

Conjugated Polymers in Bioelectronics

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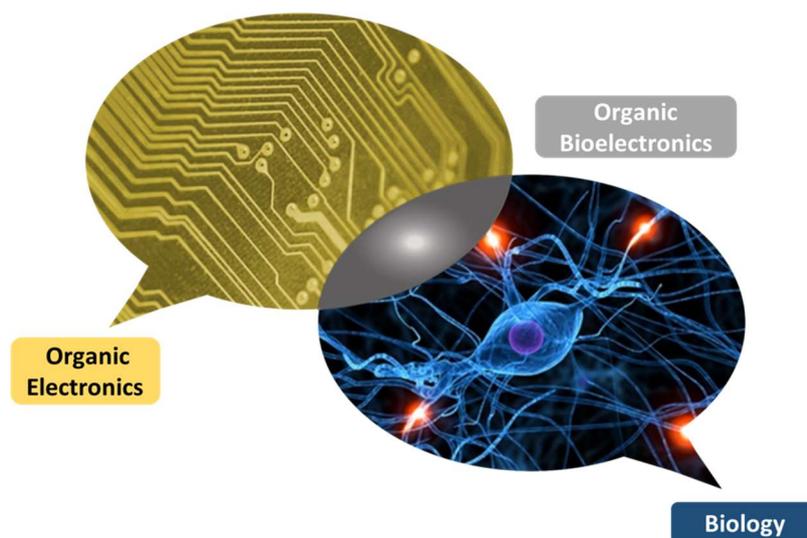
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The emerging field of organic bioelectronics bridges the electronic world of organic semiconductor-based devices with the soft, predominantly ionic world of biology. This crosstalk can occur in both directions; for example, a biochemical reaction may change the doping state of an organic material generating an electronic read-out. Conversely, an electronic signal from a device may stimulate a biological event. Cutting-edge research in this field results in the development of a broad variety of meaningful applications, from biosensors and drug delivery systems to health monitoring devices and brain/machine interfaces. Conjugated polymers share similarities in chemical “nature” with biological molecules, can be engineered on various forms, including hydrogels that have Young’s moduli similar to soft tissues and are ionically conducting. The structure of organic materials can be tuned through synthetic chemistry, and their biological properties can be controlled using a variety of functionalization strategies. Finally, organics electronic materials can be integrated with a variety of mechanical supports giving rise to devices with form factors that enable integration with biological systems. Whilst these developments are innovative and promising, it is important to note that the field is still in its infancy, with many unknowns and immense scope for exploration and highly collaborative research. The first part of this account details the unique properties that render conjugated polymers as excellent biointerfacing materials. We then offer an overview of the most common conjugated polymers that have been used as active layers in various organic bioelectronics devices, highlighting the importance of developing new materials. These materials are the most popular ethylenedioxythiophene derivatives as well as conjugated polyelectrolytes and ion-free organic semiconductors functionalized for the biological interface. We then discuss several applications and operation principles of the state of the art bioelectronics devices. These devices include electrodes applied to sense/trigger electrophysiological activity of cells as well as electrolyte gated field effect and electrochemical transistors used for sensing biochemical markers. Another prime application

example of conjugated polymers is cell actuators. Modulating externally the redox state of the underlying conjugated polymer films controls the adhesion behavior and viability of cells. These smart surfaces can be also designed in the form of three dimensional architectures owing to the processibility of conjugated polymers. As such, cell loaded scaffolds based on electroactive polymers enable integrated sensing or stimulation within the engineered tissue itself. A last application example is organic neuromorphic devices, an alternative computing architecture that takes inspiration from biology, and in particular from the way the brain works. Leveraging ion redistribution inside conjugated polymer upon an electrical field and its coupling with electronic charges, conjugated polymers can be engineered to act as an artificial neuron or synapse with complex, history-dependent behavior. We conclude our account by highlighting main factors that need to be considered for the design of a conjugated polymer for applications in bioelectronics - although there can be various figures of merit given the broad range of applications as emphasized in this account.



