluble polymers are often used to synthesize CP nanoparticles. The diameter of PPY nanoparticles prepared by this method is generally approximately 50–100 nm.

In addition, Li et al. developed a composite matrix of IL-PPY-Au. Three ionic liquid aqueous solutions based on imidazole with varying alkyl chain lengths ([C_nmim]Br, n = 2, 6, 12) were employed to synthesize the liquid ionic-polypyrrole (IL-PPY) material. The ionic liquid (IL) acted as a solvent during synthesis, facilitating the polymerization of pyrrole and the corresponding PPY derivative. Subsequently, Au microparticles were electrodeposited to enhance electrical conductivity and facilitate the immobilization of numerous biological molecules on the PPY electrode. The findings indicate that the introduction of ILs with longer chains not only significantly reduces the particle size of IL-PPY composites but also enhances the contact area, effectively increasing the number of folded conductive films on the electrode. This, in turn, expands the charge transfer area on the electrode and substantially improves the biosensor's conductivity. The synergy of [C12mim]Br, PPY, and Au microparticles establishes an optimized platform for enzyme immobilization, proving to be an effective approach for fabricating highly sensitive biosensors. This work not only presents an advanced biomolecular immobilization matrix for biosensor fabrication with heightened sensitivity but also highlights the potential application of ionic liquids in CP synthesis [95]. In addition, research on the manufacture of PPY nanotubes and their use as electrodes has been conducted, achieving a maximum conductivity of 30.4 S/cm for a diameter of 95 nm [96][97].

2.3. The Use of PANi in the Fabrication of the Transducer

2.3.1. Effect of PANi Polymerization on Transducer Fabrication

PANi is the second most extensively investigated CP [79][98]. Several chemical oxidative methods, such as enzymatic synthesis, polymerization under photo-stimulation, free-radical polymerization [99][100], and electrochemical methods [101], are commonly used for PANi synthesis. PANi exhibits redox activity, nonlinear optical characteristics, and high electrical conductivity coupled with proton and ionic transfer [101]. It also demonstrates stability in harsh chemical surroundings and a high thermal resistance. Depending on its degree of oxidation, PANi exists in different forms: fully oxidized pernigraniline base, half-oxidized emerald base, and fully reduced base. Among these, PANi is stable and conductive [79][98]. PANi offers

many advantages: a simple synthesis method, good environmental stability, low cost, and the capability to electrically switch between conductive and resistive states [102][103]. Unfortunately, its use in sensing applications is limited owing to its low processability, lack of flexibility, non-biodegradability, and chronic inflammation when implanted in humans [102][104]. Polymeric materials, such as polyphenanthroline, have the unique capability of facilitating direct electron transfer between the active centers of biomolecules and electrodes [105]. In certain instances, a combination of two polymers, PPy and PANi, has been employed to immobilize enzymes on the electrode surface [36]. In the literature, various considerations are frequently discussed when selecting electrochemical biosensors and immunosensors, including factors such as simplicity, high sensitivity, robustness, mass production, miniaturization, multiplexing, and portability. This review excludes the application of CPs in the absence of biological recognition molecules to construct chemical sensors, except for nonenzymatic glucose detection scenarios, regardless of whether the target analyte is a biomolecule.

2.3.2. Effect of PANi Structure and Morphology on Transducer Fabrication

PANi has gained widespread popularity as a CP owing to its straightforward synthesis and intriguing attributes such as chemical stability, flexibility, and ease of processing in solution. It is responsible for both p-doping and n-doping. The primary charge carrier in PANi can be manipulated by adjusting the pH of the dopant or by attaching organic or inorganic components to the polymer chain [16]. Furthermore, PANi can be synthesized with a wide variety of morphologies and electrical conductivities using both chemical and electrochemical techniques. The electrical conductivity of PANi is intimately linked to its oxidation state because PANi exhibits three distinct oxidation states corresponding to acid/base doping. Consequently, its electrical conductivity can be finely tailored within the range of 10^{-7} to 300 S/cm [106][107]. Its ease of preparation, high electrical conductivity, and high environmental stability make PANi suitable for use in sensor applications. For example, it can be used as a pH-switching electrically conducting biomaterial, an electrically active redox biopolymer, and a matrix for nanocomposite CP preparation. Methods have been developed for the preparation of PANi-based nanocomposite biopolymers. The electrical properties of PANi can be regulated by protonation or charge transfer doping.

