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Conducting Polymers as Elements of Miniature Biocompatible Sensor

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http://dx.doi.org/10.5772/intechopen.75715

Abstract

Conducting polymers (CPs), the so-called "fourth generation of polymeric materials", can solve essential problems in biosensing technologies due to their unique material properties and implementation in innovative device systems. CPs have excellent biocompatibility. They can provide advantageous interfaces for bioelectrodes owing to their hybrid conducting mechanics, combining both electron and ionic charge carriers. Many (i.e. glucose) biosensors use immobilized enzymes to form a selective layer on CP structure. Miniaturization of sensors is a new requirement. Mini sensors are portable and wearable with low utilization of sample and cost-effective technology of production.

Keywords: conducting polymers, nanomaterials, sensing devices, biosensors, miniaturization, biocompatibility

1. Introduction

Green electronics represents an occurring area of research aimed at identifying compounds of natural origin and establishing cost-reasonable ways for the synthetic materials that have utility in environmentally safe and/or biocompatible devices. There are several biocompatible sensing technologies that can perform innumerable physical and physiological measurements. Apart from carbon-based nanomaterials, other active sensing components are widely reported. These materials include polymers, semiconductors and metallic conductor-based nanomaterials as well as ionic and metallic liquids.

Carbon-based technologies are meant to address the energy and cost inefficiency issues posed by their inorganic counterparts. Organic electronics (based on i.e. conjugated polymers, CPs)

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entered the research field in the 1970s holding the high promise of delivering cost-reasonable and energy-efficient materials and devices. Despite intense effort of the scientific community during the past 30 years, the efficiency and stability of organic semiconductors endure at current times' major obstacles in their development as solid challengers of the inorganic materials [1–3]. Consequently, the large-scale rapid replacement of hard core inorganic counterparts, like the ones active in high-speed processors, integrated circuits, and solar cell modules, with organic components is not immediately expected [1–3]. However, the "soft" nature of carbonbased components confers them a serious benefit over the inorganic materials, enabling production of flexible, conformable and even extremely thin electronic equipment [4].

Conducting polymers, the so-called "fourth generation of polymeric materials", can provide effective methods for the diagnosis and treatment of different disorders, that is, diabetes. Conducting polymers have often excellent biocompatibility. They can provide favorable interfaces for bioelectrodes owing to their hybrid conducting processes, combining both electron and ionic charge carriers. Many (i.e. glucose) biosensors use immobilized enzymes to construct a selective layer on CP structure. Miniaturization of sensors is a new demand. Mini sensors are portable and wearable with low utilization of sample. New biosensors with a market size of a US\$13 billion annual turnover have quickly become valuable instruments in the healthcare. Actually, glucose biosensors (accounting for 85% of the total biosensor market) have notably mended the quality of life of diabetics [5].

2. Green electronic materials: conducting polymers

Conducting polymers (CPs) have occurred as competitive sensing materials for biological sensing applications. Their convenience of synthesis by chemical or electrochemical routes at ambient conditions, functionalization with monomer, dopant, monomer/dopant ratios and oxidation state to enhance the conductivities over 15 orders of magnitude, biocompatibility and low energy optical transitions have caused a significant concern. CPs have been synthesized by differing procedures, namely, electrochemical dip-pen lithography, mechanical stretching, electrospinning and template-directed electrochemical synthesis [6].

Since CPs were discovered, they have found many utilization. The swift progress in conductive polymer technologies is a significant motivating force for utilization of these materials as alternatives [7, 8] to conventional conductors, such as copper and gold [9, 10], as elements in the construction of electromagnetic devices. Regardless of that, the conductivity of polymers is lower than in metals, it has been presented to be adequate to construct antennas [11, 12]. Simultaneously, appearing green materials are contemplated to achieve a more aspiring purpose, designated by the integration of biocompatible, biodegradable and cost-reasonable electronics, such as the monitoring or the diagnosis of humans with environmentally benign technologies. Examples of the most common conductive polymers are shown in **Tables 1** and **2** [11–14] and **Figure 1**. Among the different conducting polymers, poly(3,4-ethylenedioxythiophene) (PEDOT) is one of the most encouraging materials for bioelectronics due to its relatively high conductivity, stability and more importantly its organic nature and good compatibility with bioorganic molecules such as enzymes compared to other CPs. Nevertheless, because of

Conducting Polymers as Elements of Miniature Biocompatible Sensor 55 http://dx.doi.org/10.5772/intechopen.75715

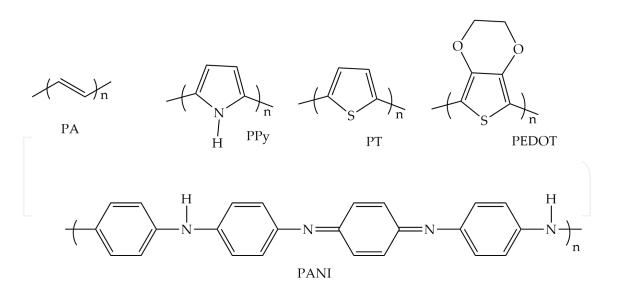


Figure 1. The most common CPs as sensor elements.

its poor solubility and processability, PEDOT is often mixed with PSS to generate water soluble poly(3,4-ethylenedioxythiophene):poly(styrene sulphonate)—PEDOT:PSS, which was developed and patented in 1988 by Bayer AG [15]. Doping of PSS could disrupt the combination of the PEDOT chains and lower their electrochemical efficiency [16]. Despite the fact that water soluble PEDOT:PSS can be applied to generate conducting thin films, the resulting planar layer lacks morphological benefit, having only restricted accessible surface in comparison with processable colloidal interface materials [16].

To date, some electrical conductors have been applied in implantable biological interfaces such as cardiac patches [17], neural interfaces [18], electroceuticals [19] and on-command drug delivery platforms [20]. Although classic inorganic electrical materials (i.e. metals and semiconductors) are not appropriate for a seamless biointerface because of the need for extracellular functionalities, the semiconducting polymers seem to be valuable alternatives for these applications [21]. Controlling this limited biocompatibility in flexible electronic materials endures a challenge, and is recently drawing fair research efforts in the bioelectronics group.

Conducting polymer	Maximum conductivity (S/CM)	Type of doping
Polyacetylene (PA)	200–1000	n, p
Polyparaphenylene (PPP)	500	n,p
Polyaniline (PANI)	5	n, p
Polyparavinylene (PPV)	1–1000	р
Polyparaphenylene sulphide (PPS)	3–300	р
Polypyrrole (PPY)	40–200	р
Polythiophene (PT)	10–100	р
PEDOT:PSS	100–1500	р

Table 1. The conductivity of the most common CPs.

