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Highly Conductive Polymer PEDOT:PSS - Application in Biomedical and Bioelectrochemical Systems

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Abstract: **This review deals with the use of the highly conductive polymer PEDOT:PSS in biomedical and bioelectrochemical systems. The examples of toxic effects on living cells, positive effects of PEDOT:PSS on the viability of cells and tissues are given. The properties of the polymer, methods of increasing its electrical conductivity by its modification with various nanoparticles and nanomaterials are discussed. Examples of using PEDOT and its composites in bioelectrochemical devices, such as biosensors and biofuel cells, are considered. Changes in the characteristics of biosensors and biofuel cells under the influence of PEDOT are discussed.**

Keywords: **highly conductive polymer PEDOT:PSS; biomedical andbioelectrochemical systems; application of PEDOT:PSS; biosensors; biofuel cells**

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Contents

1. INTRODUCTION

Currently, much attention is paid to the creation of various composite materials and mixtures for effective integration and conjunction with biological material; further use of such compositions can lead to the creation of analytical devices based on them – biosensors; the creation of energy-producing system – biofuel cells (BFCs); the creation of systems with the biomedical perspective. Recent studies show that polymer compounds such as chitosan, polyethylene glycol, polyaniline, polyvinyl alcohol, and so forth play an important role in composite materials. Some of the promising polymers that draw attention are poly(3,4-ethylenedioxythiophene) – PEDOT and poly(3,4-ethylenedioxythiophene): polysterenesulfonic acid – PEDOT:PSS. In the oxidized state, PEDOT is one of the most stable polymers known. When combined with polystyrene sulfonic acid (PSS) as a counter ion, PEDOT forms a polyelectrolyte complex that has the properties of a stable dispersion that can be produced on an industrial scale. PEDOT:PSS is a polymer

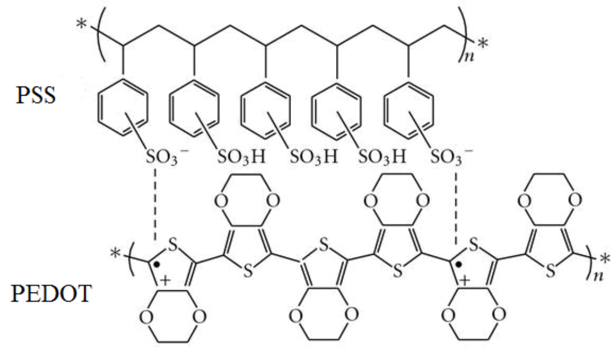

Fig. 1. *The chemical formula of PEDOT:PSS.*

that is formed by two basic molecules – EDOT (3,4-ethylenedioxithiophene) and PSS (polysterenesulfonic acid); the chemical formula of PEDOT:PSS is given in **Fig. 1**. Some of the sulfonyl groups of PSS are deprotonated and carry a negative charge. PEDOT is a conjugated polymer and carries positive charges. The charged macromolecules form a macromolecular salt.

Although the practical importance of the said polymers is highlighted, there remains much to learn about PEDOT:PSS and its properties.

In this review, main characteristics of PEDOT/PEDOT:PSS are described, they are important from a practical perspective enabling the use of this polymer as the basis of analytical and technical systems.

2. ALTERATION OF PHYSICAL-CHEMICAL PROPERTIES OF PEDOT:PSS AFTER ITS MODIFICATION WITH DIFFERENT MATERIALS

An important characteristic of polymers in any bioelectrochemical devices is their conductivity. PEDOT:PSS is considered to be one of the most promising conductive materials and it is used in device production in various fields: in displays, touch panels, polymer and photoelectrochemical cells, organic light-emitting diodes [1], as a coating in electroluminescent layers [2], as a sensitive element in photo-voltaic devices [3], in memory cells [4], resistive switches [5] and others. Electron transfer in the PEDOT polymer is carried out by a system of conjugated bonds due to electron exchange reactions between neighboring redox sites and is accompanied by conjugated movement of dopant anions along the polymer chain. Thus, PEDOT and PEDOT:PSS have a mixed electron-ion type of conductivity. Addition of metal nanoparticles that actively inject electrons, into such a polymer matrix can contribute to the production of nanostructures with the increased conductivity. Researchers are constantly searching for new ways to improve the conductive properties of PEDOT-based films. One of the most common treatment for improving the conductivity of PEDOT:PSS is to include various nanomaterials and nanoparticles in the composition of the polymer. For instance, in [6] authors sought to investigate the conductivity of PEDOT:PSS films containing gold nanoparticles and inferred that the conductivity of these films is due to hopping charge transport. They examined the absorption spectra in the visible region and volt-ampere characteristics in a wide range of electric fields at the macro (in planar structures) and micro levels (using a conducting atomic force microscope) in the films on the basis of electroactive polymer PEDOT:PSS and gold/silver nanoparticles. It was shown that the behavior of the current-voltage characteristics of nanocomposite films depends on the magnitude of the electric field. It was also found that addition of the gold nanoparticles to PEDOT:PSS in weak fields leads to an increase in volume conductivity by almost two orders of magnitude (due to donor-acceptor interactions), a 50% decrease in the activation energy of conductivity, and an increase in sensitivity to adsorbed oxygen.