Liu et al. developed a chemo-resistive sensor using PANi nanofibers adorned with Au nanoparticles for detecting volatile sulfur compounds in human breath. The Au/PANi gas sensor electrodes showed exceptional sensitivity to H_2S and CH_3SH [108]. The sensor successfully detected sulfur compounds in human breath after the consumption of raw garlic. Another study of the PANi nanofibers were horizontally ordered within the insulating gap region of an interdigitated electrode using a template-free electrochemical polymerization process [109]. The Top of Form incorporation of Au nanoparticles onto PANi nanofibers was achieved through a redox reaction involving chloroauric acid and PANi in its emeraldine form. The resulting Au/PANi gas sensor electrodes exhibited exceptional sensitivity when exposed to hydrogen sulfide (H_2S) at concentrations below 1 ppm and methyl mercaptan (CH_3SH) at concentrations less than 1.5 ppm. The sensor's capability to detect volatile sulfur compounds in human breath was demonstrated by exposing it to the exhaled breath of a healthy volunteer who had consumed raw garlic [110]. Han et al. synthesized zero-dimensional conductive nanoparticles using a chemical oxidative polymerization method. PANi particles, 20–30 nm in size, displayed remarkable conductivities of up to 24 S/cm. The synthesis involved octyl trimethylamine bromide and ferric chloride as the model compound and oxidizing agent, respectively [111][112][113].

2.4. The Use of PTh and P3HT Derivatives in the Fabrication of the Transducer

2.4.1. Effect of the Polymerization of PTh and P3HT Derivatives on Transducer Fabrication

PTh is notable for its stable and high conductivity (10^3 S/cm), which depends on the type of dopant and the polymerization process. PTh is inherently nontransparent and highly solvent-resistant [114]. Previous studies have investigated the impact of the conjugated sequence length in PTh on its conductivity. Specifically, oligomers composed of 11 thiophene units demonstrated conductivity comparable to that of higher-molecular-weight PTh. This aligns with the observation that short thiophene oligomers possess polymer-like characteristics, with the conductivity and carrier mobility increasing with the conjugation length up to the hexamer of thiophene. Transparency is a crucial attribute in applications that prioritize electrical conductivity, such as photographic films coated with antistatic materials, where a transparency level exceeding 90% is necessary [115]. The transparency of CPs has been enhanced through methods such as dilution, which can affect conductivity. Approaches used for diluting PTh include block copolymerization, grafting alkyl side chains onto the π -conjugated backbone, blending with a transparent polymer, and producing composites through the polymerization of thiophene absorbed in an insulating polymer.

Furthermore, methods such as plasma polymerization, electrochemical procedures, and the thin-layer deposition of PTh can be employed [116]. Plasma polymerization has the advantage of producing exceptionally thin defect-free layers that firmly adhere to various substrates without the need for solvents. Given that thiophene is an electron-rich aromatic ring