Introduction

The interfacing of living systems with modern microelectronics represents humankind's most aspirational endeavour; one that impacts a broad range of fields from philosophy (origins of consciousness) to medicine (new tools for treating disease and disability). Starting with the work of Galvani in the 18th century, experiments with electricity and living tissues shed light into the workings of the brain, led to the development of implantable electronic devices such as the cardiac pacemaker and the cochlear implant, and inspired "neuromorphic" concepts in information processing. Today, brain/machine interfaces that control prosthetic limbs are being developed for people with limited mobility, and deep-brain stimulation is increasingly being used as a treatment for the symptoms of Parkinson's disease. *In vitro* systems in which electronics interface with cell cultures and intact tissues are being developed as alternatives to animal testing used in drug screening and pre-clinical trials. At the same time, the pharmaceutical industry is beginning to explore "bioelectronic medicines", aiming to replace systemic administration of certain drugs with electrical stimulation from implanted devices. Further into the future, electronic tattoos will monitor our health on a continuous basis, providing a wealth of data that will revolutionize medicine and help personalize disease treatment.

Key to these technologies is the high-quality interface between tissue and electronics. Current technologies use inorganic materials such as metals and ceramics, which means that major incompatibilities exist in terms of chemical structure (organic *vs.* inorganic) as well as mechanical (low *vs.* high Young's modulus) and electrical (ionic *vs.* electronic conduction) properties at the two sides of this interface. These differences limit the information transfer between the disciplines of biology and electronics and diminish the scope and lifetime of bioelectronic systems. Organic electronic materials have been proposed as a solution to these issues (Figure 1).¹ They share similarities in chemical "nature" with biological molecules, can

be engineered on various forms, including hydrogels that have Young's moduli similar to soft tissues and are ionically conducting. Furthermore, the structure of organics can be tuned through synthetic chemistry, and their biological properties can be controlled using a variety of functionalization strategies. Finally, organics electronic materials can be integrated with a variety of mechanical supports giving rise to devices with form factors (conformable, stretchable, fibrous, 3D porous) that enable integration with biological systems. A variety of devices that use organic electronic materials and therefore take advantage of these features have already been described (Figure 1): One prominent example is conducting polymer electrodes, which are being developed for applications in electrophysiology.^{2,3} The same materials are also being used as electrically-active tissue engineering scaffolds that control protein conformation and cell adhesion and function.⁴ Organic thin film transistors take advantage of signal amplification to deliver powerful biosensors.⁵⁻⁷ Organic electronic ion pumps leverage the mixed electronic/ionic conductivity of organic materials to achieve drug delivery with exquisite spatiotemporal control.^{8,9} The same property of mixed conductivity leads to devices with "neuromorphic" behaviour that enable new ways to process and store information.^{10,11}

Although a few of the devices mentioned above utilise small molecules (for example, the organic field-effect transistors), the majority of work has been on conjugated polymers (CPs) in either intentionally doped or pristine form. This is probably due to the fact that CPs can be processed in forms (hydrogels, fibers, 3D scaffolds) that facilitate the interface with biology, while maintaining their electrical properties. In this review, therefore, we focus on CPs and discuss their synthesis, properties and some of the applications in bioelectronics.