The PEDOT:PSS with conductivity of about 3000 Cm×cm^{-1} was obtained quiet recently. The main strategy to increase the conductivity is to change the properties of the polymer when it interacts with various solvents, such as DMSO (dimethylsulfoxide). In addition to the effect of increased conductivity, the authors [7] found that the range of potential, within which the PEDOT:PSS demonstrates highly conductive properties, expands to the region of negative potentials. This characteristic can be used later on when using PEDOT:PSS as part of chemical sensors where high material conductivity is required at particular potentials.

In [8], the authors propose a method for manufacturing flexible conductive structures of PEDOT:PSS polymer and reduced graphene with a multilayer structure. The resulting capacitance value of such composites was about 193 F/g at a current density of 500 mA/g. The obtained material was highly stable – the capacitive component remained at the level of 90% after 1000 cycles, which indicates the prospect of using this approach to manufacture flexible energy storage devices. The works [9,10] demonstrate the possibility of multi-stage formation of composite transparent coatings with increased conductivity based on the carbon nanotube system - conductive PEDOT:PSS polymer. The produced coatings are characterized by a combination of low surface resistance (89 Om) and high optical transparency (about 81%). The main advantage of the obtained coatings is their mechanical stability to bending deformations.

Yan et al. [11] were the first to discover that completely isolated halloysite nanotubes

(HNTs) improve the electrical conductivity of PEDOT:PSS films by several orders of magnitude in the case of simple mixing. Due to this effect a highly porous and highly conductive composition of PEDOT:PSS-HNTs was created. By modifying the mixing process, the authors created a flexible conducting hybrid structure with a high specific surface. They propose a mechanism according to which colloidal particles with size of several dozens of nanometers are tightly packed in channels formed by PEDOT:PSS particles. In this case, the resulting conductivity is several orders of magnitude higher than that of the PEDOT:PSS located outside the nanotubes.

The formation of "sandwich structures" based on the successive repetition of procedures of metal oxide layers and polymer deposition led to the creation of composite materials {PEDOT/MnO_2}x [12] and {PEDOT/NiO}x [13]. Such structures make it possible to increase the capacitance characteristics of materials while maintaining high charge-discharge rates, which is used in supercapacitors.

Cross-linking of PEDOT:PSS with diglycidyl ether of bisphenol A results in production of the electrically conductive films with increased water resistance. Moreover, there is no evidence of decrease in the electrical properties of the film as thermal stability increases. The researchers proposed a promising technique of creation of electrodes that can be used in biological environments where contact with water is often unavoidable.

3. STIMULATING AND TOXIC EFFECTS OF PEDOT:PSS ON CELLS

One of the basic properties of any polymer for potential use in bioelectrochemical devices is the biocompatibility of the material. This term is usually used for the description of the implantable devices. The materials used in implants should be chemically and biologically inert, non-allergenic and non-toxic. Several studies have indicated that the PEDOT:PSS polymer is used in biomedical studies showing its good compatibility with the cells of different tissues. The review [15] emphasized a growing interest in the development of neural prosthetic devices from organic nanomaterials which was driven by recent advances in nanotechnology. An ideal material should have the properties that allow seamless binding and long lifetime. As a result, a great number of tests show that lots of nanomaterials, synthesized primarily for various purposes, are able to detect neural signals and stimulate the neurons. It is worthy of note that PEDOT is among the polymer materials, which exhibit the said properties. This polymer has extremely high conductivity, chemical stability in the oxidized state and great biocompatibility. The applications of polymers during exploration of tissue regeneration may give us an answer to questions regarding peculiarities of the organism response induced by the insertion of the stent (tensile elastic construction in the form of a cylindrical frame which is inserted in the clearance of hollow organs, providing expansion of the site reduced by pathological process). The scientists [16] explored the potential application of the PEDOT thin films for the stents with the aim to elucidate the extent of their effects on cell adhesion and proliferation, to determine their role in physical-chemical processes. As a matter of fact, this research focused on study of the stimulating effects of PEDOT. The authors demonstrated that all tested PEDOT films were cytocompatible, contributed to adsorption of serum albumin and increased cell survival, and PEDOT:PSS promoted cell proliferation. Finally, the authors have concluded that the applications of nanomaterials in medicine may improve the relationship between medicine and bioelectronics; the use of PEDOT:PSS and PEDOT:TOS polymers (PEDOT doped with anions such as tosylate) stimulates regeneration processes during implantation of cardiovascular devices.

