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REVIEW

New directions in medical biosensors employing poly(3,4-ethylenedioxy thiophene) derivative-based electrodes

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Abstract Demand is growing in the field of medical diagnostics for simple, disposable devices that also demonstrate fast response times, are easy to handle, are cost-efficient, and are suitable for mass production. Polymer-based microfluidic devices meet the requirements of cost efficiency and mass production and they are suitable for biosensor applications. Conducting polymer-based electrochemical sensors have shown numerous advantages in a number of areas related to human health, such as the diagnosis of infectious diseases, genetic mutations, drug discovery, forensics and food technology, due to their simplicity and high sensitivity. One of the most promising group of conductive polymers is poly(3,4-ethylenedioxythiophene) (PEDOT) and its derivatives due to their attractive properties: high stability, high conductivity (up to 400–600 S/cm) and high transparency. This review paper summarizes newly developed methods associated with the application of PEDOT to diagnostic sensing.

Keywords Biosensor · Conductive polymer · PEDOT · Electrochemistry · Microfabrication

Abbreviations

PEDOT, PEDT	Poly(3,4-ethylenedioxythiophene)
EDOT	3,4-Ethylenedioxythiophene
PSS	Poly(styrene-sulfonate)
PDMS	Poly(dimethlysiloxane)
ITO	Indium tin oxide
CP	Conductive polymer
MIP	Molecularly imprinted polymers

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Introduction

In recent years, the demand has grown in the field of medical diagnostics for simple, disposable devices that also demonstrate fast response times, are easy to handle, are cost-efficient, and are suitable for mass production. Such devices are especially valuable in developing countries. Microfluidics and related biosensor technologies offer the potential to fulfil these criteria through an interdisciplinary combination of approaches from nanotechnology, polymer chemistry and medical science: by manipulating small amounts of fluids, routine laboratory tests can now be miniaturized and automated via handheld microchips.

A biosensor can be generally defined as a device that consists of a biological recognition system and a transducer. The interaction of the analyte with the bioreceptor is designed to produce an effect measured by the transducer, which converts the information into a measurable signal. Electrochemical sensing is one of the simplest detection methods in microfluidics. This technique directly converts the recognition event into an electrical signal so that it can be easily computerized [1, 2]. Polymer-based devices are suitable for microprocessing and for meeting the requirements of cost efficiency and mass production, but the link between the polymeric base and the signal processing unit is usually a metal microelectrode array, which increases the cost of production and the environmental impact of these type of sensors. This review will concentrate on recent advances in biosensors, where the metal microelectrodes are replaced or modified with conductive polymers.

Electrochemical detection

Due to rapid development in this field, the use of electrochemical biosensors is becoming more widespread, as these sensors are able to provide information on the different products of recognition events based on the kinetics and time dependency of the electrochemical reactions [3–5]. The electrochemical assay is simple, reliable, has a low detection limit and a wide dynamic range due to the fact that the electrochemical reactions occur at the electrode–solution interfaces. Microelectrodes are powerful and versatile tools in the study of electrochemical processes of mechanistic and/or analytical interest. They experience high mass transport rates but little interference from interfacial capacitance or solution resistance effects. These advantageous properties are due to the small size of these devices. Microelectrodes can be used in highly resistive environments; they can work in very small sample volumes and enable the detection of very small amounts of material. The improved mass transport properties facilitate the measurement of higher exchange current densities and electron transfer rate constants and also allow the study of fast coupled chemical reactions. Unfortunately, microelectrodes record currents in the nanoampere range, which requires very sensitive equipment and the correct electrical insulation of the experimental setup. Electrochemical systems are extremely sensitive to the processes that take place on the surfaces of the electrodes, and in this sense they are promising candidates for use as direct transducers in biomedical applications. Several types of electrochemical methods are used; the most common are cyclic voltammetry (CV), amperometry and impedance spectroscopy (EIS). In cyclic voltammetry, the electrode potential ramps linearly with time and the current is measured. The absolute value of the current increases as the potential reaches the redox potential of the analyte. The oxidation–reduction process is characteristic of the system and can be used to qualify and quantify the electrochemical components. In amperometry, the potential of the working electrode is kept constant and the change in the current is measured during the biological event. Electrochemical impedance spectroscopy (EIS) combines analyses of both the resistive and capacitive properties of materials, based on the perturbation of the system by a small-amplitude sinusoidal (AC) signal. The impedance of the system can be scanned over a wide range of AC signal frequencies, and the equivalent circuit models fitted to the impedance curves are useful tools for characterizing the system.