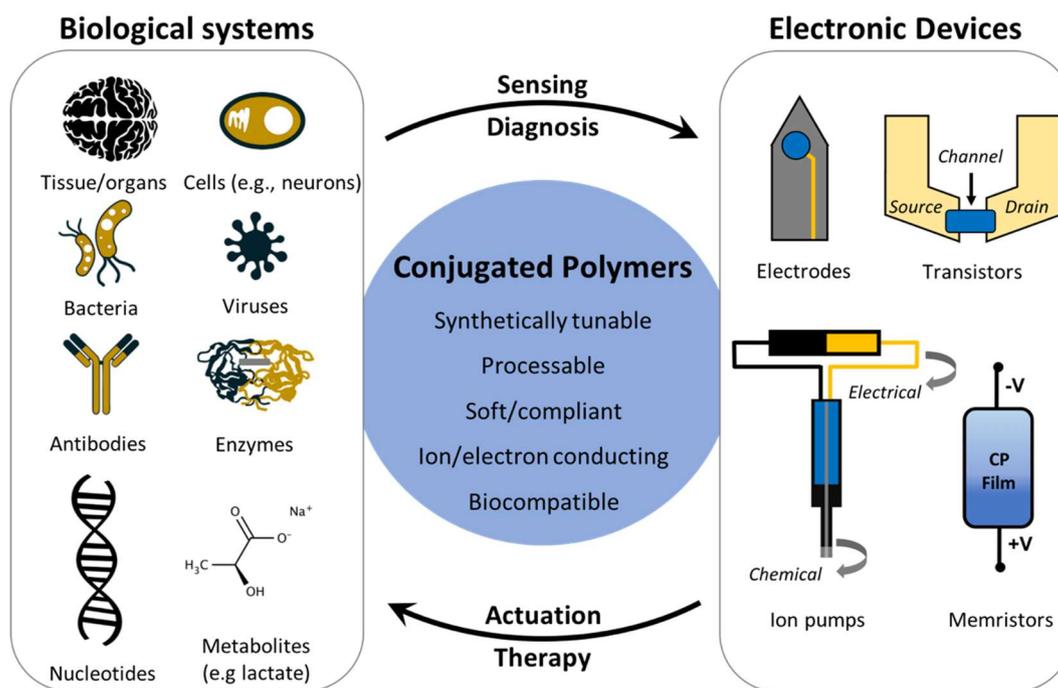


Figure 1. The unique set of properties of conjugated polymers which lead to state of the art devices used for sensing or actuation.

What makes CPs promising for bio-interfacing?

CPs comprise of planar, rigid aromatic repeat units, which typically template an extended, ribbon-like macromolecular conformation. Thin film microstructure facilitates electronic coupling between chains, essential for charge transport, arising from a combination of relatively weak Van der Waals intermolecular associations from both side chains and aromatic π stacking, as well as both dipolar interactions and electrostatic forces (when doping is present). This renders them as “soft” materials, in contrast to “hard” silicon which forms three dimensional networks of strong, rigid covalent bonds. This soft nature of organics contributes to their tendency to swell in aqueous environment and to the mechanical compatibility with biological systems, but also enables low-temperature, solution processing particularly beneficial for processing the material with biological entities such as enzymes, which would otherwise easily denature under extreme conditions. Material processing can be performed by

a variety of techniques such as spin coating, bar coating, printing and vapour phase deposition. The mechanical softness allows fabrication of bendable, stretchable devices on a wide range of substrates, from glass and plastics to textiles and even paper. Moreover, thin films of CPs can be transparent, which opens up access to optical analysis techniques.

CPs allow control of chemical structure and film morphology in order to build specific properties into the material itself. Basic structures can be thought of as a blank canvas, and chemists conveniently have access to a wide palette of “brushes” to conceive tailored molecular designs starting from a wide library of polymeric structures. For instance, their compatibility with biological systems can be further optimised if necessary by either integrating biomolecules into the conjugated backbone to enable specific associations with proteins/cells or by choosing naturally occurring materials such as indigo derivatives or carotenoids as starting points in the synthesis of complex organic bioelectroactive materials. Additionally, they can be functionalised to allow for adhesion to artificial substrates. The polarity of charge transport, on the other hand, can be controlled by chemical manipulation of the frontier molecular orbital energy levels of the conjugated electron system. Thin film morphology, subsequently the transport properties, can be dictated through the size and shape of the side chains, while their composition can also determine aqueous and ionic uptake.

Biological events involve controlled ionic fluxes in an aqueous environment. Constructing devices that sense or trigger biological events therefore requires the use of materials that are not only biocompatible and soft, but also transduce biological signals into electrical ones and vice versa. Once doped, CPs can transport hole carriers (p-type), electron carriers (n-type) or they can be classified as ambipolar (supporting the transport of both carriers). Importantly, they can also transport ionic carriers (cations and anions). In fact, the ions taken up by the film from the aqueous media (which is the biological fluid) change electronic (and physicochemical) properties of the CP dramatically and reversibly (within the electrochemical window imparted

by the electrolyte), the process known as electrochemical doping/dedoping. The mobility of ions in the film is facilitated when the CP provides regions for transport that can be hydrated. Efficient ion penetration close to the polymer backbone is enhanced by coulombic attraction from the high polaron density of the conjugated systems. Polaron formation in the CP can significantly distort the local molecular environment, with subsequent effect on film microstructure; this means that any modification on charge density (e.g. through ionic uptake) tremendously affects morphology and electronic properties, in contrast to inorganics, where rigid covalent lattices are not affected by such changes. Upon modification of redox state, the films typically undergo expansion and contraction. This translates into further rationale for the design of water-swelling CPs, given that large free volumes result in an improved ability to accommodate ions and biomolecules and ultimately promote efficient ion transduction.