The work [17] reported the development of a dual component coating that could help stabilize a cochlear implant (a medical device which is intended to compensate for hearing loss). This coating is a combination of an arginine-glycine-aspartic acid, alginate hydrogel and the PEDOT polymer. The use of this coating significantly improved implant performance, lowered electrode impedance, improved charge delivery and locally enhanced the level of a trophic factor. In addition, the authors wrote that this coating is biocompatible with the organism tissues.

The studies [18-21] provide the results of the experiments on the development of the layer around nerve cells with the use of the conductive polymer PEDOT:PSS to obtain biomaterial with high electrical conductivity for direct electrical contact between electrically active cells such as heart cells, neurons, cells of the skeleton muscle. The authors described a technique which can be used for this procedure. It was found that nerve cells can perceive the concentration of the monomer EDOT (10 mM) for 72 hours retaining 80% of the survived cells. PEDOT could be delivered to the neuronal cells which are present in the tissue sample using 0.5-1.0 mA/mm^2 electrodes. Living cells kept viability in the polymer for 120 hours. The "PEDOT-neuron" composite yielded lower impedance by 1-1.5 order of the magnitude; a significant increase in the capacity of charge delivery was also observed. The application of PEDOT for the development of these hybrid electrode layers is effective to prevent negative effects of short circuits at the electrode- tissue interface.

Meanwhile, several studies have indicated that the PEDOT:PSS films show antibacterial activity. For instance, in the work [22] the biohybrid film (BHF) was prepared by a combination of PEDOT, chitosan and polyvinyl alcohol. To obtain BHF a set of samples were selected by varying the concentrations of chitosan. Poly(vinyl alcohol) is the compound acting as a glue, thereby, improving mechanical properties such as strength of the film. The resultant biohybrid film presented high antibacterial activity in respect to Gram positive bacteria (*Staphylococcus aureus*). The researchers [23] reported a simple strategy for creating an efficient photo thermal nanocomposite based on PEDOT:PSS and agarose. This nanocomposite shows high antibacterial activity against both Gram-positive and Gram-negative bacteria. The exposure of the composition to IR light is related to photo thermal conversions, leading to efficient death of approximately 100% of pathogenic bacteria within 2 minutes. PEDOT with nanoparticles of fluoro hydroxyapatite, distributed uniformly on its matrix to cover orthopedic implants, has also antibacterial effects against Gram-positive and Gram-negative bacteria [24].

To improve the conductivity, PEDOT is frequently modified, as is shown above, by different nanomaterials. Notably, these compositions may have antimicrobial properties. For instance, in the work

[25], nanohybrid coatings on the basis of PEDOT with inclusions of the particles of graphene oxide and modified additionally with poly-diallyldimethylammonium chloride demonstrate (1) low roughness of the surface that prevents bacterial adhesion to surfaces and (2) positive charge that may be efficient in killing the bacteria. These properties are useful in biomedical devices to create cardiovascular stents and surgical devices.

Thus, an addition of different compounds into the PEDOT solution influences the properties in respect to different living cells. The question concerning biocompatibility of the polymer PEDOT:PSS relative to bacterial cells is yet to be answered and needs further exploration.

4. APPLICATIONS OF PEDOT:PSS FILMS IN BIOELECTROCHEMICAL SYSTEMS

4.1. Application of PEDOT:PSS films for the formation of biosensor receptors

Let us consider examples of the use of PEDOT:PSS films for the creation of bioelectrochemical devices. Most frequently, publications focus on the use of PEDOT as a component for the amperometric enzyme-based biosensor. Researchers in [26] suggested a biosensor on the basis of glucose oxidase entrapped in PEDOT-based microcuvettes. A signal was recorded during detection of hydrogen peroxide resulting from the enzymatic reaction. A biosensor had high sensitivity with a rapid signal generation occurring within 20 s. This procedure is universal and can be applied to any enzyme.