CPs	Synthesis	Properties	Application
Polypyrrole (PPy)	Electrochemical and chemical synthesis	High conductivity (up to 160 S cm ⁻¹) when doped with iodine; opaque, brittle, amorphous material	Biosensors, antioxidants, drug delivery, bioactuators, neural prosthetics, cardiovascular application
Polythiophenes (PT)	Electrochemical and chemical synthesis	Good electrical conductivity and optical property	Biosensors, food industry
Polyaniline (PANI)	Electrochemical and chemical synthesis	Belongs to the semi- flexible rod polymer family; requires simple doping/dedoping chemistry; exists as bulk films or dispersions; high conductivity up to 100 S cm ⁻¹	Biosensors, antioxidants, drug delivery, bioactuators, food industry, cardiovascular application
Poly(3,4-ethylenedioxythiophene) (PEDOT)	Electrochemical and chemical synthesis	High temperature stability; ability to suppress the so-called "thermal runaway" of the capacitor; transparent conductor; moderate band gap and low redox potential; conductivity up to 210 S cm ⁻¹	Biosensors, antioxidants, drug delivery, neural prosthetics

Table 2. Properties of the CPs.

2.1. Surface modification of conducting polymers

Surface modification of the CPs for incorporating biomolecules has been obtained by both physical and chemical moderations. Such modifications can be applied to create both physical and chemical guidance cues, which can be adapted for the required biomedical utilization [22]. Chemical modification has been extensively studied using biomolecules as dopants (biospecific dopants such as peptides, proteins and neurotrophins) [23, 24] or by immobilizing bioactive moieties on the surface of the material [24].

For example, neural microelectrodes are commonly used in chronic, long-term implantations. Due to the fact, highly stable materials are needed that can tolerate the implantation procedure as well as the presence of biochemical environment in living tissue. Polypyrrole, however, has a poorly defined chemical structure in which there is a notable amount of α - β' coupling. The presence of these defect sites along the polymer chain induces structural disorder, limits the electrochemical response and has been implicated as the primary site of polymer breakdown due to over-oxidation [23]. Moreover, oxidized polypyrrole is unstable to reduction by relatively weak, but biologically relevant, reducing agents such as dithiothreitol and glutathione [23], which act as a p-dopants.

Physical modification has been investigated by enlarging surface roughness by different processes such as generating microporous layers using polystyrene sphere templates, creating composites of nanoparticles and polylactide [25], growing CPs within hydrogels [18] and mixing with biomolecules to yield "fuzzy" structures.

The electrode coatings used are rather soft [26] and can be tailored at the micrometer, nanometer and molecular scale to have fibrillary, nodular, fuzzy, tubular [27] or porous surface morphologies [25]. As a consequence, most tissue- and device-compatible surface tempering of the electrode would be bringing electrical activity, bioactivity, mechanical softness and architectural properties on a similar scale to that of cells in tissues. The surface roughness character of the conducting polymer layers can be tailored by modification of the conducting polymer synthesis temperature [22]. Exceptional adaptation of the surface roughness characteristics is important because rougher topology corresponds with increasing of surface area, which would expand the signal conduction by growing the interface with neurons. For example, polypyrrole films synthesized at a lower temperature (418°C) were rougher than the same layers achieved at 2518°C [28]. Kmecko et al. [29] presented that the introduction of carbon nanotubes as dopants to PPy and PEDOT prefers the creation of bumps and grows the surface roughness. Functionalization of CPs with biomolecules has permitted engineers to modify CPs with biological sensing elements, and to turn ON and OFF different signaling routes demanded for several cellular mechanisms to form conducting polymers that extend cell proliferation/differentiation. Moreover, dopants can be applied as intermediates to allow further modification of CPs, that is, doping with poly(glutamic acid) supplies a carboxylic acid pendent group, which can be functionalized further by covalent binding to any amino group, such as those found in polylysine and laminin [30].

The electrochemical character of the CPs can be varied by modifying the dopant concentration. Electrical conductivities can be varied by as much as 15 orders of magnitude by changing the dopant concentrations so that control is feasible over the all ranging from insulator to semiconductor and then to metal [31]. The usually used dopants contain aromatic sulphonate variants such as *p*-toluenesulphonate, styrene, sodium benzenesulphonate to dope the polymers [32]. Other appropriate dopants for oxidation polymerization contain buffer salts, I_2 , BF_4 , perchlorates and FeCl₃ (**Table 3**). Biological dopants include laminin peptide sequences, hydroxyapatite or a silk-like polymer with fibronectin units and polysaccharides [22]. Nevertheless, a main disadvantage of introducing dopants is the possible diffusion of the dopant into the culture medium with effects on cytotoxicity and deterioration of the electrical characteristics of the CP layer itself. For example, dodecyl sulphate-doped PPy layers undergo structural modifications after 7 days of soaking in deionized water [23].

The scope of possible dopants is huge as long as the selected dopant is charged. On the other hand, covalent methods can be used to more constantly functionalize CPs. The monomer can be synthesized with required functional groups and then polymerized, or post-polymerization covalent modification is also possible. It is crucial to note that the steric effects of any introduced functional group may interrupt the planarity of the conjugated arrangement, which could in turn lower the conductivity [22].

Polymer	Conductivity (S cm ⁻¹)	Dopant	Conductivity after doping (S cm ⁻¹)	Ref.
PEDOT	6×10^{-4}	polystyrene sulphonate (PSS)	10	[33]
PPY	10 ⁻² -10 ⁻³	ClO ₄ -	10	[34]
PT	10–10 ⁻³	BF_4	10–20	[34]
PT	10–10 ⁻³	SO3-	10–20	[34]
Table 3. Exa	amples of common CP do	pants in biological use.	Der	

2.2. Conducting polymers as effective electron relays in sensor devices

Effective electron transfer between the biorecognition species (e.g. an enzyme) and the electrode is challenging element when creating enzymatic biosensors. Classically, the distance among the active centre of the enzyme and the electrode surface is too long for direct electron transfer (DET) owing to the protective disk of the enzyme. Because electron transfer (ET) *via* a tunneling mechanism is rarely observed in classic electrodes, establishing electron relays that allow for fast ET, thus avoiding free-diffusing redox species between the electrode and the enzyme, is vital [35]. Due to the fact, organic electronic materials present very attractive expectants for molecular wiring owing to their polymeric essence and conducting character [36].