that can be oxidized, highly conductive PTh can be obtained through p-doping. The electrochemical oxidation process promotes the formation of robust, adherent polymeric films, and the thickness of the polymer films can be varied by varying the polymerization duration in the electropolymerization process ^[117]. PTh has the advantage of being optically controllable, apart from exhibiting typical CP characteristics. In addition, the monomer can be easily functionalized, which facilitates the adjustment of optical properties along with conducting properties. PTh derivatives exhibit good processability in solution, which promotes uniformity in the fabrication process of PTh thin-film transducers ^[118]. In particular, because of the processability and solubility of PTh derivatives, their design, molecular weight, and π overlap between chains can be easily fine-tuned. The structure and degree of improvement in conductivity and processability in a solution depend significantly on the synthetic design and reaction pathways. The popularity of PTh serves as a leading example used to understand the importance of material synthesis ^[119]. A significant breakthrough has been achieved in the modulation of the formation of beta-substituted thiophene monomers and their sequential polymerization, resulting in solution-processable PTh derivatives ^[120]. Interesting results have been obtained in terms of improved conductivity after p-doping, and these results serve as the basis for exploring diverse potential applications for PTh-based materials.

The enhanced performance of PTh derivatives was achieved through the in situ polymerization of conjugated poly[(thiophene-2,5-diyl)-co-(benzylidene)]. This approach generates additional valence bonds on graphite and graphene oxide sheets, offering insight into the collective impact of the structure and doping on cyclic stability ^[120]. The intriguing and unconventional behavior of the less ordered, quasi-amorphous, conjugated polymers indicates their potential for attaining superior charge transport properties through electrochemical polymerization. In addition, a notable study focused on creating a polythiophene lactosylate biointerface and its interaction with Erythrina Cristagalli lectin, explored through differential pulse voltammetry. The polymerization of the 3-(3-azidopropoxy) thiophene monomer in the ionic liquid [Bmim][BF₄] allows the postpolymerization structure to facilitate lactose or ferrocene grafting through a Cu(I)-catalyzed click reaction. This newly glycosylated CP biointerface serves as a foundation for developing a label-free, real-time electrochemical biosensor to investigate protein–carbohydrate interactions, enabling rapid protein analysis ^[121].

2.4.2. Effect of the Morphology and Structure of the Polymerization of PTh and P3HT Derivatives on Transducer Fabrication

The molecular structure and fine-tuning of the crystallinity in PTh are crucial for achieving high charge mobility in the transducer. High electrical conductivity in PTh can be realized by forming conductive PTh layers on a dielectric substrate ^[122]. PTh can function as a layer that is suitable for metal electroplating, which has been difficult to achieve with insulating substrates ^[120]. In particular, P3HT can undergo recrystallization in the presence of common non-crystalline polymers such as PS and PMMA to form nanofibrous composite films. Shimomura et al. produced transparent conductive P3HT nanofibers using polymer composites with PMMA and AuCl₃ oxidation solution ^[123]. Furthermore, flexible conductive membranes with high electrical conductivity have been realized by appropriately adjusting the optimal ratio of acetonitrile and a boronic agent ^[124]. Notably, PTh serves as an activating layer that facilitates the formation of smooth, conductive nickel nanoparticles on an insulating matrix ^[125]. The stability of PTh-functionalized multiwalled carbon nanotube (MWCNTs) binary composites has been achieved using sodium bis(2-ethylhexyl) sulfosuccinate micelles prepared via oxidative polymerization ^[126]. The combination of binary mixtures and the incorporation of entangled silver nanoparticles has paved the way for the development of ternary nanocomposites. These ternary composites exhibit superior performance, with an enhanced electrical conductivity of 80.76 S/cm. This improvement can be attributed to the efficient charge transport facilitated by the PTh interlayer, which effectively serves as a conductive bridge between MWCNTs and silver nanoparticles ^[120]. Enhanced conductivity plays a pivotal role in promoting accurate sensing, because analytes respond to variations in conductivity or resistance ^[127].