The common concept of the field-effect transistor is based around the idea that it is constructed of ceramic and semiconductor materials coated with metal. The study [27] shows that it is possible to develop all-organic field-effect transistors which include elements – channel, source, drain, gate – made from PEDOT:PSS. The combination of PEDOT:PSS and ferrocene, as a mediator, allowed measurement of glucose in the range from 0.001 to 100 mM. The biosensor was successfully applied to detect glucose levels in saliva. In [28], a similar transistor was used to determine both glucose and lactate. For immobilization of the enzymes, a simple, fast and reproduction procedure has been performed based on one-step electrochemical co-deposition of the glucose oxidase enzyme (GOD) or lactate dehydrogenase (LDH) and the particles of *Ni-Al* Layered double hydroxide (**Fig. 2**).

The studies [29,30] reported that grapheme was utilized to modify PEDOT: PSS-based glucose biosensors, and now it is not necessary to use artificial mediators for electron transfer.

PEDOT:PSS is used not only as a component of glucose biosensors, but also in combination with other enzymes. For instance, the study [31] reported on a highly sensitive disposable amperometric biosensor

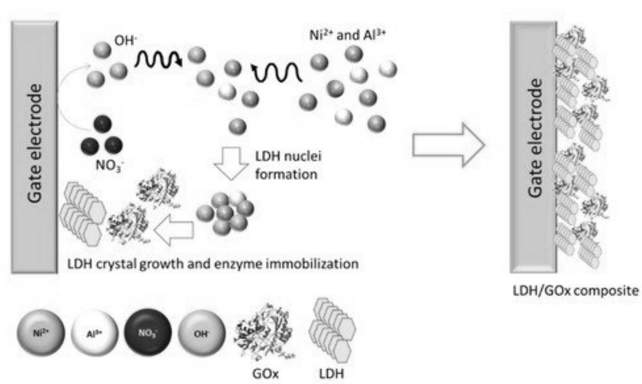

Fig. 2 *Processes occurring at a PEDOT:PSS-based thin films gate electrode; nitrate recovery contributes to an increase in OH level leading to the deposition of the composite of a dual hydroxide/enzyme. Taken out from Gualandi et al, 2020* [28], *under a Creative Commons Attribution 4.0 Internationa; License. Published by Multidisciplinary Digital Publishing Institute (MDPI).*

for detecting triglycerides based on Au/PEDOT:PSS nanocomposite deposited by inkjet-printing on screen-printed graphite electrodes and co-immobilization of lipase, glycerol kinase and glycerol-3-phosphate oxidase. The designed biosensor had a wide detection limit (0–531 mg/dl), its sensitivity was 2.66 μA/mM, a response time was 30 s, and detection limit was as low as 7.88 mg/dL. The work [32] presented an amperometric biosensor based on PEDOT and multi-wall carbon nanotubes for detection of organophosphorus compounds using the enzyme acetylcholinesterase. Detection limit of malathion was 1fM in linear range from 1 fM to 1μM. The study [33] described the formation of a biosensor based on the principle of electrochemiluminescence (ECL) imaging for ethyl alcohol identification. The biosensor was based on the enzyme (alcohol dehydrogenase) immobilized in the matrix from PEDOT:PSS and graphene. Biosensor was applied to detect the concentration of ethanol in real beverages; detection limit was $2.5 \cdot 10^{-6}$ M.

Nafion was used to prepare biocompatible medium for biologically active compounds, to improve adhesion and binding force between the PEDOT:PSS film and the electrode interface, as well as to prevent exfoliation of enzymatic molecules for PEDOT modification in [34]. Ascorbate oxidase was used as a basis of the biosensor. PEDOT modification had pronounced water resistance, preventing sensitive element to be exfoliated from the electrode that is important while carrying out experiments in aqueous media. The biosensor (sensitivity of 158.1μA/mM and detection limit of 0.193 μM) was applied to determine the ascorbic acid content of juices.

PEDOT: PSS is applied not only in enzymatic biosensors, but in the other types of sensors as well, for example, immunosensors. An example of the use of PEDOT:PSS, as a component of immunosensors, is an amperometric device which measures the content of clenbuterol, medical preparation, stimulating the growth in milk [35]. The authors used a competitive scheme of analysis, where horseradish peroxidase enzyme was the label of an antigen. The detection limit for clenbuterol was 0.196 ng/ml. The article [36] described the aptasensor based on electrochemical impedance spectroscopy. The paper electrode was modified with PEDOT: PSS and grapheme to provide conductivity and sensitivity, the surface was then functionalized with amino- and carboxyl groups, and then with aptamers. This biosensor was sensitive to carcinoembryonal antigens in the linear range from 0.77 to 14 ng/ml^{-1}; it would be able to assist in the diagnosis of cancer at an early stage.