Doped PPy was the first CP presented to provide an electron relay among the surface of the electrode and the active centre of an enzyme [37, 38]. Nevertheless, owing to deficient electrochemical stability (potentially affecting long-term functionality) [39], attempts moved to other materials such as PEDOT, a polythiophene derivative which appeared as a more stable expectant owing to its low bandgap and high electrochemical stability in the oxidized state [40]. The first example of a PEDOT-based glucose sensor with potential for long-term measurements was presented by Kros et al. [41]. They physically introduced a positively charged polymer in the conducting substrate of the biosensor, permitting more effective ET as a result of the grown electrostatic interaction between the positively charged entrapped polymer and the negatively charged enzyme (Figure 2A). An optional procedure to enhance the electron relay in CPs postsynthesis involves intermixing with redox hydrogels, which have been presented to reveal rapid substrate and counter-ion diffusion effects with high flexibility and quick electron transfer rates. The non-conducting nature of such hydrogels hinders their effective and spatially placed immobilization on the active electrode surface, and mixing them with CPs can thus overcome this issue resulting in an ideal electron-transfer strategy. PEDOT:PSS was used to improve the deficient performance of a mediator-based biosensor by its introduction into nanocomposite enzyme electrodes, emerging in enhanced electron hopping in terms of the electron diffusion coefficient and charge transfer resistance (Figure 2B) [42]. Going one step further, Bao et al. investigated intrinsically conducting nanostructured polyaniline (PANI)-redox hydrogels [43]. In another strategy, a CP-based glucose-permeable redox hydrogel was created by crosslinking polymer acid-templated PANI together with glucose oxidase, leading to the electrical wiring of the enzyme and permitting electrocatalytic oxidation of glucose at low oxidation potentials (Figure 2C) [44]. Recently, CP hydrogels with high permeability to enzymes were utilized to produce metabolite biosensors with excellent sensing character without the need for a mediator (Figure 2D) [45].

Conducting Polymers as Elements of Miniature Biocompatible Sensor 59 http://dx.doi.org/10.5772/intechopen.75715

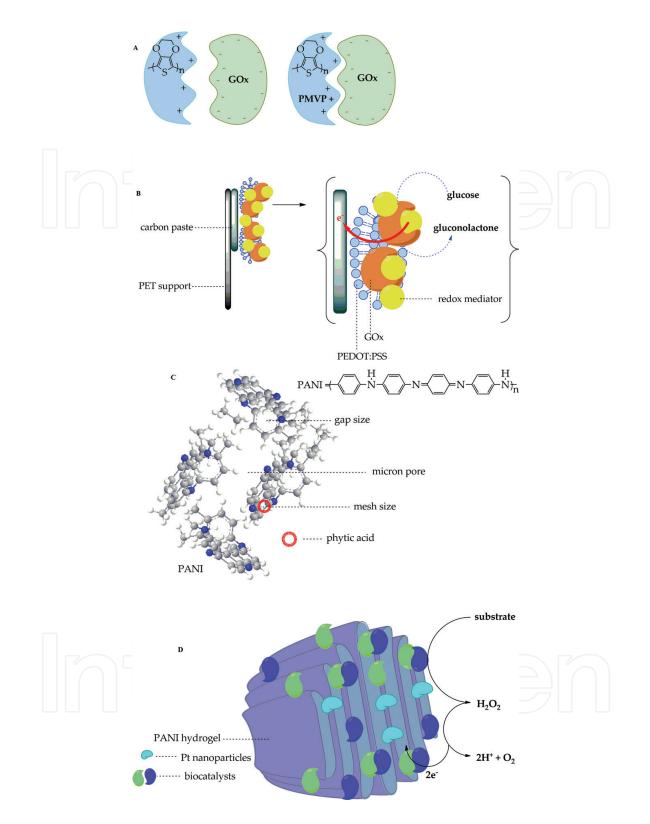


Figure 2. Organic conducting materials as effective enzyme immobilization supports and transducers for different body metabolite determination. (A) Electrostatic binding (weak and strong) of glucose oxidase (GOx) onto a PEDOT and PEDOT supplied with positively charged PMVP, poly(*N*-methyl-4-pyridine), according to [41]. (B) Schematic diagram of the working electrode coated with ferrocene-branched polyethylenimine, PEDOT:PSS and GOx for glucose detection, according to [42]. (C) Phytic acid gelated and doped PANI hydrogel according to [44]. (D) The PANI hydrogel matrix including Pt nanoparticles and the proper biocatalysts for the detection of uric acid, cholesterol and triglyceride, according to [45].

2.3. Biocompatibility of CPs

Among the effective presentations of organic bioelectronics, ultra-thin electronic systems for surgical, point-of-care [46], diagnostic implants [47], ambient intelligence for daily-life assistance [48], soft robotics [49], conformable and self-sustaining bioelectronic elements for sports and recreation [48], or even disposable (biodegradable) electronics [50] for food packaging [51] or throw-away applications [52] can be listed. The connection of novel electronic elements with biosensing constituents will open the possibility for investigating disposable diagnostic and drug delivery platforms. This topic has been recently reviewed in detail [53, 54]. The organic bioelectronics field may prove to be the satisfactory host for greeting natural and nature-inspired carbon materials and a perfect base for achieving the ambitious purpose of "green" and sustainable electronics future.

Conducting polymers of pyrrole and thiophene connected by ester linkages have been considered for the generation of temporary scaffolds for cell attachment and proliferation for tissue engineering applications [22]. Moreover, these scaffolds are biodegradable [55]. The possibility of growing cells on CPs has proven the biocompatibility of these polymers [21, 56]. Additionally, recently the biocompatibility of PPy and PEDOT layers and PPy and PEDOT nanotubes was estimated by utilizing a dorsal root ganglion model [57]. The implantation of CPs *in vivo* for several weeks has led to only minimal inflammation, again pointing to low toxicities and good tissue compatibility [21, 55]. Moreover, Abidian and Martin [18] successfully presented that PEDOT nanotubes could record neuronal spikes about 30% more than control sites with a high signal-to-noise ratio (SNR) for 7 weeks post-implantation *in vivo*. In addition, there have been a number of reviews on CPs with regard to biomedical applications [22, 27, 55, 58–63].