In addition to improvements in conductivity, sensitivity, and processability, mechanical flexibility is an equally vital consideration for the application of PTh in transducers. Achieving desirable mechanical properties has proven to be a significant challenge for PTh derivatives, such as P3HT ^[128], an alkylated derivative of PTh, and widely investigated tetrafluoro-7,7,8,8-tetracyanoquinodimethane p-conjugated electrically of CP. P3HT exhibits commendable solubility in a variety of organic solvents, contributing to its superior film-processing properties. Furthermore, it is commercially available ^[129]. Because P3HT has been successfully used in all-organic solar cells and all-organic field effect transistors, research groups have investigated its potential as a thermoelectric material. Crispin et al. evaluated the thermoelectric properties of P3HT films doped with nitronium hexafluorophosphate ^[130]. Maximum performance was observed in a sample with a 31% doping level. It was also demonstrated that bulky PF₆ anions inhibit the formation of crystallites at low doping levels, but with an increasing doping level, the structural order increases in line with the electrical conductivity. This challenge has impeded progress in organic electronics and their industrial implementation. Typically, semiconductive-based polymers exhibit limited stretchability because of their high crystallinity resulting from their rigid molecular structure and strong π - π interactions. This has led to a growing demand for CPs with improved intrinsic stretchability ^[131].

Both PTh and P3HT, while flexible and bendable to a certain extent, lack adequate robustness to repeated bending processes. This mechanical instability can introduce fluctuations in the electrical properties of P3HT-based flexible devices [59]. To address this issue, researchers have developed high-molecular-weight carbon chains with disiloxane moieties in the side chains to enhance the tensile strength. Moreover, investigations into the molecular structure and physical properties of substituted thiophene have confirmed the outstanding mechanical flexibility of certain derivatives. The impact of side chains on chain mobility and the glass transition temperature (T_g), a measure of flexibility, in prepared substituted polymers has also been investigated [132]. Specifically, bulkier side-chain substituents tend to increase stiffness, resulting in a higher T_g because bond rotations are constrained. This restriction on bond rotation can be achieved by using branched side chains, such as the P3HT isomer poly(3-2-methylpentylthiophene), which features a methyl-branched side chain instead of the typical linear chain polymers. The inclusion of a methyl group in the side chain limits the rotation of adjacent C-C bonds, rendering the side chain stiffer than the linear chain in P3HT. Branched side chains restrict chain movement and reduce crystallization-induced phase separation, which is a crucial factor determining the stability of the transducer layer in sensors [133]. As shown in **Figure 5**, Shin et al. presented a straightforward approach for enhancing the NO₂ sensing capability of an organic field-effect transistor (OFET) sensor operating at room temperature. The approach involved incorporating a nano P3HT film with reduced graphene oxide (rGO) through phase-supported cutting and a coating separation technique. The synergy between the nanoporous P3HT, which serves as a pathway for analyte diffusion, and the rGO, which acts as an adsorption site, leads to significant changes in the electrical properties of the nanoporous P3HT/rGO OFET when it comes in contact with NO₂ gas molecules. This underscores the potential of OFETs as effective NO₂ sensors. More specifically, novel nanoporous OFET sensors featuring rGO-integrated nanoporous P3HT membranes exhibit a significantly improved response, with rGO amounts of approximately 61.3%, when exposed to 10 ppm NO₂ gas. In contrast, sensors based on nonporous P3HT/PS/rGO composite membranes showed a response of approximately 17.7%. Moreover, the novel nanoporous OFET sensors exhibited exceptional response and recovery characteristics, with a response time of approximately 62 s and a recovery time of approximately 145 s. They also showed high sensitivity at approximately 1.48 ppm⁻¹ and excellent selectivity [134].