Conductive polymers in biomedical applications

Conductive polymers are excellent candidates for replacing/modifying electrodes in polymer-based systems because they behave in an electrically similar manner to metals and inorganic semiconductors, and they also possess attractive properties such as ease of synthesis and flexibility of processing. Recently, a comprehensive review was published on the applications of conductive polymers in biomedical engineering [6], but significant developments have occurred in the last few years in this area, especially in the use of poly(3,4-ethylenedioxythiophene) (PEDOT). Several new methods have been used to enhance the sensitivity, applicability and/or specificity of these sensors based on PEDOT, for example the incorporation of nanoparticles into the polymer matrix, ink jet printing/patterning of the conducting polymers, molecular imprinting for specific detection, the creation of organic transistors from conducting polymers to improve sensor sensitivity, or the embedding of cells into the conducting polymer matrix for direct stimulation. This review will discuss these new directions of special interest in the field of medical sensing.

Properties of polythiophene derivatives

Conducting polymers (CP) that have inherent ion/electron transfer properties can provide a bridge between the biological event to be examined and the metal electrode for the measuring electronics. Doping is the process of oxidizing (p-doping) or reducing (n-doping) a neutral polymer and providing a counter anion or cation (dopant). Upon doping, a CP system with a net charge of zero is produced due to the close association of the counterions with the charged CP backbone. Dopants can catalyze the polymerization of monomers during synthesis and change the physical properties and biological affinity of the conducting polymer [7]. In most cases, large or highly charged dopants are strongly bound to the polymer matrix and do not diffuse away with long periods of incubation in solution. The binding properties of the dopant are crucial to polymer sensor electrodes because they provide the affinity to the biological species to be monitored.

Poly(3,4-ethylenedioxythiophene) (PEDOT or PEDT, Fig. 1) is a polythiophene that has received much attention over the last few years. It was developed by the Bayer AG research laboratory in Germany in the late 1980s, and became one of the most exciting polymers for practical applications [8] due to its advantageous properties: it has a low oxidation potential, and in the oxidized state it exhibits high stability and high conductivity (up to 400–600 S/cm). In the oxidized state, thin PEDOT film is light blue and turns transparent during reduction. In general, the color changes of an electrochromic polymer originate from electrochemical doping–dedoping redox processes, which involve ion transport in and out of the polymer matrix in order to balance the electronic charge. PEDOT can be

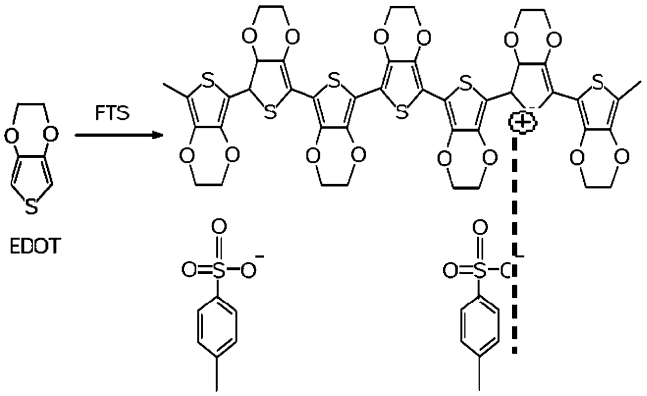

Fig. 1 The chemical structure of PEDOT

produced from 3,4-ethylenedioxythiophene (EDOT) by both chemical oxidative or electrochemical polymerization processes [36].

The most frequently used dopant for PEDOT is poly (styrene sulfonate) (PSS), which has a high molecular weight, and is to some extent physically trapped by and stably integrated into the CP. However, small dopants like tosylate (*p*-toluene sulfonate) can diffuse more easily out of the CP and can be exchanged with other ions in the surrounding environment [13]. Thus, the properties of the CP can be regulated via the dynamic doping and dedoping process that occurs during oxidation and reduction of the CP [11, 29].