3. Organic electronic-based sensing platforms for body metabolites

3.1. Metabolite sensing of body fluids

Blood is the most generally used body fluid for metabolite level monitoring. Nevertheless, owing to the wealth of electroactive elements, electrochemical determination procedures become somewhat challenging, and the usually observed biofouling of the sensing electrodes poses further restrictions [5, 64]. CPs bearing sustainable surface modifications (i.e. incorporation of electron mediators, permselective membranes) can offer precious instruments towards modern and more accurate diagnostic devices. An antibody-mediated amperometric platform was designed by Wei et al. to avoid the interfering signals often encountered in complex systems (blood) when utilizing enzymatic-mediated amperometric determination. A PPy matrix favored for immobilization of the capture antibody, on top of a 16-array gold electrochemical sensor, which could therefore determine creatinine fast and accurately in whole blood, resulting in a point-of-care (POC) assay for allograft dysfunction (**Figure 3A**) [65]. Liao et al. recently investigated a flexible organic electrochemical transistor (OECT) platform based on PEDOT:PSS to selective detection of urea and glucose in saliva samples [66]. To exclude electrochemical interference in saliva, thus increasing sensitivity and selectivity, the gate electrodes were modified with oppositely

charged bilayer polymeric layers for both anionic and cationic charge exclusion of interferes. Moving towards multiplexing, a PEDOT:PSS-based OECT biosensing platform integrated with microfluidics was investigated for contemporary screening of glucose, lactate and cholesterol in human saliva samples [5]. The final tool was tested with human volunteers before and after exercise to present comparative differences in their metabolite profiles under stimuli (**Figure 3B**) [67]. In a similar procedure, contemporary sensing of lactate and glucose was presented by integrating two OECT-based tools, each with a separate microfluidic channel. They created a prototype portable glucose sensor by linking a smartphone with the sensing platform through Bluetooth connection, highlighting the ease of integration of such devices for POC systems [68].

3.2. Metabolite sensing from whole cells

Determination of cellular metabolites under different stimuli or environmental conditions can give useful prospects for drug discovery and toxicology. Larsen et al. used PEDOT:tosylate microelectrodes as an all polymer electrochemical chip for the determination of potassiuminduced transmitter release from neuron-like cells, presenting the potential of the procedure

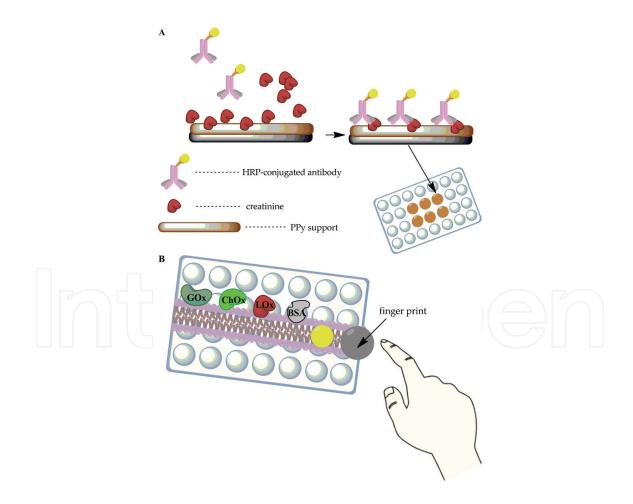


Figure 3. Integrated point-of-care systems based on organic electronics. (A) Scheme of the conducting polymer electrochemical sensor for the direct measurement of creatinine from serum, according to [65]. (B) Schematic demonstrating the OECT-based multianalyte system, according to [67]; BSA, bovine serum albumin; ChOx, cholesterol oxidase; GOx, glucose oxidase; HRP, horseradish peroxidase; lox, lactate oxidase.

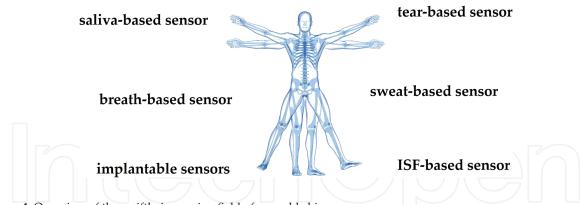


Figure 4. Overview of the swiftly increasing field of wearable biosensors.

for drug screening applications [69]. To enhance the electrocatalytic effect of the sensing electrode, the PEDOT:PSS gate can also be supplied with electrodeposited Pt nanoparticles [70]. Owing to the high surface area of the nanoparticles and the high specificity of the biocatalyst, the authors obtained very sensitive detection of the crucial metabolites such as glucose and lactate from live cells. Lactate production in tumor cell cultures derived from real patients was also studied using an OECT circuit. Lactate production could be measured from a few cells, underlining the sensitivity of the tool in a highly complex milieu, thus shown its potential for utilization in *in vivo* applications for cancer diagnostics [71]. Also, recently, Curto et al. presented a multiparametric on-chip platform integrated with microfluidics for cell cultures, using among other in-line methods the OECT-based detection of glucose produced by the cells as a measure to validate their improved differentiation under stimuli conditions [72].

3.3. Wearable metabolite biosensors

An indisputable trend in biosensor technology is on-body continuous monitoring of metabolites using wearable devices (**Figure 4**) [1]. Wearable biosensor applications aim to transform centralized hospital-based care systems to home-based personal medicine, reducing healthcare cost and time for diagnosis. Electrochemical transducers offer many benefits as wearable sensors for physiological monitoring, and can be easily integrated onto textile materials or directly on the skin.

Sweat-based wearable sensors, although mostly focused on a small number of physical or electrophysiological parameters, can yield crucial information about the health status of a patient based on levels of vital metabolites [73]. Wearable biosensors can be either textile/plastic-based or epidermal (tattoo)-based systems [74]. Epidermal biosensors supply better contact with skin but commonly exhibit shorter lifetimes than the textile-based tools. Such biosensors were first developed in 2009 by Kim et al. for continuous monitoring of physical parameters [75] and, shortly thereafter, Jia et al. combined this route with biorecognition elements to generate the first printed tattoo-based biosensor [76]. A screen-printed electrode on no permanent tattoo paper was investigated with carbon and silver (Ag)/AgCl serving as the working and reference electrodes, respectively. The working electrode was also modified with carbon nanotubes carrying a mediator together with lactate oxidase for endlessly monitoring lactate in sweat during exercise [76].

CPs are specially beneficial for wearable sensor technology owing to their compatibility with production on flexible solids [77]. In a very interesting way, Pal et al. investigated PEDOT:PSS

electrodes on flexible fully biodegradable silk protein fibroin supports using a simple photolithographic process and an aqueous ink composed of the CP and carrier proteins (**Figure 4B**) [78]. In an almost identical route by the same scientific group, silk proteins including fibroin and sericin were modified with photoreactive methacrylate groups for use as substrate inks for water-dispersible PEDOT:PSS that was micropatterned to investigate a biodegradable bioelectrode for glucose sensing *in vitro* [79]. This pathway presents a new trend for generating an entirely organic and free-standing system with controllable biodegradability including scalability and processability, leading to applications in wearable or implantable bioelectronics [80].