Current Conjugated Polymers

As is often the case with emerging technologies, the lack of appropriate materials limits applications. For the field of organic bioelectronics, the range of materials is in fact quite narrow, i.e., most of the devices so far rely on well-established CPs such as polypyrrole (Ppy), polyaniline and, predominantly, polythiophene derivatives such as the poly(3,4-ethylenedioxythiophene) doped with poly(styrenesulfonate) (PEDOT:PSS) (Figure 2a-c). Early use of CPs was largely based on Ppy and anilines, however, these materials were found to be relatively unstable and easily over-oxidized. The films tend to be brittle/rigid and the insolubility of the polymer in organic solvents has limited their wide range use. These limitations have promoted polymers based on the EDOT repeat unit, where the di-oxy bridge protects and stabilizes the aromatic thiophene ring from irreversible oxidation – as these materials are often exposed to aqueous environments rich in oxidative species and need to support significant charge densities or current injection, stability to overoxidation is a necessary requirement that has vaulted PEDOT-based polymers to organic bioelectronic popularity.

PEDOT was first developed as an antistatic coating,¹² but has received attention in the organic electronic community as a transparent conductor or electrochromic material. Another reason for the current popularity of PEDOT in bioelectronics, is that it is readily available from a number of commercial vendors as a monomer, dispersion (at various grades and ratios with polyanions), and in the form of pre-cast films under a number of trade names. In addition, it can be processed through various deposition techniques such as electrochemical polymerization, vapor phase polymerization (VPP), allowing for integration into a wide range of pre-existing fabrication protocols/procedures.

PEDOT derivatives

Due to its high conductivity and electrochemical stability, substantial work has been carried out in extending the PEDOT family. Through electrochemical polymerization, the dopant (stabilizing anion) could be modified by changing the medium in which electropolymerization is performed. Conducting films with different morphologies as well as electrical and mechanical properties can be obtained by varying the anion type, the solvent in which the polymerization takes place.^{13,14} Most commonly, chloride anions, as well as small molecular anions such as tosylate, or polyanions such as PSS were employed. A variety of negatively charged biomolecular agents such as synthetic lipids, sugars, and laminin peptides and even living cells can be incorporated into the network during electrochemical synthesis of PEDOT.¹⁴⁻¹⁶ VPP has also been employed,¹⁷ whereby an Fe(III) salt is coated on a surface, and exposed to EDOT vapor in order to oxidatively polymerize the PEDOT film. In this case, other molecules such as gelatin, PEG, enzymes can be included in the precursor solution and thus VPP provides a facile way to make functional composite films.¹⁸ Chemically reactive groups can also be introduced to the EDOT monomer itself, acting as a synthetic reaction site to add additional functionalities to the backbone.^{19,20}

Amongst the most popular formats are commercially available dispersions, including the format of choice in bioelectronics, PEDOT synthesized in the presence of PSS which is incorporated into the polymer to compensate the positively charged PEDOT (PEDOT:PSS). These inks can be purchased, pre-formulated to appropriate viscosity for printing, and coated over large areas. Addition of co-solvents, dopants, and crosslinkers to the (oxidatively) synthesized dispersions modulates mixed conductivity,²¹ and stability in aqueous environments. However, while PEDOT:PSS has series of useful advantages, it does not allow for further bespoke optimization and tailoring for specific applications. Furthermore, its high acidity hinders processing via different techniques such as inkjet printing. Moreover, since the macromolecular colloid has structural complexity, it is unable to act as a model system to study for extracting molecular design criteria that can link chemical structure to device performance. These considerations motivate alternative synthetic approaches to develop CPs with optimized properties.

Conjugated polyelectrolytes

Typical CPs doped with anions are composite materials comprising hole and cation conducting phases. Conjugated polyelectrolytes (CPEs), on the other hand, are single component mixed conductors that constitute charged groups covalently attached to the conjugated backbone. The CPEs are semiconducting when the pendant ions are compensated by counter ions or conducting when compensated by an electronic charge injected onto the conjugated backbone. PEDOT:S is such a CPE with pendant sulfonate group anchored onto the PEDOT backbone (Figure 2d). Due to the presence of the two oxygens whose lone pairs can stabilize the holes, the polymer film is in a conducting state. This polymer can be integrated into liposomes and in lipid bilayers on solid surfaces when combined with alkyl-ammonium salts enabling electronic conduction within lipid membranes.²² The same CPE was applied into a rose stem imparting its conductivity to the plant,²³ or used to manipulate attachment of cells cultured on the polymer

surface as a result of a change of its oxidation state/intake of charge-compensating ions as explained in the next section.²⁴ Another anionic CPE, in this case a polythiophene with a pendant sulfonate group, gives rise to a high performance accumulation mode organic electrochemical transistor (OECT) operating in aqueous media (Figure 2e).²⁵ Accumulation mode OECTs are promising for biosensing applications, where the electrochemical doping of the polymer, i.e. increase of its conductivity, is due to detection of a biological event/molecule.