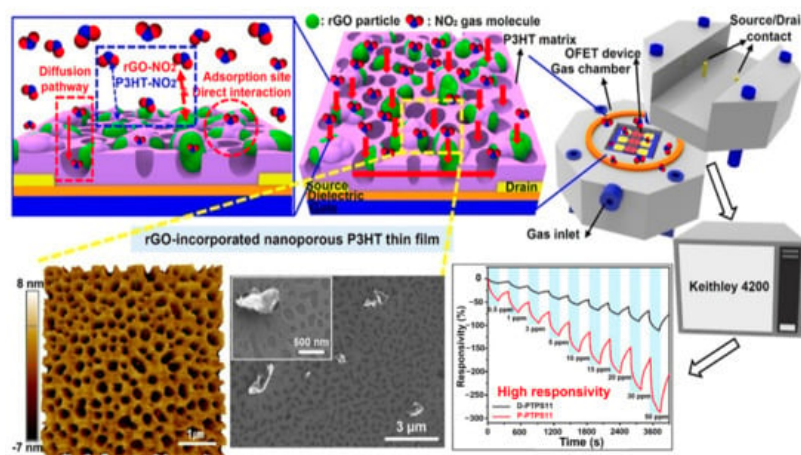


Figure 5. Schematic of the NO₂ sensing performance of an OFET based on CPs; composite of rGO-incorporated nanoporous films. (Reprint from Ref. [134] (copyright (2023) ACS Publisher).

Another approach to enhance the mechanical properties of PTh and P3HT involves substituting side chains with esters, which provides greater freedom of movement. This substitution with ester side chains leads to extended two-way conjugation, thereby improving mobility and stretchability by strengthening the amorphous structure with reinforcing agents [135]. Notably, the orientation of the crystals during the drawing process plays a crucial role in determining the conductivity. PTh disiloxane-substituted derivatives exhibit a specific stable crystallographic orientation, even when strain degree approximately 140% [136]. Control over the crystallization modes of conjugated block copolymers based on poly(3-dodecylthiophene) (P3DDT) and poly(2-vinylpyridine) can be achieved by controlling through the regioselectivity of P3DDT, as well as the melting temperature and crystallization rate using P3DDT. Such control involves poly(2-vinylpyridine) at low recovery rates and crystallization at temperatures near or below T_g [137]. Crystal growth is limited by the cylindrical block copolymer structure or the glass layer [137]. In a study focused on the formation of a stretchable active channel matrix, a mixed solution of PS-block-poly(ethylene-co-butylene)-block-polystyrene and P3HT was obtained through rotational molding. This process facilitates the in situ phase separation of P3HT nanofibers on the surface of the rubber matrix, the assembly of nanofibers into wide bundles, the formation of networks of these bundles, and the indentation of the bundles on the active rubber surface [138].

In various studies, researchers have explored different approaches to enhance the performance of conducting polymer-based devices. Chen et al. adopted a block copolymer strategy to create resilient memory devices, demonstrating

consistent performance under diverse conditions [139]. In this context, Higashihara et al. utilized Kumada–Tama catalytic transfer polycondensation and living polymerization to synthesize a triblock copolymer, achieving morphologically adjustable and elastic polymer matrices [140]. Similarly, Watts et al. produced click-processed rod-coil diblock copolymers by combining alkynyl-functionalized P3HT with azido-terminated PBA homopolymers. Furthermore, they examined the effect of bulk ratios on mechanical and morphological characteristics, especially for CP application in stretchable field-effect transistor (FET) devices [141]. In a study comparing the electronic properties and surface morphologies of P3HT and 2,3,5,6-tetrafluoro-7,7,8,8-tetracyanoquinodimethane (F4TCNQ) films doped directly in solution or through sequential doping processes [142], Joeng et al. observed that the sequential doping technique significantly increases the electrical conductivity at the equivalent doping ratio [12]. Additionally, Jacobs et al. conducted a comparative study on the electronic properties and surface morphologies of P3HT films doped with F4TCNQ, highlighting the significant enhancement in electrical conductivity achieved through sequential doping. The optimized morphology, achieved by stacking alternating layers of the polymer and dopant, resulted in thicker films with properties closely resembling their thin-film counterparts, showcasing the potential for fine-tuning these processes to improve device performance [143].