Also, the use of matrices based on PEDOT seems to be effective for DNA exploration. Electrochemical DNA biosensors have advantages over conventional techniques due to rapid, precise, highly sensitive and selective signal responses. The work [37] demonstrated that the graphite electrode modified with chitosan and PEDOT was applied to electrochemically detect interaction of DNA with anticancer medical preparation (mitomycin C is an antitumor antibiotics and a strong agent, which is able to crosslink DNA).

4.2. Applications in biofuel cells

The use of PEDOT:PSS polymer in biofuel cells (BFC) would facilitate electron transport in the system and increase the overall efficiency of these devices. So far, only a few variants of BFCs based on PEDOT are described in literature. For example, the study [38] reported that the anode for BFC was produced by successive deposition of layers of carbon, para-benzoquinone, glucose oxidase, and PEDOT. Such an electrode could work both as a glucose biosensor and as a BFC anode. The maximum specific power of such a device depended on the temperature and was equal to 18.9 and 22.5 μW/cm^2 at 25° and 37°*C*, respectively. PEDOT- and grapheme-based anode served as the basis for the immobilization of *Escherichia coli* [39]. A compact biofilm was formed on the hybrid anode due to the electrostatic interaction between negatively charged bacteria and positively charged PEDOT. The maximum power generated by such a BFC was 873 mW/m^2. Researchers [40] suggested to develop a PEDOT:PSS - and sulphonated graphene oxide-based biocompatible BFC anode. Glucose oxidase was used as a biocatalyst. It was shown that similar structure of the anode can be used both in glucose biosensor and in BFC whereas the element generates a high power density of 27±2 мA·cm^{-2}.

In [41], the creation of miniature BFCs that have higher output of electrical energy and shorter time to reach steady state (about 1 hour) is reviewed. Appliance of PEDOT polymer and an anode chamber with a volume of 12 μl is the distinctive feature of such BFC. BFC develops a power of about 423 mW×cm^{-3} and uses unadapted *Shewanella oneidensis* MR-1 bacteria as a model biocatalyst. The paper [42] presents BFCs based on microbial communities of activated sludge, which anodes are covered with chemically polymerized PEDOT films. The use of polymer made it possible to achieve power of 3.5 A/m^2 and increase the degree of wastewater treatment from 51% to 86%.

PEDOT can be used not only for bioanode modification, but also in BFC cathodes. Researchers [43] demonstrated that PEDOT was used to immobilize laccase at the BFC cathode. It was shown that electropolymerization of PEDOT with various alloying additives significantly affects the structural features and morphology of PEDOT films, increasing the active surface of the electrode, and guarantees effective fuel mass transfer through the matrix and, as a result it is a crucial step that determines the cell capacity.

The use of PEDOT enables the creation of BFCs based on flexible electrodes. In [44] PEDOT:PSS was the basis for microbial fuel cell (MFC) made of flexible stretchable fabric. The flexible *Pseudomonas aeruginosa* -based MFC generated the maximum power and current density of 1.0 μW×cm^2 and 6.3 μA/cm^2, respectively, which is comparable to or exceeds similar parameters of a flexible paper-based BFC. Such a device can be easily integrated into the next-generation of flexible electronics to implement low-power and autonomous systems. Such flexible electrodes can be used to create wearable biosensors and BFCs for monitoring human health. Researchers [45] designed a wearable BFC based on *Staphylococcus epidermidis, Staphylococcus capitis* and *Micrococcus luteus* that exist on human skin and eat sweat as a substrate. Prussian blue was used as a mediator of electronic transport, and PEDOT:PSS polymer and dimethylsulfoxide were used to ensure the conductivity and fixation of bacteria, as well as to collect electricity.

Biological fluids can be the basis of power for biofuel cells, which in its turn can be a power source for low-power devices that monitor human health (for example, continuous glucose monitoring) or perform functions that support human life (for example, cardiac pacemaker, neurostimulators, etc.). For example, the study [46] reported that human urine served as a power source for BFC. The BFC anode was a carbon film coated with PEDOT:PSS. The electrodes were inoculated with a mixture of sludge and pure human urine in a periodic mode. The BFC maintained its functionality for more than 90 days generating average stable power of 283.5 μW. Moreover, it was shown that PEDOT:PSS not only improves the electrochemical properties of the electrodes, but also contributes to the growth of the biofilm and, consequently, increases the overall energy characteristics and long-term functionality of the BFC.

5. CONCLUSION

In the present study, we show that the main property of the PEDOT:PSS polymer is low electrical resistance and the majority of the components involved in conjugation with this polymer get it. One of the prior sphere of practical application of PEDOT:PSS is medicine. It is, therefore, not surprisingly, that there is increasing attention paid to the combination of PEDOT:PSS and glucose oxidase – an enzyme used to create biosensors for glucose detection. Notably, combinations of PEDOT:PSS and nanomaterials significantly increase the detection sensitivity and enhance the stability of the electrodes. Applications of different modifications of PEDOT allows for the development of flexible bioelectrochemical devices that can be recommended both for medical and other industrial areas.