3.4. Miniaturization: implantable devices

The perspectives of implantable instruments and especially home-based metabolic monitoring can only be reached if they can be simply implanted and explanted (i.e. needle-assisted) without the necessity of complicated surgery [81]. Due to that, the implantable tool should be small, which calls for novel miniaturization of different functional elements such as electrodes, power sources, signal processing systems and sensory components. In addition, miniaturized biosensors implanted by ultrafine needles induce less tissue damage and then less inflammation and foreign body response [82]. Miniaturization of implantable instruments and particularly biosensors can be listed under: (1) miniaturization of sensing electrodes and elements and (2) miniaturization of driving electronics for power, communication and their subsequent integration/packaging. Referring to the production of miniaturized electrodes for analyte sensing, immobilization of biocatalyst onto an ultra-thin Pt wire (diameters less than 50μ m) or carbon nanofibres has been substantial [83]. The latter is convenient for generating nerve stimulating microelectrodes because of the possibility of ultra-fine dimensions and flexibility [84]. Due to subsequent improvement of the electrocatalytic feature of carbon nanofibres, these were modified with different metal nanoparticles without compromising their flexibility [85]. Recently, the advent of sub-micron lithography and its further use to produce miniaturized transistors has encouraged investigators to develop solid state electrochemical sensing systems in a transistor order [86]. Biosensors based on classic Si-based transistors as well as the incipient organic thin film transistors are being investigated for a scope of analytes. The unique electrical character of 1-D nanomaterials (CPs) [86] has led researchers to use them as channel materials and investigates sensors based on modifications induced in either gate conductance, modulation, transconduction, hysteresis or threshold voltage.

The flexible nature of polymers together with their low-temperature processing and demonstrated biocompatibility with enzymes renders them beneficial over classic Si- and glass-based materials [81]. Additionally, the soft and flexible character of polymers could reduce the possibility of tissue damage to the body during implantation and can be beneficial for applications where the instrument has to be able to adjust itself to the shape of the human body.

4. Discussion

Green electronics constitutes not only a novel term but also twenty-first century's slogan; it means an emerging area of research covered the identifying compounds of natural origin and

Device	CPS	Analyte	Ref.
Fluorescence-based biosensor	Poly(dithienotetraphenylsilane)	Dopamine	[87]
Electrochemical biosensor	Poly(bis-selenophene)-N-nonyl carbazole	Phenolic compounds	[88]
Optical LTCC biosensor	Poly(bis-thiophene) acridone	Phenolic compounds	[89]
Glucose biosensor	Langmuir-Schaefer film of <i>N</i> -hexadecyl-2,8- bis(thianthrene)phenothiazine	Glucose	[90]

Table 4. Miniature sensors based on CPs.

determining economically efficient ways for the fabrication of materials that have applicability in environmentally friendly technologies and devices. The key factor of this chapter is to generate routes for the production of human- and environmentally safe electronics in the main and the integration of such electronic circumferences with biological tissue.

Scientific researches into the class of green electronics may implement not only the original assurance of organic electronics that is to carry cost-reasonable and energy efficient materials but also achieve inconceivable functionalities for electronics, for example, benign integration into life and environment. Modern electronics technology has turned the relationship energy consumed during fabrication versus energy consumed during exploitation of the product to a complete imbalance [48]. A key prerequisite for achieving sustainability in the electronics industry is the usage of materials and technologies that have low embodied energy. In this context, it is worth to emphasize miniaturization procedures and alternative conducting materials as—CPs, which our group successfully implemented in miniature sensor devices (**Table 4**).

5. Concluding remarks

Organic electronics recently has swiftly gone to the forefront of biological applications, regardless its beginnings in wide, flexible applications realized by tools such as the organic light-emitting diode or organic photovoltaics. One of the agents responsible for the favorable outcome of organic electronics in biosensing applications is the accurate flexibility and tunability of the materials to suit the requirements in biological environment. Organic electronics can then demonstrate the technology to meet the requirements of the biosensor market. With regard to classical raised issues in terms of stability and lifetime of the biocatalyst and other biological elements, the trends in this dynamic field of organic electronic sensors are foreseen to contain the investigation of biomimetic architectures (i.e. molecular imprinted structures), harnessing the versatility in synthesis of such electronic materials. Transducer and biorecognition elements can be met as a single active agent that combines electronic functionalities and the best properties of the biological element in a more stable support, therefore, opening up modern prospects in sensor technologies in both fundamental and practical aspects.

Acknowledgements

The authors gratefully acknowledge the financial support of Wroclaw University of Science and Technology (10401/0194/17).

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References

- [1] Ma H, Acton O, Hutchins DO, Cernetic N, AK-Y J. Multifunctional phosphonic acid self-assembled monolayers on metal oxides as dielectrics, Interface modification layers and semiconductors for low-voltage high-performance organic field-effect transistors. Physical Chemistry Chemical Physics. 2012;14:14110-14126
- [2] Mei J, Diao Y, Appleton AL, Fang L, Bao Z. Integrated materials design of organic semiconductors for field-effect transistors. Journal of the American Chemical Society. 2013;135:6724-6746
- [3] Jorgensen M, Norrman K, Gevorgyan SA, Tromholt T, Andreasen B, Krebs FC. Stability of polymer solar cells. Advanced Materials. 2012;**24**:580-612
- [4] Kaltenbrunner M, White MS, Głowacki ED, Sekitani T, Someya T, Sariciftci NS, Bauer S. Ultrathin and lightweight organic solar cells with high flexibility. Nature Communications. 2012;3:770
- [5] Pappa A-M, Parlak O, Scheiblin G, Mailley P, Salleo A, Owens RM. Organic electronics for point-of-care metabolite monitoring. Trends in Biotechnology. 2018;**36**:45-59
- [6] Ahmad R, Mahmoudi T, Ahn M-S, Hahn Y-B. Recent advances in nanowires-based field-effect transistors for biological sensor applications. Biosensors and Bioelectronics. 2018;100:312-325
- [7] Peisert H, Liu X, Olligs D, Petr A, Dunsch L, Schmidt T, Chass T, Knupfer M. Highly ordered phthalocyanine thin films on a technically relevant polymer substrate. Journal of Applied Physics. 2004;**96**(7):4009-4011
- [8] Kang HS, Lee JW, Kim MK, Joo J, Ko JM, Lee JY. Electrical characteristics of pentacenebased thin film transistor with conducting poly(3,4-ethylenedioxythiophene) electrodes. Journal of Applied Physics. 2006;100(6):064508