Ion-free organic semiconductors

Side chain functionalization of high mobility CPs with nonionic polar groups, e.g. ethylene glycol side chains, allows for ion injection/transport (Figure 2f).²⁶ The efficient ion-to-electron conversion makes such polymers promising to use at the interface with biological systems. Transistors based on these semiconductors exhibited performances outpacing that of PEDOT-based OECTs of the same geometry.²⁷ Using a similar approach of side chain functionalization, a naphthalene-1,4,5,8-tetracarboxylic diimide and bithiophene copolymer was developed, exhibiting electron transport (Figure 2g). Ambipolar OECTs made thereof exhibited a record high stability in aqueous media.²⁸

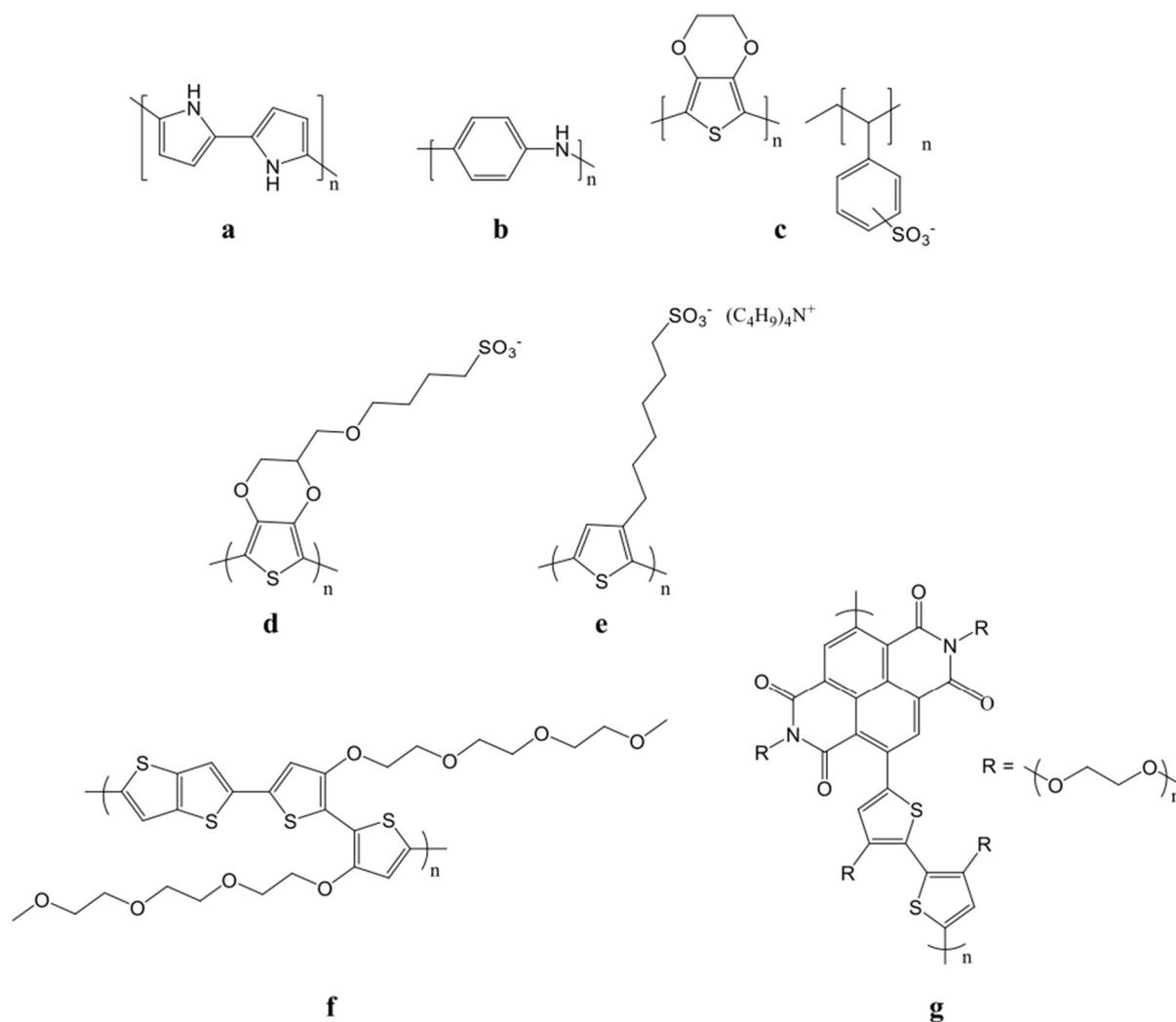


Figure 2. Current CPs in bioelectronics **a)** Ppy, **b)** polyaniline, **c)** PEDOT:PSS, **d)** PEDOT-S, **e)** PTHS, **f)** p(g2T-TT), **g)** p(gNDI-g2T)

Selected Applications of CPs in Bioelectronics

Electrodes, EGOFETs and OECTs applied as bio-chemo sensors

Electrodes coated with doped CPs are a common implementation for bio-interfacing. In most cases they are used to record local changes in potential – and thus are non-specific bioelectronic sensors, although they have been used in recording potential dependent oxidation/reduction of biomolecular species (i.e. fast scan cyclic voltammetry). Largely, this implementation of CPs

is similar to that of other recording electrodes, whereby specificity can be imparted by addition of a transduction layer or functionalization layer (i.e. ion selective membrane, or antibody). The fact that ionic species can readily penetrate the bulk of the film, and electronic carriers can be transported through the bulk, means that the effective capacitance of the film can often be two orders of magnitude higher than the capacitance of a similarly sized flat metallic electrodes, dictated by the accumulation of an electrical double layer. The need for facile collection of electronic charges means that this material must be conducting— limiting such materials to CPs such as PEDOT:PSS. Their utility, freedom of deposition, facile functionalization, and low impedance has allowed for high quality recordings of electrophysiological signals with high signal-to-noise as microelectrodes (Figure 3a),²⁹ and has enabled small-footprint, high current injection efficiency for electrical stimulation.³⁰