The question is still unanswered with regard to the biocompatibility and toxicity of PEDOT. The effects of PEDOT:PSS on neurons in the human brain have been explored and the biocompatibility of the polymer in the cells of the human brain have been shown. Additionally, PEDOT:PSS is used for fabrication of films with high antibacterial activity against Staphylococcus aureus and Escherichia coli.

On the whole, the overall direction to the use of the properties of the PEDOT:PSS polymer aims to improve the quality of life, increase the production efficiency while monitoring the environmental indicators, in other words we give the outlook of this polymer for possible applications in easy-to-follow and positively oriented trends.

REFERENCES

1. Hecht DS, Hu LB, Irvin G. Emerging transparent electrodes based on thin films of carbon nanotubes, graphene, and metallic nanostructures. *Adv. Mater.*, 2013, 23:1482-1513.
2. Chin BD. Role of the polymeric hole injection layer on the efficiency and stability of organic light emitting diodes with small molecular emitters. *J. Phys. D: Appl. Phys,* 2008, 41(21):215104. doi: 10.1088/0022-3727/41/21/215104.
3. Scharber MC, Muhlbacher D, Koppe M, Denk P, Waldauf C, Heeger AJ, Brabec CJ. Design Rules for Donors in Bulk Heterojunction Solar Cells-Towards 10% Energy Conversion Efficiency. *Adv. Mater.*, 2006, 18:789-794.
4. Scott JC, Bozano LD. Nonvolatile Memory Elements Based on Organic Material. *Adv. Mater.*, 2007, 19(11):1452-1463.
5. Pettersson LA, Ghosh S, Inganäs O. Optical anisotropy in thin films of poly(3,4-ethylenedioxythiophene)–poly(4-styrenesulfonate). *Org. Electron,* 2002, 3(3-4):143-148.
6. Kukhto AV, Pochtenny AE, Misevich AV, Kukhto IN, Semenova EM, Vorobyova SA,

Sarantopoulou E. Optical and electrophysical properties of nanocomposites based on PEDOT:PSS and gold/silver nanoparticles. *Phys. Solid State*, 2014, 56(4):827-834.

7. Park HS, Ko SJ, Park JS, Kim JY, Song HK. Redox-active charge carriers of conducting polymers as tuner of conductivity and its potential window. *Sci. Rep.,* 2013, 3(2454):1-6.
8. Yang W, Zhao Y, He X, Chen Y, Xu J, Li S, Jiang Y. Flexible conducting polymer/reduced graphene oxide films: synthesis, characterization, and electrochemical performance. *Nanoscale Res. Lett.,* 2015, 10(1). doi: 10.1186/s11671-015-0932-1.
9. Voronin AS, Simunin MM, Ivanchenko FS, Shiverskii AV, Fadeev YV, Tambasov IA, Nemtsev IV, Matsynin AA, Khartov SV. Preparation and investigation of composite transparent electrodes of poly(3, 4-ethylenedioxythiophene) polystyrene sulfonate/single-wall carbon nanotubes. *Tech. Phys. Lett,* 2017, 43(9):783-786.
10. Ventura IA, Zhou J, Lubineau G. Investigating the Inter-Tube Conduction Mechanism in Polycarbonate Nanocomposites Prepared with Conductive Polymer-Coated Carbon Nanotubes. *Nanoscale Res. Lett.*, 2015, 10:485.
11. Yan H, Zhang P, Li J, Zhao XL, Zhang K, Zhang B. PEDOT/PSS-Halloysite Nanotubes (HNTs) Hybrid Films: Insulating HNTs Enhance Conductivity of the PEDOT/PSS Films. *Sci. Rep.*, 2015, 5:18641.
12. Nizhegorodova AO, Kondratiev VV. Synthesis and electrochemical properties of composite materials based on poly-3,4-ethylenedioxythiophene with manganese dioxide inclusions. *Russ. J. Electrochem.*, 2014, 50(12):1157-1163.
13. Nizhegorodova AO, Apraksin RV, Kondratiev VV. Electrochemical properties of composite materials based on poly-3,4-Ethylenedioxythiophene with nickel oxide inclusions. *Russ. J. Electrochem.*, 2015, 51(10):908-915.
14. Park MU, Lee SM, Chung D. Model system of cross-linked PEDOT:PSS adaptable to an application for an electrode with enhanced water stability. *Synth. Met.*, 2019, 258:116195.
15. Fattahi P, Yang G, Kim G, Abidian MR. A Review of Organic and Inorganic Biomaterials for Neural Interfaces. *Adv Mater*, 2014, 26(12):1846-1885.
16. Karagkiozaki V, Karagiannidis PG, Gioti M, Kavatzikidou P, Georgiou D, Georgaraki E, Logothetidis S. Bioelectronics meets nanomedicine for cardiovascular implants: PEDOT-based nanocoatings for tissue regeneration. *Biochim. et Biophysica Acta*, 2013, 1830:4294-4304.
17. Chikar JA, Hendricks JL, Richardson-Burns SM, Raphael Y, Pfingst BE, Martin DC. The use of a dual PEDOT and RGD-functionalized alginate hydrogel coating to provide sustained drug delivery and improved cochlear implant function. *Biomaterials*, 2012, 33:1982-1990.
18. Richardson-Burns SM, Hendricks JL, Foster B, Povlich LK, Kim DH, Martin DC. Polymerization of the conducting polymer poly(3,4-ethylenedioxythiophene) (PEDOT) around living neural cells. *Biomaterials*, 2007, 28:1539-1552.
19. Venkatraman S, Hendricks JL, Richardson-Burns SM, Jan E, Martin D, Carmena JM. PEDOT coated microelectrode arrays for chronic neural recording and stimulation. 2009, *4th International IEEE/EMBS Conference on Neural Engineering*. doi: 10.1109/ner.2009.5109313.
20. Wilks S. Poly(3,4-ethylene dioxythiophene) (PEDOT) as a micro-neural interface material for electrostimulation. *Front Neuroeng.*, 2009, 2. doi: 10.3389/neuro.16.007.2009.
21. Richardson-Burns SM, Hendricks JL, Martin DC. Electrochemical polymerization of conducting polymers in living neural tissue. *J. Neural Eng.*, 2007, 4(2):6-13.
22. Khan S, Narula AK. Bio-hybrid blended transparent and conductive films