- [9] Herth E, Rolland N, Lasri T. Circularly polarized millimeter-wave antenna using 0-level packaging. IEEE Antennas and Wireless Propagation Letters. 2010;9:934-937
- [10] Herth E, Seok S, Rolland N, Lasri T. Wafer level packaging compatible with millimeterwave antenna. Sensors and Actuators A: Physical. 2012;173(1):238-243
- [11] Pudas M, Halonen N, Granat P, Vhkangas J. Gravure printing of conductive particulate polymer inks on flexible substrates. Progress in Organic Coating. 2005;54(4):310-316
- [12] Bai H, Shi G. Gas sensors based on conducting polymers. Sensors. 2007;7(3):267-307
- [13] Herth E, Guerchouche K, Rousseau L, Calvet LE, Loyez C. A biocompatible and flexible polyimide for wireless sensors. Microsystem Technologies. 2017;**23**:5921-5929
- [14] Woods M, Batchelor J. Low-profile slot antenna integrated with a thin polymer nonmetallic battery. In: Antennas and Propagation Conference (LAPC); Loughborough. 2013. pp. 441-445
- [15] Jonas FD, Heywang GD, Schmidtberg W. AgB Festst off-Elektrolyte und diese enthaltende Elektrolyt-Kondensatoren. 1989
- [16] Alemu D, Wei H, Ho K, Chu C. Highly conductive PEDOT:PSS electrode by simple film treatment with methanol for ITO-free polymer solar cells. Energy & Environmental Science. 2012;5:9662-9671
- [17] Shin SR, Jung SM, Zalabany M, Kim K, Zorlutuna P, Kim SB, Nikkhah M, Khabiry M, Azize M, Kong J, Wan T, Palacios T, Dokmeci MR, Bae H, Tang X, Khademhosseini A. Carbon-nanotube-embedded hydrogel sheets for engineering cardiac constructs and bioactuators. ACS Nano. 2013;7:2369-2380
- [18] Abidian MR, Martin DC. Multifunctional nanobiomaterials for neural interfaces. Advanced Functional Materials. 2009;19:573-585
- [19] Famm K. A jump-start for electroceuticals. Nature. 2013;2013(496):159-161
- [20] Wu CH, Cao C, Kim JH, Hsu CH, Wanebo HJ, Bowen WD, Xu J, Marshall J. Trojan-horse nanotube on-command intracellular drug delivery. Nano Letters. 2012;12:5475-5480
- [21] Schmidt CE, Shastri VR, Vacanti JP, Langer R. Stimulation of neurite outgrowth using an electrically conducting polymer. Proceedings of the National Academy of Sciences of the United States of America. 1997;94:8948-8953
- [22] Ravichandran R, Sundarrajan S, Reddy Venugopa J, Mukherjee S, Ramakrishna S. Applications of conducting polymers and their issues in biomedical engineering. Journal of the Royal Society Interface. 2010;7:S559-S579
- [23] Cui XY, Martin DC. Electrochemical deposition and characterization of poly (3,4-ethylenedioxythiophene) on neural microelectrode arrays. Sensors and Actuators B: Chemical. 2003;89:92-102
- [24] Zhong YH, Yu XJ, Gilbert R, Bellamkonda RV. Stabilizing electrode-host interfaces: A tissue engineering approach. Journal of Rehabilitation Research and Development. 2001;38:627-632

- [25] Yang JY, Martin DC. Microporous conducting polymers on neural microelectrode arrays.I. Electrochemical deposition. Sensors and Actuators B: Chemical. 2004;101:133-142
- [26] Yang JY, Martin DC. Impedance spectroscopy and nanoindentation of conducting poly(3,4-ethylenedioxythiophene) coatings on microfabricated neural prosthetic devices. Journal of Materials Research. 2006;21:1124-1132
- [27] Abidian MR, Kim DH, Martin DC. Conducting polymer nanotubes for controlled drug release. Advanced Materials. 2006;18:405-409
- [28] Guimard NK, Gomezb N, Schmidt CE. Conducting polymers in biomedical engineering. Progress in Polymer Science. 2007;32:876-921
- [29] Kmecko T, Hughes G, Cauller L, Jeong-Bong L, Romero-Ortega M. Nanocomposites for neural interfaces. Materials Research Society Symposia Proceedings. Materials Research Society. 2006;926E:0926-CC04-06
- [30] Song HK, Toste B, Ahmann K, Hoffman-Kim D, Palmore GTR. Micropatterns of positive guidance cues anchored to polypyrrole doped with polyglutamic acid: A new platform for characterizing neurite extension in complex environments. Biomaterials. 2006;27:473-484
- [31] Malhotra BD, Singhal R. Conducting polymer based biomolecular electronic devices. Pramana. 2003;**61**:331-343
- [32] Cui X, Lee VA, Raphael Y, Wiler JA, Hetke JF, Anderson DJ. Surface modification of neural recording electrodes with conducting polymer/biomolecule blends. Journal of Biomedical Materials Research. 2001;56:261-272
- [33] Crispin X, Jakobbson FLE, Crispin A, Grim PCM, Andersson P, Volodin A, van Haesendonck C, van der Auweraer M, Solaneck WR, Berggren M. The origin of the high conductivity of PEDOT-PSS plastic electrode. Chemistry of Materials. 2006;18:4354-4360
- [34] Tourillon G, Garnier F. Effect of dopant on the physicochemical and electrical properties of organic conducting polymers. The Journal of Physical Chemistry. 1983;87:2289-2292
- [35] Sekretaryova AN, Vagin M, Beni V, Turner APF, Karyakin AA. Unsubstituted phenothiazine as a superior water-insoluble mediator for oxidases. Biosensors & Bioelectronics. 2014;53:275-282
- [36] Vallejo-Giraldo C, Kelly A, Biggs MJ. Biofunctionalisation of electrically conducting polymers. Drug Discovery Today. 2014;**19**:88-94
- [37] Schuhmann W, Zimmermann H, Habermüller K, Laurinavicius V. Electron-transfer pathways between redox enzymes and electrode surfaces: Reagentless biosensors based on thiol-monolayer-bound and polypyrrole-entrapped enzymes. Faraday Discussions. 2000;2000:245-255
- [38] Swann MJ, Bloor D, Haruyama T, Aizawa M. The role of polypyrrole as charge transfer mediator and immobilization matrix for d-fructose dehydrogenase in a fructose sensor. Biosensors & Bioelectronics. 1997;12:1169-1182