Whereas electrodes are considered passive components for biosensors, transistors have been targeted as means to locally amplify and transduce biological signals. These devices consist of a channel (consisting of an intrinsic or doped semiconductor), through which a drain current passes. A change in the sensing environment, either a direct change in gate potential (i.e. the firing of an electroactive cell, or an enzymatic reaction), or a change in charge accumulation or local impedance that would in turn influence the gate current or effective gate bias at the channel, modulates the current through the channel. The efficiency or sensitivity of the sensor is thus defined by the magnitude of current change in response to the change in effective gate bias (this is called the transconductance).

When the channel is in direct contact with a sensing environment which is externally gated, the transistor is said to be “electrolyte gated”. While inspired by traditional ion selective or biosensing inorganic transistors, these transistors with a channel comprising of organic materials roughly fall into two main classes: electrolyte-gated organic field effect transistors (EGOFETs), and OECTs. EGOFETs are usually formed from more traditional organic

electronic polymers and small molecules – they are functionalized at either the gate-electrode/electrolyte interface, the channel/electrolyte interface, or buried underneath the channel material – leading to multiple modes of functionalization and sensitivity.⁶ While EGFETs rely on accumulation of charges at the electrolyte/channel interface, OECTs operate through bulk changes in channel conductivity, leading to an extremely high transconductance dictated by volumetric capacitance. These devices can be functionalized similar to EGFETs, and thus can be used ion selective, biomolecular/enzymatic sensors, and as sensors of electrophysiological activity (Figure 3b and c).^{5,31-33} From a materials perspective, OECT materials can be either doped, or intrinsic, but they should possess high volumetric capacity, and should not pose a significant barrier for ion injection.³⁴