Due to its property profile, PEDOT is used for different purposes: antistatic and electrostatic equipment, solid-state capacitor electrodes, substrate for metal deposition in printed circuit boards, carrier-conducting material in organic light-emitting diodes (OLED), and electrodes for inorganic electroluminescent lamps [8, 9]. Very recently, the thermistor behavior and piezoresistive behavior of PEDOT/PSS have been reported in relation to its possible application to biosensors [58, 59]

Compared with other conducting polymers, little research has been done on the development of biosensors based on poly(3,4-ethylenedioxythiophene) (PEDOT) derivatives [7–9], although this material is a promising biosensor systems. It combines high stability in its oxidized state with high conductivity and compatibility with aqueous electrolytes [7, 8, 10]. Moreover, PEDOT shows excellent stability against biological reducing agents due to its more ordered molecular structure [12, 19, 22]. The superior electrochemical stability of PEDOT can be attributed to the dioxyethylene bridging group, which blocks coupling along the backbone. Numerous dopant types have been introduced, ranging from small salt ions to polymers or biospecific dopants, such as peptides, proteins and neurotrophins [14–16, 26].

Detailed structural studies of thin films of tosylate-doped PEDOT were performed by Aasmundtveit et al. with in situ grazing-incidence diffraction [12]. A pseudo-orthorhombic unit cell containing four monomers and one tosylate ion per cell was found. A paracrystalline state was observed, which could explain the high conductivity of PEDOT. The observed anisotropy of the thin film agrees well with the observed optical anisotropy of the material [15]. The PEDOT can shrink by up to 5% of its original thickness during washing steps. This shrinking effect can be used to trap enzymes, nanoparticles or nanofibers in a CP matrix by adding them to the washing solvent [16, 17, 24]. The composite film points to a promising future for the development of stable biosensors [17, 25].

Application of PEDOT in biosensors

Neural processes

Neural microelectrodes that aid the study of neural functions or the treatment of neural diseases have been extensively investigated in order to achieve better application performance, particularly in relation to the stimulation and recording of signals from neural cells. Due to their stability in biological environments and their affinity to neurons, the electrode surface has become a critical factor. Conductive polymer coatings have been intensively used to modify the recording surfaces of traditional electrodes with the intent of improving long-term performance [21]. PEDOT has recently also been introduced into this field. It was found to be stable under constant polarization conditions and is able to retain its conductivity even after storage at high temperature [18–20]. PEDOT films have been presented as being superior at maintaining electrochemical activity, with only a 30% loss in charge-carrying capacity following 400 redox cycles, and an 11% reduction in conductivity following 16 h of in vivo polarization [29]. Xiao et al. [18] have developed an adenosine 5′-triphosphate (ATP)-doped PEDOT for neural recordings. ATP has long been known to be an activator of sensory nerves [27, 28]. Green et al. discussed the challenges of neural interfaces, and emphasized that PEDOT derivatives have been found to be some of the best materials in terms of stability, resistivity to biochemical agents, conductivity, and reduced toxicity [23]. They drastically decrease the recording site impedance in neural electrodes, which reduces thermal noise and signal loss through shunt pathways. PEDOT also reduces the amount of low-frequency drift in local field potential recordings, and PEDOT-coated electrodes are suitable for recording neural activity in vivo for extended periods [30].

Very recently, synthetically produced, anionically modified laminin peptides were used to dope PEDOT electrodeposited onto platinum (Pt) electrodes [60]. It was demonstrated that large peptide dopants produced softer

PEDOT films with a minimal decrease in electrochemical stability compared to the conventional dopants. Cell studies revealed that the modified PEDOT retained neurite outgrowth bioactivity but that the effect was strongly dependent on the initial cell attachment.

Selective detection of dopamine

Several investigations have been performed in which PEDOT electrodes have been used to measure the concentration of specific components in human blood or in other biological fluids by electrochemical methods. The most important advance is the use of PEDOT-based electrodes to enable the selective detection of these components.