In a study by Hynynen et al., as shown in **Figure 6**, the sequential doping approach was employed by exposing a P3HT film to F4TCNQ vapor. They demonstrated that the crystalline structure of the film could be modulated by varying the doping level [144]. Their work also revealed that the molecular weight of P3HT had a relatively modest effect on the film conductivity, and they reported an electrical conductivity of 12.7 S/cm [145]. A recent approach for doping P3HT films involves the use of organic molecular dopants such as electron acceptors. These dopants induce ground-state charge carrier transfer in the semiconductor polymer host, creating polarons and bipolaron after that [146]. However, dopant anions remain in the film and often result in drastically reduced solubility. Therefore, aggregation is a major issue in polymer dopant liquid mixtures. To avoid such phenomena, P3HT solutions should be diluted and maintained at a high temperature to prevent aggregation. Using conventional solution processing, a P3HT film achieved an electrical conductivity of 4×10^{-4} S/cm [147]. A problem with bulk doping methods is that large dopant amounts, such as rGO, adversely affect the morphology of the P3HT film and lead to aggregation, which inhibits the achievement of higher conductivity levels [148]. **Figure 7** shows the performance of Hynynen's OFET sensor.

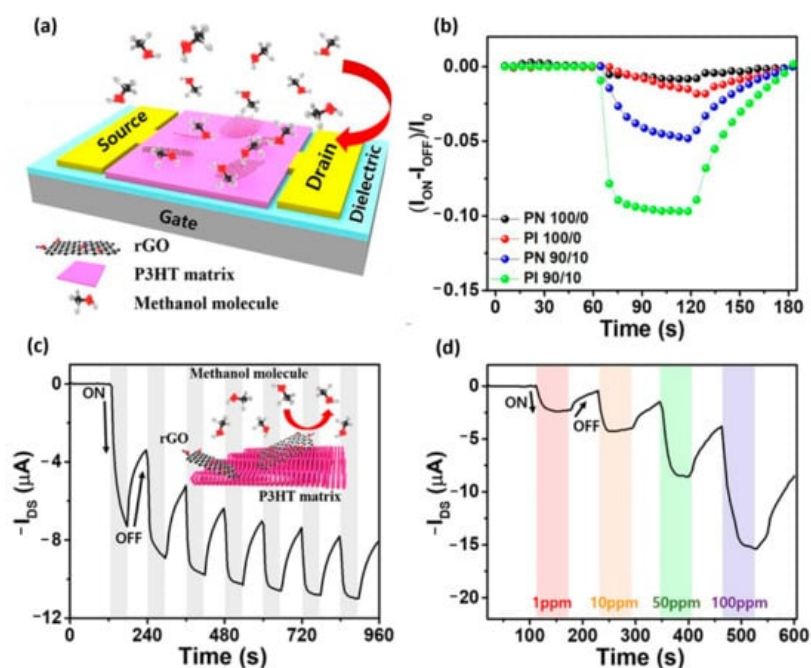


Figure 6. Design of OFET sensor based on CPs. (a) the photo-irradiated P3HT and rGO composite films were used in the OFET configuration. (b) Comparison of responses of OFET sensors based on pristine P3HT, pristine P3HT/rGO (90/10), photo-irradiated bare P3HT, and photo-irradiated P3HT/rGO (90/10) to 10 ppm methanol vapor. (c) Photo-irradiated P3HT/rGO showed consistent methanol vapor sensing (90/10). (d) The composite depicts the interactions between methanol vapor and rGO molecules, and it shows how a photo-irradiated P3HT/rGO (90/10) sensor responds to different methanol vapor concentrations. Testing of the OFET sensor was performed in a continuous environment [149]. (Reprint from Ref. [149] (copyright (2021) Elsevier Publisher).