- [39] Pud AA. Stability and degradation of conducting polymers in electrochemical systems. Synthetic Metals. 1994;66:1-18
- [40] Kros A, Sommerdijk NAJM, Nolte RJM. Poly(pyrrole) versus poly(3,4-ethylenedioxythiophene): Implications for biosensor applications. Sensors and Actuators B: Chemical. 2005;106:289-295
- [41] Kros A, van Hovell WFM, Sommerdijk NAJM, Nolte RJM. Poly(3,4-ethylenedioxythiophene)-based glucose biosensors. Advanced Materials. 2001;13:1555-1557
- [42] Wang J-Y, Chen L-C, Ho K-C. Synthesis of redox polymer nanobeads and nanocomposites for glucose biosensors. ACS Applied Materials & Interfaces. 2013;5:7852-7861
- [43] Pan L, Yu G, Zhai D, Lee HR, Zhao W, Liu N, Wang H, Tee BC, Shi Y, Cui Y, Bao Z. Hierarchical nanostructured conducting polymer hydrogel with high electrochemical activity. Proceedings of the National Academy of Sciences. 2012;109:9287-9292
- [44] Mano N, Yoo JE, Tarver J, Loo YL, Heller A. An electron-conducting cross-linked polyaniline-based redox hydrogel, formed in one step at pH 7.2, wires glucose oxidase. Journal of the American Chemical Society. 2007;129:7006-7007
- [45] Li L, Wang Y, Pan L, Shi Y, Cheng W, Shi Y, Yu G. A nanostructured conductive hydrogels-based biosensor platform for human metabolite detection. Nano Letters. 2015;15:1146-1151
- [46] Pollock NR, Rolland JP, Kumar S, Beattie PD, Jain S, Noubary F, Wong VL, Pohlmann RA, Ryan US, Whitesides GM. A paper-based multiplexed transaminase test for lowcost, point-of-care liver function testing. Science Translational Medicine. 2012;4:152ra129
- [47] Tybrandt K, Forchheimer R, Berggren M. Logic gates based on ion transistors. Nature Communications. 2012;3:871
- [48] Irimia-Vladu M. "Green" electronics: Biodegradable and biocompatible materials and devices for sustainable future. Chemical Society Reviews. 2014;43:588-610
- [49] Martinez RV, Branch JL, Fish CR, Jin L, Shepherd RF, Nunes RMD, Suo Z, Whitesides GM. Robotic tentacles with three-dimensional mobility based on flexible elastomers. Advanced Materials. 2013;25:205-212
- [50] Irimia-Vladu M, Troshin PA, Reisinger M, Shmygleva L, Kanbur Y, Schwabegger M, Bodea R, Schwödiauer A, Mumyatov JW, Fergus V, Razumov G, Sitter H, Sariciftci NS, Bauer S. Biocompatible and biodegradable materials for organic field-effect transistors. Advanced Functional Materials. 2010;20:4069-4076
- [51] Tao H, Brenckle MA, Yang M, Zhang J, Liu M, Siebert SM, Averitt RD, Mannoor MS, McAlpine MC, Rogers JA, Kaplan DL, Omenetto FG. Silk-based conformal, adhesive, edible food sensors. Advanced Materials. 2012;24:1067-1072
- [52] Tobjork D, Osterbacka R. Paper electronics. Advanced Materials. 2011;23:1935-1961

- [53] Angione MD, Pilolli R, Cotrone S, Magliulo M, Mallardi A, Palazzo G, Sabbatini L, Fine D, Dodabalapur A, Cioffiand N, Torsi L. Carbon based materials for electronic bio-sensing. Materials Today. 2011;14:424-433
- [54] Svennersten K, Larsson KC, Berggren M, Richter-Dahlfors A. Organic bioelectronics in nanomedicine. Biochimica et Biophysica Acta. 2011;1810:276-285
- [55] Rivers TJ, Hudson TW, Schmidt CE. Synthesis of a novel, biodegradable electrically conducting polymer for biomedical applications. Advanced Functional Materials. 2002;12:33-37
- [56] Garner B, Georgevich A, Hodgson AJ, Liu L, Wallace GG. Polypyrrole–heparin composites as stimulus-responsive substrates for endothelial cell growth. Journal of Biomedical Materials Research. 1999;44:121-129
- [57] Abidian MR, Corey JM, Kipke DR, Martin DC. Conducting-polymer nanotubes improve electrical properties, mechanical adhesion, neural attachment, and neurite outgrowth of neural electrodes. Small. 2010;6:421-429
- [58] Ahuja T, Mir IA, Kumar D. Biomolecular immobilization on conducting polymers for biosensing applications. Biomaterials. 2007;28:791-805
- [59] Kenry YJC, Lim CT. Emerging flexible and wearable physical sensing platforms for healthcare and biomedical applications. Microsystems & Nanoengineering. 2016;2:1-19
- [60] Gong S, Schwalb W, Wang Y, Chen Y, Tang Y, Si KJ, Shirinzadeh B, Cheng W. A wearable and highly sensitive pressure sensor with ultrathin gold nanowires. Nature Communications. 2014;5:1-8
- [61] Kim SY, Park S, Park HW, Park DH, Jeong Y, Kim DH. Highly sensitive and multimodal all-carbon skin sensors capable of simultaneously detecting tactile and biological stimuli. Advanced Materials. 2015;27:4178-4185
- [62] Pang C, Lee G-Y, Kim T-I, Kim SM, Kim HN, Ahn SH, Suh KY. A flexible and highly sensitive strain-gauge sensor using reversible interlocking of nanofibres. Nature Materials.
 2012;11:795-801
- [63] Segev-Bar M, Landman A, Nir-Shapira M, Shuster G, Haick H. Tunable touch sensor and combined sensing platform: Toward nanoparticle-based electronic skin. ACS Applied Materials & Interfaces. 2013;5:5531-5541
- [64] Krishnan S, Weinmanb CJ, Oberb CK. Advances in polymers for anti-biofouling surfaces. Journal of Materials Chemistry. 2008;18:3405-3413
- [65] Wei F, Cheng S, Korin Y, Reed EF, Gjertson D, Ho CM, Gritsch HA, Veale J. Serum creatinine detection by a conducting-polymer-based electrochemical sensor to identify allograft dys-function. Analytical Chemistry. 2012;84:7933-7937
- [66] Liao C, Mak C, Zhang M, Chan HL, Yan F. Flexible organic electrochemical transistors for highly selective enzyme biosensors and used for saliva testing. Advanced Materials. 2015;27:676-681