One of the most interesting examples is the detection of dopamine in the presence of ascorbic acid and other disturbing factors [37, 44]. Dopamine is a catecholamine that plays a vital role in the function of the central nervous, renal, hormonal and cardiovascular systems. The development of methods for the quantification of dopamine in blood and biological fluids is currently the focus for intense investigations. Since dopamine is easily oxidizable, an electrochemical method is an ideal choice to quantitatively determine it; however, the electrochemical oxidation of dopamine at conventional electrodes is found to be difficult because (a) the electrode surface is fouled due to the adsorption of oxidation products, (b) interference arises due to the coexistence of ascorbic acid in biological fluids, which also undergoes oxidation at more or less the same potential, and (c) the concentration of ascorbic acid is much higher (1000×) than that of dopamine in these samples, which results in poor selectivity and sensitivity for dopamine detection. Hence, the development of a dopamine sensor using voltammetric protocols for the detection of dopamine in the presence of excess ascorbic acid is a challenging task. Recently, Kumar et al. [31] demonstrated that, unlike on the bare glassy carbon electrode, there is significant peak separation in voltammetric signals of dopamine on PEDOT-coated glassy carbon electrodes in the presence of ascorbic acid in the solution. The results showed a 0.2 V separation between the peaks from dopamine and ascorbic acid. This peak separation can be explained by a combination of effects, such as the electrostatic interactions responsible for the negative shift in the peak potential of the oxidation of ascorbic acid, by the weak hydrophobic interactions of dopamine with the "reduced" regions of the polymer matrix, and/or by electron transfer mediation of the PEDOT (redox process) [31]. It was shown that the PEDOT-modified glassy carbon electrode could detect dopamine at a concentration of 1 μM even in the presence of ascorbic acid at concentrations as high as 1 mM (a 1:1000 ratio), which reflects the difference in their concentrations under physiological conditions. The modified electrodes also showed excellent antifouling properties. Furthermore, an analytical protocol involving square-wave voltammetry was developed using a PEDOT-coated microchip electrode for the determination of uric acid in the concentration range of 1–20 μM in the presence of excess ascorbic acid [32]. An improvement in sensitivity for dopamine was achieved by doping the PEDOT electrodes with gold nanoparticles [33, 34]. The nanocomposite of gold nanoparticles and PEDOT was synthesized through a sequence of chemical and electrochemical routes. The PEDOT matrix was recognized as being responsible for the peak separation (selectivity) and for the catalytic oxidation of the dopamine and uric acid. The inclusion of the nanometer-sized gold particles allowed the sensitivity of the biosensor to be improved to nanomolar concentrations. These new generations of nanocomposites are expected to enhance the value of electroanalytical techniques, as it is possible to tune their properties to suit particular analytical needs.

Enzyme electrodes

Enzyme electrodes where the electrode surface is covered by a thin layer (10–200 nm) of immobilized enzyme are well known and also available commercially. The function of the enzyme provides selectivity through its biological affinity for a particular substrate molecule. The kinetics of the enzyme reaction are monitored via the rate of formation of product or the disappearance of a reactant. If either the product or reactant is electroactive, reaction status can be monitored directly using amperometry. Therefore, such electrochemical reactions can be utilized for the construction of amperometric biosensors. Sarmaa et al. have published a detailed review on this type of enzyme electrode [35]. Conductive polymer electrodes have frequently been used as the substrate material for the enzymes because they bind proteins with high affinity by physical adhesion. Enzymes can also be immobilized in conductive polymer by an electrochemical method, which has several advantages over conventional methods [38]. First, the amount and spatial distribution of enzyme in the polymer matrix can easily be controlled by manipulating preparation parameters such as the monomer and enzyme concentrations in the electrodeposition solution. Second, it is also feasible to immobilize the enzyme on the surface of the electrode with a one-step process regardless of the type and geometry of substrate to be deposited.