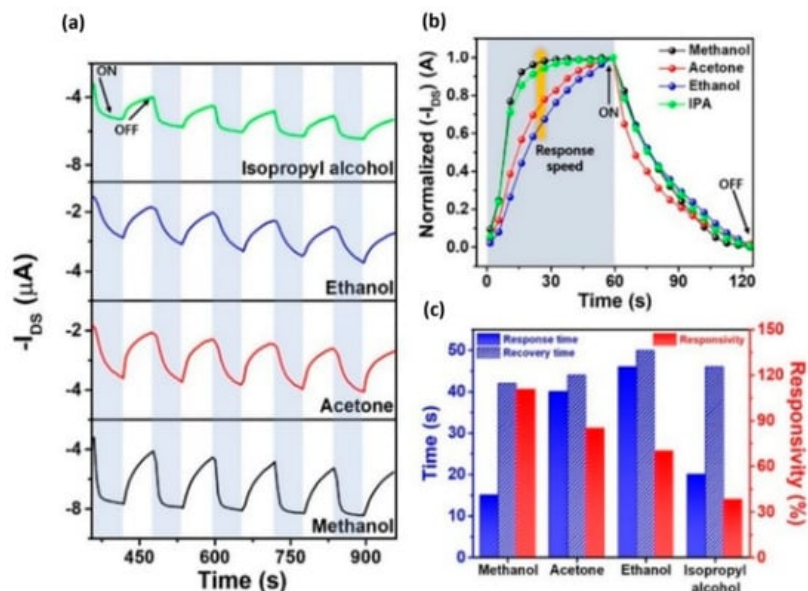


Figure 7. OFET sensor's ability to identify VOC vapors based on CPs. After exposure to 10 ppm of polar VOC vapors, namely methanol, acetone, ethanol, and isopropyl alcohol, photo-irradiated P3HT/rGO (90/10)-based OFET sensors showed the responses and normalized drain currents displayed in (a,b). (c) Corresponding responsivity (right axis) and response/recovery time (left axis) for 60-s on/off pulses. $V_{GS} = -10$ V and $V_{DS} = -40$ V were the constant voltages used for the OFET sensor test [149]. (Reprint from Ref. [149] (copyright (2021) with permission from Elsevier Publisher).

2.5. The Use of PEDOT in the Fabrication of the Transducer

In contrast to many other CPs, PEDOT offers superior conductivity, higher transparency, and exceptional environmental stability. Nevertheless, this material has drawbacks: it is insoluble in both water and organic solvents. This makes it challenging to use in molding or spin coating techniques. To address the solubility and processability issues, Bayer developed a graft copolymer of PEDOT with PSS polymerized in an aqueous colloidal suspension. This innovation has provided an effective solution to the processing difficulties associated with PEDOT, making PEDOT:PSS suitable for use in sensor fabrication [58][150].

2.5.1. Effect of PEDOT Polymerization on Transducer Fabrication

PEDOT is one of the most extensively researched CPs, primarily because of its exceptional stability and high electrical conductivity. The initial enhancement of this polymer focused on achieving a soluble CP without the presence of α,β - and β,β -coupling in its backbone. PEDOT can be synthesized using standard oxidative or electrochemical polymerization techniques [128][151]. It exhibits transparency within the matrix and exceptional stability in its oxidized state. The behavior of PEDOT, which encompasses aspects such as solubility and stability, has been investigated by incorporating a water-soluble polyelectrolyte. PSS served as a dopant and facilitated charge-balancing in the polymerization process to form PEDOT:PSS. The synergy between PEDOT and the PSS electrolyte resulted in several notable properties, such as water solubility, a high conductivity of approximately 10 S/cm, excellent architectural light transmittance, and remarkable stability [152]. High-density PEDOT:PSS can withstand prolonged exposure to a 100 °C air temperature for over 1000 h, with minimal changes in its electrical properties. It is noteworthy that the reported conditioning of PEDOT nanoparticles mainly involved the relative solubility regime of the 3,4-ethylenedioxythiophene (EDOT) monomer in aqueous solutions. PEDOT thin films can attain impressive conductivity levels, with values reaching up to 6259 S/cm, whereas single-crystal nanowires can surpass this level, reaching 8797 S/cm. PEDOT synthesis typically involves three primary polymerization methods: oxidative chemical polymerization involving EDOT-based monomers in the presence of various oxidants, electrochemical polymerization conducted in a three-electrode setup using EDOT-based monomers, and transition-metal-mediated coupling techniques. PEDOT itself is insoluble, and the addition of other polymers is often necessary to enhance its solubility and overall processability. PDMS is the most commonly used material for this purpose, and it enhances PEDOT's stability in aqueous environments. Because of their remarkable biocompatibility, PEDOT and its derivatives, such as PEDOT:PSS, have found widespread applications in diverse biomedical fields, including bone, heart, and nervous tissue engineering, as well as drug delivery systems [153][154].