PEDOT:PSS:Chitosan exhibiting electro-active and antibacterial properties. *Eur. Polym. J.,* 2016, 81:161-172.

23. Ko Y, Kim J, Jeong HY, Goomin Kwon, Kim D, Ku M, Yang J, Yamauchi Y, Kim HY, Lee C, You J. Antibacterial poly (3,4-ethylenediox ythiophene):poly(styrene-sulfonate)/agarose nanocomposite hydrogels with thermo-processability and selfhealing. *Carbohydr. Polym.*, 2019, 203:26-34.
24. Madhan Kumar A, Adesina AY, Hussein MA, Ramakrishna S, Al-Aqeeli N, Aktar S, Saravanan S. PEDOT/FHA nanocomposite coatings on newly developed Ti-Nb-Zr implants: Biocompatibility and surface protection against corrosion and bacterial infections. *Mater. Sci. Eng. C*, 2019, doi: 10.1016/j.msec.2019.01.012.
25. Hsu CC, Cheng YW, Liu CC, Peng XY, Yung MC, Liu TY. Anti-Bacterial and Anti-Fouling Capabilities of Poly(3,4-Ethylenedioxythiophene) Derivative Nanohybrid Coatings on SUS316L Stainless Steel by Electrochemical Polymerization. *Polymers,* 2020, 12(7):1467; doi: 10.3390/polym12071467.
26. Park J, Kim HK, Son Y. Glucose biosensor constructed from capped conducting microtubules of PEDOT. *Sens Actuators B Chem,* 2008, 133:244-250.
27. Shim NY, Bernards DA, Macaya DJ, DeFranco JA, Róisín MN, Owens M, Malliaras GG. All-Plastic Electrochemical Transistor for Glucose Sensing Using a Ferrocene Mediator. *Sensors,* 2009, 9:9896-9902.
28. Gualandi I, Tessarolo M, Mariani F, Arcangeli D, Possanzini L, Tonelli D, Scavetta E. Layered Double Hydroxide-Modified Organic Electrochemical Transistor for Glucose and Lactate Biosensing. *Sensors,* 2020, 20(12):3453; doi: 10.3390/s20123453.
29. Wisitsoraat A, Pakapongpan S, Sriprachuabwong C, Phokharatkul D, Sritongkham P, Lomas T, Tuantranont A. Graphene–PEDOT:PSS on screen printed carbon electrode for enzymatic biosensing. J. *Electroanal. Chem.*, 2013, 704:208-213.
30. David M, Barsan MM, Brett CMA, Monica Florescu. Improved glucose label-free biosensor with layer-by-layer architecture and conducting polymer poly(3,4-ethylenedioxythiophene). *Sens Actuators B Chem.*, 2018, 255 (3):3227-3234.
31. Phongphut A, Sriprachuabwong C, Wisitsoraat A, Tuantranont A, Prichanont S, Sritongkham P. A disposable amperometric biosensor based on inkjet-printed Au/PEDOT-PSS nanocomposite for triglyceride determination. *Sens Actuators B Chem,* 2013, 178:501-507.
32. Kaur N, Thakur H, Prabhakar N. Conducting polymer and multi-walled carbon nanotubes nanocomposites based amperometric biosensor for detection of organophosphate. *J. Electroanal. Chem.*, 2016, 775:121-128.
33. Gao Y, Li J, Yang X, Xiang Q, Wang K. Electrochemiluminescence Biosensor Based on PEDOT:PSS-Graphene Functionalized ITO Electrode. *Electroanalysis,* 2014, 26:382-388.
34. Wen Y, Xu J, Li D, Liu M, Kong F, He H. A novel electrochemical biosensing platform based on poly(3,4-ethylenedioxythiophene): poly(styrenesulfonate) composites. *Synth. Met.*, 2012, 162:1308-1314.
35. Talib NAA, Salam F, Sulaiman Y. Development of highly sensitive immunosensor for Clenbuterol detection by using poly(3,4-ethylele dioxythiophene)/graphene oxide modified screen-printed carbon electrode. *Sensors,* 2018, 18:4324-4336.
36. Yen YK, Chao CH, Yeh YS. A Graphene-PEDOT:PSS Modified Paper-Based Aptasensor for Electrochemical Impedance Spectroscopy Detection of Tumor Marker. *Sensors,* 2020, 20:1372.
37. Kuralay F, Demirci S, Kiristi M, Oksuz L, Oksuz AU. Poly(3,4-ethylenedioxythiophene) coated chitosan modified disposable electrodes for DNA and DNA–drug