Glucose sensing

According to the World Health Organization, around 200 million people (~3% of the population) suffer from diabetes worldwide, and its incidence is increasing rapidly. Diabetes

is a syndrome of disordered metabolism resulting in abnormally high blood sugar levels. Optimal management of diabetes involves patients measuring and recording their own blood glucose levels. Enzyme electrodes have long been used for glucose sensing. The devices are essentially electrodes (usually Pt) that are coated with a gel containing glucose oxidase. They usually measure the amount of hydrogen peroxide produced by the reaction between glucose and glucose oxidase. The O_2/H_2O_2 couple can also been replaced with a redox mediator, such as conjugated polymers with immobilized enzyme, in glucose sensing based on amperometry. Park et al. [39] reported a glucose oxidase-containing hollow microtubule electrode produced from PEDOT:PSS on ITO glass by microfabrication. It was shown that it was possible to produce conducting polymer microtubules containing glucose oxidase by capping their openings with a conductive composite and electrochemical polymerization. Nanostructured PEDOT with a dispersion of metal nanoparticles was constructed by Santhosh et al. for glucose monitoring [40]. The electrochemical deposition of palladium nanoparticles and glucose oxidase immobilization in nanofibrous PEDOT was performed by cyclic voltammetry sequentially in order to fabricate the modified electrode. The reliability and practicality of this type of sensor were tested by estimating the glucose concentration in human serum samples using a PEDOT–Pd/glucose oxidase-modified electrode and then comparing this value with a commercial glucose meter. The two results obtained agreed to within 3.24%. The glucose biosensor exhibited high sensitivity (detection limit of 75 μM of glucose) and good linearity in current response for a wide range of concentrations (0.5–30 mM). Excellent sensitivity was achieved by Chiu et al. using a Prussian blue dopant for PEDOT [42]. Prussian Blue or its derivatives are used to improve electron transfer from the biochemical reaction to the CP and therefore improve sensor sensitivity and selectivity. Macaya et al. [41] developed a new approach for glucose sensing. A conducting polymer transistor was built from patterned poly(3,4-ethylenedioxythiophene):poly(styrene sulfonate) film (used as source/drain electrodes) and Pt (used as the gate electrode; Fig. 2A). A PDMS (poly(dimethlysiloxane)) well was used to confine the analyte/enzyme solution in the PEDOT/PSS channel. The sensitivity of this sensor was in the range of glucose concentrations in human saliva. A similar organic thin-film transistor-based glucose sensor was constructed by Liu et al. (Fig. 2B), but in this case the glucose oxidase enzyme was entrapped in polymer matrix during the electrochemical polymerization [43]. Under optimized testing conditions, this sensor showed a rapid response time and high sensitivity. A linear relationship has been observed between the drain current and glucose concentration in the range from 1.1 to 16.5 mM. This range

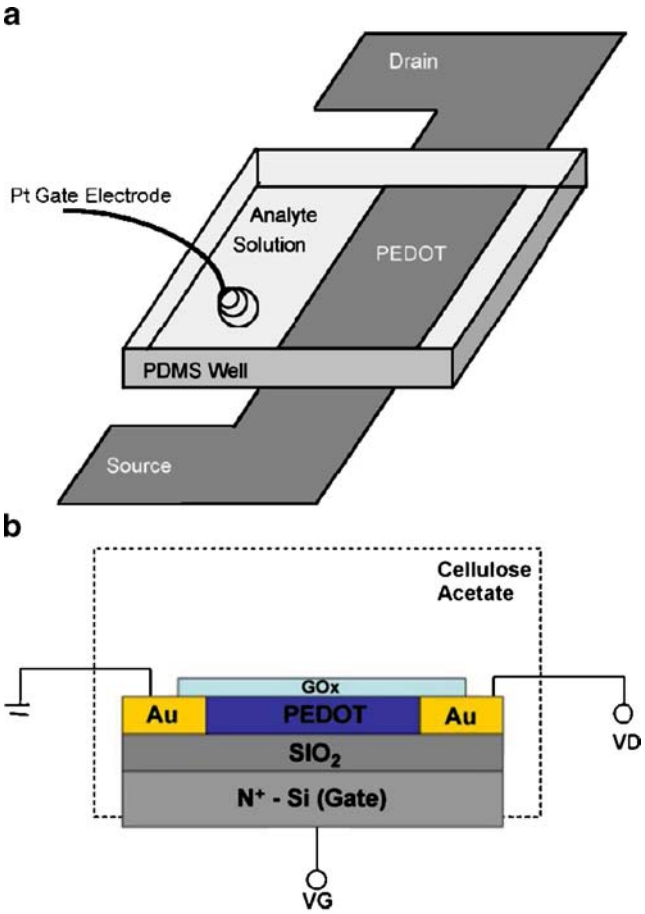

Fig. 2A–B PEDOT-based organic transistors: **A** from [41] and **B** from [43]