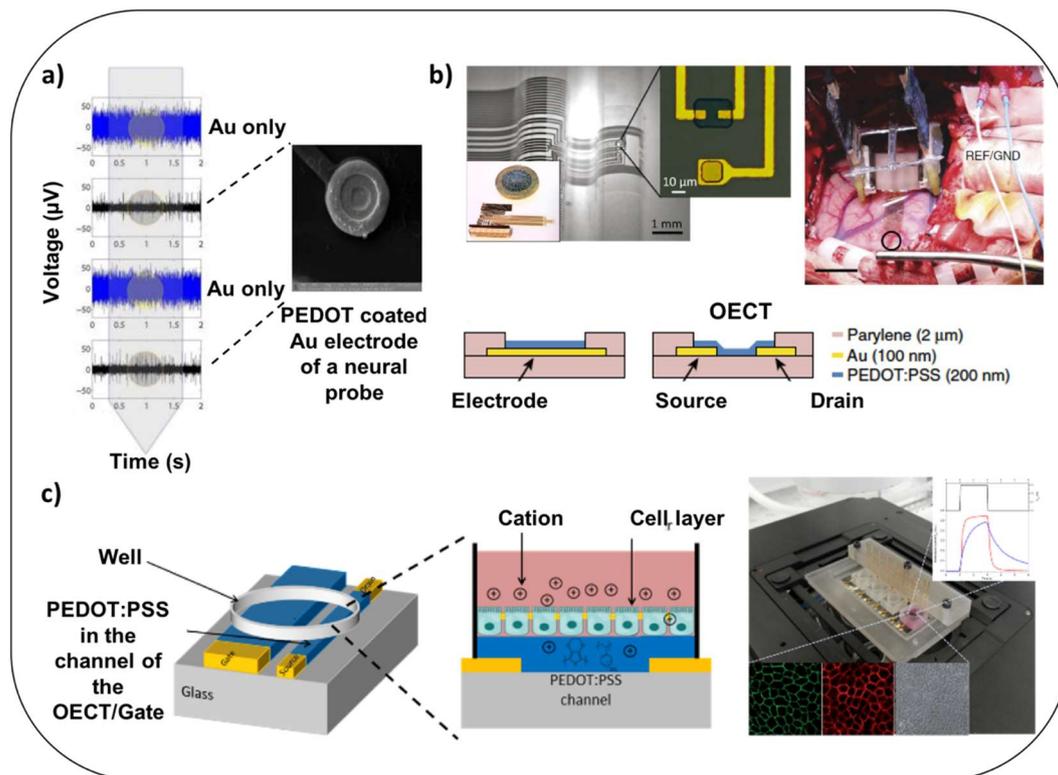


Figure 3. (a) PEDOT coated Au electrodes of a neural probe exhibit lower noise floor than bare electrodes,²⁹ (b) an OECT and organic electrode array on a flexible substrate to measure

activity of cortical neurons as well as the surgical placement of the electrode array on the surface of human brain,^{31,32} (c) OECT measuring the health of cells *in vitro*.³³

Bioactive/electro-responsive surfaces and Tissue engineering scaffolds

In most cases, organic bioelectronic devices are based on solution cast thin films of CPs, similar to biopolymer coatings used in cell culture studies which encourage cells to adhere and differentiate *in vitro*. The nature of the surface, such as its softness or the topography, onto which cells adhere affects biological signaling pathways. For instance, when the surface is a synthetic material that is unknown to cells, proteins such as integrins, used by cells to interact with a surface, or multi-adhesive matrix proteins such as fibronectin may induce signaling pathways triggering cell death. CPs can reversibly undergo changes in physicochemical properties (such as the pH, wettability and roughness) both in the bulk and surface as their electrochemical state is switched. This renders CPs quite unique for interfacing with cells as while they can be used to electrically stimulate cells (electric fields can guide the development and regeneration of many tissues), the modulation of physicochemical properties of the films gives an indirect tool to change the adhesion behavior of cells. In fact, neurite length and branching in primary neuronal cultures were improved by CP based electrical stimulation (Figure 4a).³⁵ When cell growth factors were incorporated into CP films, they can be released to trigger neurite growth factor upon electrical stimulation (Figure 4b).³⁶ Seminal work on CP-cell interactions demonstrated that the adhesion of bovine aortic endothelial cells depended on the redox state of the underlying Ppy coated surface.³⁷ This phenomenon, i.e. cells distinguish between oxidized and reduced surfaces of CPs, was shown with other cell types and CP films as well.³⁸ One of the commonly proposed mechanisms is related to the change in the pH of the film surface upon electrochemical reduction/oxidation, which in turn changes the conformation and adsorption of proteins present in the extracellular matrix (ECM), specifically that of the

fibronectin, an adhesive glycoprotein crucial for cell attachment to substrates (Figure 4c and d).³⁹