In biosensors, PEDOT:PSS, in combination with graphene oxide (GO), is used as a conductive substrate for the immobilization of glucose oxidase to perform enzyme-based glucose detection. More recently, PEDOT:PSS and GO have been used in gold microelectrodes, leading to improved electrochemical, biochemical, and mechanical properties of the microelectrodes and making them suitable for neural implant applications. PEDOT has been electrochemically deposited

onto biodegradable magnesium microwires, and the microwires have been used for recording nerve signals. These PEDOT-coated Mg microwires were further spray-coated with poly(glycerol sebacate) for use as an insulating layer. The resulting microelectrode exhibited performance comparable to that of equivalent platinum (Pt) microelectrodes commonly used in clinical settings. The PEDOT-coated microelectrode exhibited superior electrical properties compared with the Pt electrode, with a charge storage capacity five times that of Pt and lower impedance within the frequency range of 1 MHz to 0.1 Hz. Furthermore, the Mg-based electrode demonstrated similar neural recordings in vivo ^[155].

2.5.2. Effect of PEDOT Morphology and Structure on Transducer Fabrication

Fully organic implants have been developed using PEDOT, with ongoing research focused on improving their biocompatibility and biodegradability. For instance, the Ferlauto group fabricated an all-organic transient neural probe consisting of a polycaprolactone substrate and a packaging material, with PEDOT:PSS-ethylene glycol as the electrode material ^[156]. These electrodes were implanted in the visual cortex of mice, and neural activity was measured during rest, induced seizures, and visual stimulation. The study demonstrated the electrodes' long-term effectiveness, and they remained functional months after implantation. While PEDOT:PSS is not inherently biodegradable, the authors hypothesized that electrode degradation is related to hydrolysis, which is ascribed to the electrode's adsorption of hydrogen peroxide in the environment ^{[157][158]}. They also suggested that the transient probe resulted in a less pronounced glial scar compared with no transient polyimide probes, facilitating microglia access for the phagocytosis of delaminated PEDOT:PSS. Furthermore, the results indicated the complete degradation of the electrode after 1 year at 37 °C and pH 12, with an acceleration factor of approximately 2.5 compared with pH 7.4 ^[159]. This gradual degradation was also evident when electrode implantation resulted in only a small glial scar after nine months. In another study, Pradhan et al. developed a fully organic, biocompatible, and bioabsorbable temperature sensor using silk and PEDOT:PSS. Silk, a natural protein obtained primarily from silkworms, was utilized as the sensor's substrate and housing material. The conductive layer was composed of PEDOT:PSS dispersed in photoreactive sericin, a biodegradable variant of silk. This dispersion in biodegradable sericin provided the controllable degradation of PEDOT:PSS, allowing the entire sensor to completely degrade within 10 days in a protease solution. This technique was also employed to fabricate PEDOT:PSS-based silk sensors for glucose, dopamine, and ascorbic acid detection ^[151]. Lupu et al. demonstrated sinusoidal voltages for the enhanced incorporation of enzymes into polymers during electrolysis, developing a tyrosinase-based dopamine biosensor attached to a PEDOT membrane ^[160].

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