covers human blood glucose levels (3.85–8.25 mM). Setti et al. introduced a new preparation method for producing microelectrodes from PEDOT. Printing PEDOT and enzymes with a commercial inkjet printer, a complete amperometric glucose biosensor based on the detection of hydrogen peroxide was produced (Fig. 3) [38]. The horseradish peroxidase retained its functionality after thermal inkjet printing. The biosensor showed very good sensitivity and remarkable operational stability. Enzyme sensors were also used recently for determining other chemicals such as lactate, alcohol and glycerol [45, 47]. Alcohol dehydrogenase was deposited onto Au nanoparticles that were dispersed in PEDOT:PSS to create an ethanol sensor [46]. Experimental results indicated that the Au nanoparticles dispersed in the PEDOT:PSS matrix had large specific surface areas and good biocompatibilities, and that they are well suited to the immobilization of biomolecules or enzymes.

Immunosensors

An antibody is a complex biomolecule that exhibits very specific binding capabilities for specific structures. An

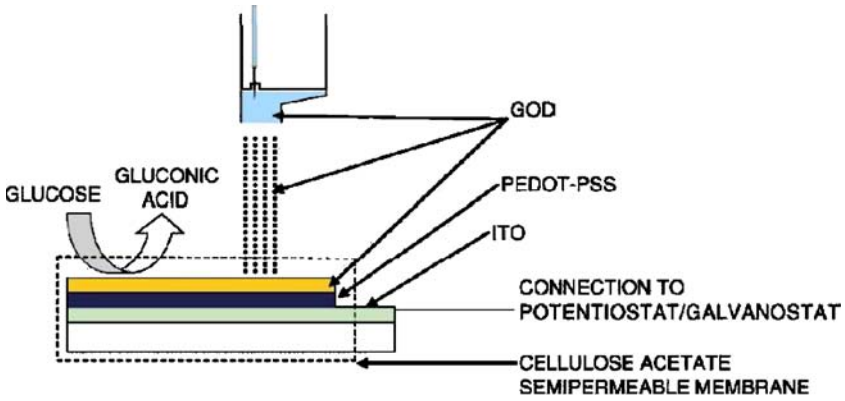

Fig. 3 Schematic diagram of the prototype of the complete GOD (glucose oxidase) inkjet-printed electrode from [38]

antigen-specific antibody "fits" its unique antigen in a highly specific manner. Antibodies are used in immunosensors where only the specific analyte of interest, the antigen, fits into the antibody's binding site. The immobilization of antibodies on the surface of the electrode is one of the key issues when developing these types of biosensors. Several research groups have achieved excellent results in binding antibodies to conductive polymers [48], but only a few of them have used PEDOT as the base polymer. Physical adsorption is the simplest method of immobilization and one of the first approaches used for biosensors, but controlling the concentration of the immobilized compound is difficult and immobilization is not stable due to the weak noncovalent forces involved, which decrease the lifetime of the biosensor. Another drawback is that compound adsorption can reduce the sensitivity of the sensors by limiting the number of sensor elements.

An alternative to adsorption is physical entrapment of the desired biomolecule during sensor production, which is one of the most extensively used techniques. Mouffouk et al. have described a method in which a biotin-functionalized EDOT derivative was used to produce the conductive polymer film [49]. They also miniaturized the system by optimizing the electrodeposition process on a 10 μm diameter Pt disk microelectrode, which worked as a sensor with a low detection limit. Avidin could be detected at the 10^{-16} mole level [48].