interaction sensing. *Colloids Surf B Biointerfaces*, 2014, 123: 825-830.

38. Nien PC, Wang JY, Chen PY, Chen LC, Ho KC. Encapsulating benzoquinone and glucose oxidase with a PEDOT film: Application to oxygen-independent glucose sensors and glucose/O_2 biofuel cells. *Bioresour. Technol.*, 2010, 101(14):5480-5486.
39. Wang Y, Zhao C, Sun D, Zhang JR, Zhu JJ. A Graphene/Poly(3,4-ethylenedioxythiophene) Hybrid as an Anode for High-Performance Microbial Fuel Cells. *ChemPlusChem*, 2013, 78:823-829.
40. Inamuddin B, Ahamed MI, Asiri AM, AlAmry KA. Biocompatible mediated bioanode prepared by using poly(3,4-ethylene dioxy thiophene) poly(styrene sulfonate) (PEDOT:PSS) and sulfonated graphene oxide integrated enzyme for biofuel cells applications. **Mat. Sci. for En. Tech**., 2018, 1(1):63-69.
41. Jiang H, Halverson LJ, Dong L. A miniature microbial fuel cell with conducting nanofibers-based 3*D* porous biofilm. *J. Micromech. Microeng.*, 2015, 25:125017.
42. Kang YL, Ibrahim S, Pichiah S. Synergetic effect of conductive polymer poly(3,4-ethylenedioxythiophene) with different structural configuration of anode for microbial fuel cell application. *Bioresour. Technol.*, 2015, 189:364-369.
43. Wang X, Sjöberg-Eerola P, Eriksson JE, Bobacka J, Bergelin M. The effect of counter ions and substrate material on the growth and morphology of poly(3,4-ethylenedioxythiophene) films: Towards the application of enzyme electrode construction in biofuel cells. *Synth. Met.*, 2010, 160(13-14):1373-1381.
44. Pang S, Gao Y, Choi S. Flexible and stretchable microbial fuel cells with modified conductive and hydrophilic textile. *Biosens. Bioelectron.*, 2018, 100:504-511.
45. Mohammadifar M, Tahernia M, Yang JH, Koh A, Choi S. Biopower-on-Skin: Electricity generation from sweat-eating bacteria for self-powered E-Skins. *Nano Energy,* 2020, 104994; doi: 10.1016/j.nanoen.2020.104994.
46. Salar-Garcia MJ, Montilla F, Quijada C, Morallon E, Ieropoulos I. Improving the power performance of urine-fed microbial fuel cells using PEDOT-PSS modified anodes. *Appl. Energy*, 2020, 278:115528; doi: 10.1016/j.apenergy.2020.115528.