- [67] Pappa AM, Curto VF, Braendlein M, Strakosas X, Donahue MJ, Fiocchi M, Malliaras GG, Owens RM. Organic transistor arrays integrated with finger-powered microfluidics for multianalyte saliva testing. Advanced Healthcare Materials. 2016;5:2295-2302
- [68] Ji X, Lau HY, Ren H, Peng B, Zhai P, Feng S-P, Chan PK. Highly sensitive metabolite biosensor based on organic electrochemical transistor integrated with microfluidic channel and poly(N-vinyl-2-pyrrolidone)-capped platinum nano-particles. Advanced Materials Technologies. 2016;1:1600042(1-8)
- [69] Larsen ST, Vreeland RF, Heien ML, Taboryski R. Characterization of poly(3,4-ethylenedioxythiophene): Tosylate conductive polymer microelectrodes for transmitter detection. Analyst. 2012;137:1831-1836
- [70] Strakosas X, Huerta M, Donahue MJ, Hama A, Pappa AM, Ferro M, Ramuz M, Rivnay J, Owens RM. Catalytically enhanced organic tran-sistors for in vitro toxicology monitoring through hydrogel entrap-ment of enzymes. Journal of Applied Polymer Science. 2017;134(1-7):44483
- [71] Braendlein M, Pappa AM, Ferro M, Lopresti A, Acquaviva C, Mamessier E, Malliaras GG, Owens RM. Lactate detection in tumor cell cultures using organic transistor circuits. Advanced Materials. 2017;29:1605744
- [72] Curto VF, Marchiori B, Pappa AM, Ferro MP, Braendlein M, Rivnay J, Fiocchi M, Malliaras GG, Ramuz M, Owens RM. Organic transistor platform with integrated microfluidics for in-line multi-paramentric in vitro cell monitoring. Microsyst. Nano. 2017;17028(1-12):3
- [73] Heikenfeld J. Technological leap for sweat sensing. Nature. 2016;529:475-476
- [74] Parrilla M, Cánovas R, Jeerapan I, Andrade FJ, Wang J. A textile-based stretchable multiion potentiometric sensor. Advanced Healthcare Materials. 2016;5:996-1001
- [75] Kim DH, Lu N, Ma R, Kim YS, Kim RH, Wang S, Wu J, Won SM, Tao H, Islam A, Yu KJ, Kim TI, Chowdhury R, Ying M, Xu L, Li M, Chung HJ, Keum H, McCormick M, Liu P, Zhang YW, Omenetto FG, Huang Y, Coleman T, Rogers JA. Epidermal electronics. Science. 2011;333:838-843
- [76] Jia WZ, Bandodkar AJ, Valdés-Ramírez G, Windmiller JR, Yang Z, Ramírez J, Chan G, Wang J. Electrochemical tattoo biosensors for real-time noninvasive lactate monitoring in human perspiration. Analytical Chemistry. 2013;85:6553-6560
- [77] Khodagholy D, Curto VF, Fraser KJ, Gurfinkel M, Byrne R, Diamond D, Malliaras GG, Benito-Lopez F, Owens RM. Organic electrochemical transistor incorporating an ionogel as a solid state electrolyte for lactate sensing. Journal of Materials Chemistry. 2012;22:4440-4443
- [78] Pal RK, Farghaly AA, Wang C, Collinson MM, Kundu SC, Yadavalli VK. Conducting polymer-silk biocomposites for flexible and biodegradable electrochemical sensors. Biosensors & Bioelectronics. 2016;81:294-302
- [79] Kurland NE, Dey T, Kundu SC, Yadavalli VK. Precise patterning of silk microstruc-tures using photolithography. Advanced Materials. 2013;25:6207-6212

- [80] Kurland NE, Dey T, Wang C, Kundu SC, Yadavalli VK. Silk protein lithography as a route to fabricate sericin microarchitectures. Advanced Materials. 2014;**26**:4431-4437
- [81] Vaddiraju S, Tomazos I, Burgess DJ, Jain FC, Papadimitrakopoulos F. Emerging synergy between nanotechnology and implantable biosensors: A review. Biosensors & Bioelectronics. 2010;25:1553-1565
- [82] Kvist PH, Iburg T, Aalbaek B, Gerstenberg M, Schoier C, Kaastrup P, Buch-Rasmussen T, Hasselager E, Jensen HE. Biocompatibility of an enzyme-based, electrochemical glucose sensor for short-term implantation in the subcutis. Diabetes Technology & Therapeutics. 2006;8(5):546-559
- [83] Crespi F. In vivo voltammetric detection of neuropeptides with micro carbon fiber biosensors: Possible selective detection of somatostatin. Analytical Biochemistry. 1991;194(1):69-76
- [84] Receveur RAM, Lindemans FW, De Rooij NF. Microsystem technologies for implantable applications. Journal of Micromechanics and Microengineering. 2007;17(5):R50-R80
- [85] Tamiya E, Sugiura Y, Takeuchi T, Suzuki M, Karube I, Akiyama A. Ultra-micro glutamate sensor using platinized carbon Fiber electrode integrated counter electrode. Sensors and Actuators B: Chemical. 1993;10(3):179-184
- [86] Forzani ES, Zhang H, Nagahara LA, Amlani I, Tsui R, Tao N. A conducting polymer nanojunction sensor for glucose detection. Nano Letters. 2004;4(9):1785-1788
- [87] Baluta S, Malecha K, Zając D, Sołoducho J, Cabaj J. Dopamine sensing with fluorescence strategy based on lowtemperature co-fired ceramic technology modified with conductingpolymers. Sensors and Actuators B: Chemical. 2017;252:803-812
- [88] Cabaj J, Jędrychowska A, Świst A, Sołoducho J. Tyrosinase biosensor for antioxidants based on semiconducting polymer support. Electroanalysis. 2016;28:1383-1390
- [89] Jędrychowska A, Malecha K, Cabaj J, Sołoducho J. Laccase biosensor based on low temperature co-fired ceramics for the permanent monitoring of water solutions. Electrochimica Acta. 2015;**165**:372-382
- [90] Cabaj J, Sołoducho J, Jędrychowska A, Zając D. Biosensing invertase-based Langmuir-Schaefer films: Preparation and characteristic. Sensors and Actuators B: Chemical. 2012;166-167:75-82



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