Molecularly imprinted polymers

Molecularly imprinted polymers (MIPs) represent a new class of materials that have artificially created receptor structures (Fig. 4). MIPs are considered to be appropriate alternatives to biological receptors for use in sensors principally due to their high stability. MIPs can be synthesized for analytes for which no receptor or enzyme is available or when they are too expensive. Additionally, the polymerization step is fully compatible with the microfabrication used in sensor technology. MIP sensors have been developed for herbicides, sugars, nucleic acid and amino acid derivatives, drugs, and toxins [50]. The limiting step in the development of MIP sensors was the difficulty involved in integrating highly crosslinked polymers with transducers. The utilization of conductive polymers with electrochemical transduction has solved this problem. A microfluidic system for detecting morphine using a combination of a molecularly imprinted polymer (MIP) and electrochemical sensing techniques has been developed in order to realize an electrochemical PEDOT-based morphine sensor [51]. The experimental data showed that the

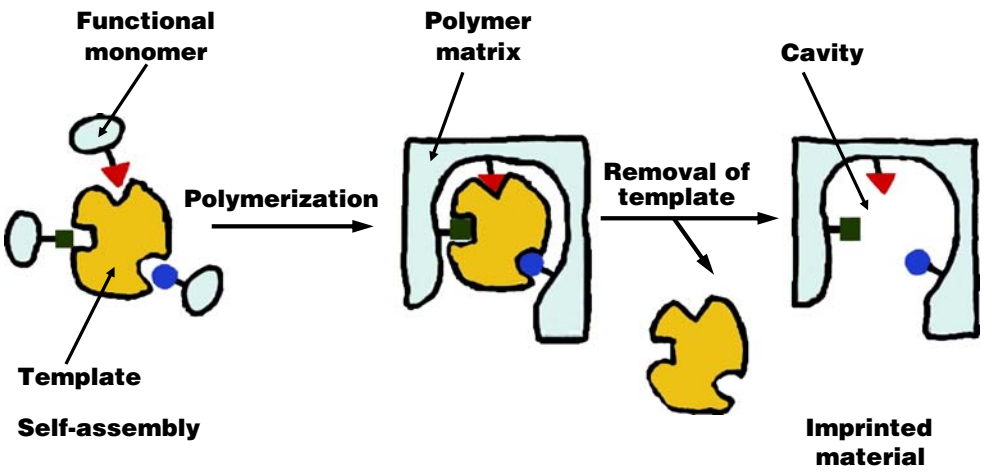

Fig. 4 Steps involved in molecular imprinting

morphine–MIP microfluidic system successfully detected morphine with concentrations ranging from 0.01 to 0.2 mM. This novel combination of microfluidics, MIP, and electrochemical techniques provides a promising system for biosensors. Amperometric detection of nicotine was carried out on a titanium dioxide (TiO_2)/(PEDOT)-modified electrode by a molecular imprinting technique [51]. In order to improve the conductivity of the substrate, PEDOT was coated onto the sintered electrode by in situ electrochemical polymerization of the monomer. Preliminary results have shown that the imprinted electrodes can also detect nicotine in a complicated blood plasma system.

Embedding of cells into conductive polymer electrodes

Significant improvements in the performance of electrode-based biomedical devices can be achieved by increasing integration at the electrode–tissue interface. Recently, a new process was introduced for polymerizing PEDOT around living cells (Fig. 5) [52]. Living cells embedded in the conductive polymer matrix remained viable for at least 120 h following the polymerization. A comprehensive study was made of the properties of the resulting PEDOT electrodes, and the PEDOT+live neurons. Furthermore, the cells can be removed from the PEDOT matrix to generate a neural cell templated biomimetic conductive substrate with cell-shaped features that are attractive to cells. The neural cell-templated PEDOT coatings on electrodes also significantly enhanced the electrical properties of the electrode [52].

Microbial sensing

Microbes have a number of advantages when used as sensing materials in the fabrication of biosensors. Although purified enzymes have very high specificity for their substrates or inhibitors, their application in biosensors may be limited because of the tedious, time-consuming and costly enzyme purification, the requirement for multiple enzymes to generate the measurable product, or the need for cofactor/coenzyme. Microorganisms provide an ideal alternative to these bottlenecks. Recently, Odaci et al. [53] introduced this new method into biosensor preparation. Bacterial cells (*Pseudomonas fluorescens*) were entrapped on a thiophene-based conducting polymer and then covered with a dialysis membrane to avoid the leakage of biological material during the measurements. The response characteristics of the resulting system were examined for glucose. The biosensor showed a good linear range, a good repeatability and a high operational stability. Although enzymes are usually more stable in their natural environment (i.e., in cells, where coenzymes and activators are also present), the major disadvantage of microbial biosensors compared to enzyme sensors is the slow response, which has been attributed to slow diffusion through the cell membranes.

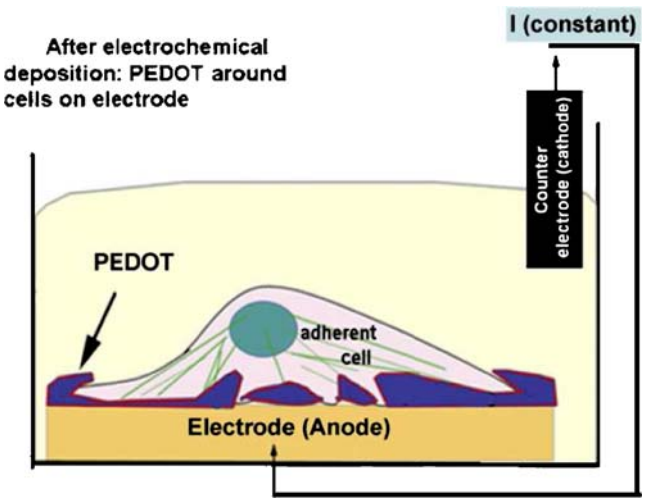

Fig. 5 Embedded cells in PEDOT, from [52]

Challenges and future directions

The research and development efforts of the recent years have quickly brought PEDOT to the forefront of the field of conducting polymers. Its properties, namely its high conductivity in combination with its excellent stability and its relatively high transparency to visible light, have allowed the material to become industrially useful. As a result, PEDOT and its derivatives have found their way into several current biosensor applications. The synthetic chemistry of PEDOT and its derivatives provides a high level of structural flexibility, which leads to great variety in the properties of the resultant polymers. We can foresee the development of many other applications in the future, especially in systems where structure and function relationships are involved. Although most of the current applications of PEDOT and its derivatives are still based on coating $InTO_2$ glass/metal/glassy carbon electrodes, in recent years a new all-polymer system has also been invented. Hansen et al. developed a new method for integrating conducting polymers into nonconductive polymer substrates [54], which was a good starting point for the further development of all-polymer biosensors. Since the polymer electrodes have lower conductivities than metal ones, and there is a need to miniaturize the systems, micropatterning of the all-polymer electrodes is a crucial part of sensor development. Recently a simple, cost-effective method was developed for the direct fast patterning of PEDOT-tosylate electrodes. This method is based on the fact that PEDOT-tosylate loses its conductivity in the oxidized state [55]. The applicability of all-polymer microdevices to biosensors has already been demonstrated [Jain T, et al. (2009) Characterization of PEDOT-tosylate microelectrodes for biosensor applications; submitted to

Biosens Bioelectron]. In all-polymer microfluidic sensors, as well as the electrode the fluidic circulation system (which enables the transport of the sample to the sensor surface) is also important. Conventional micropumps and valves become less reliable when the system is reduced to microdimensions, and they are unsuitable for full integration with the microfluidic device. Recently, great progress was achieved in this field with the design of an all-polymer pump and a strain gauge using PEDOT-tosylate [56, 57]. The all-polymer pump is an array of asymmetric electrodes, and its operation is based on AC electroosmotic effect. The strain gauge utilizes the piezoresistive properties of PEDOT-tosylate. Although these systems are not yet used in biosensors, their integration into microfluidic devices is very promising. As this happens, even more applications will emerge, enabling PEDOT and its analogs to maintain their position as the world's most popular conducting polymers used in all-polymer microdevices.

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