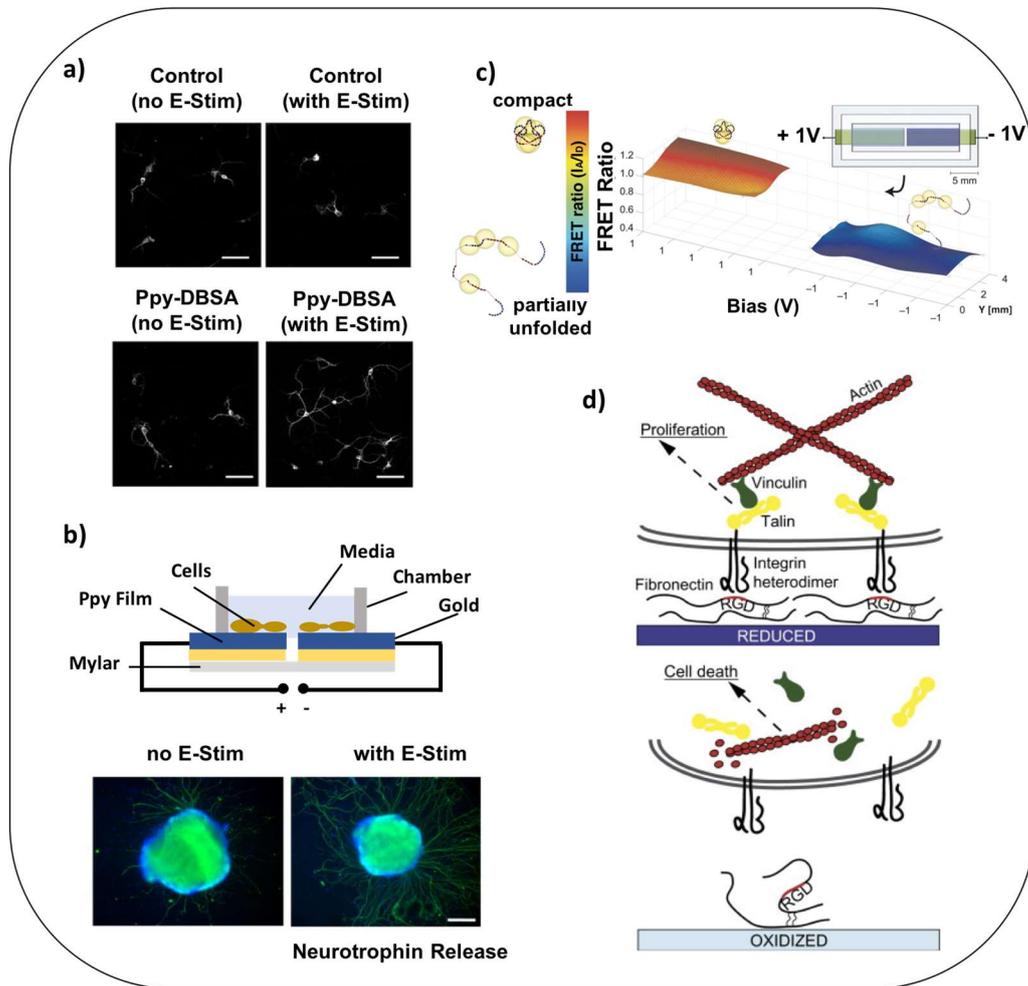


Figure 4. (a) Electrical stimulation using a Ppy film improved neurite growth in primary cortical neurons,³⁵ (b) a similar film releases incorporated neurotrophins when stimulated, improving neurite outgrowth from cochlear neural explants,³⁶ (c) the redox state of a CP film modulates the protein conformation,³⁹ (d) as well as cell attachment and viability.³⁸

In the last decade, concerns related to the physiological relevance of 2D cell culture models accelerated work on 3D analogues which can replace the CP films deposited on planar substrates. As the non-cellular component of the tissue, ECM provides physical scaffolding to cells and organizes them into a functional tissue with a unique topography and composition,

providing necessary biochemical cues for cells to function. As well as their soft nature and low-to-absent toxicity, when CPs are processed to have a porous architecture that enables a support for 3D cell growth, they have potential to mimic the ECM. For instance, a poly(lactic-co-glycolic acid) fibrous scaffold coated with Ppy delivered electrical as well as mechanical stimulation (based on the volume change of CP as a result of electrochemical switch) to human pluripotent stem cells.⁴⁰ This electroactive scaffold demonstrated an increased expression of cardiac markers for stimulated as well as unstimulated protocols. As such, even without using the stimulation function, the inherent electrical conductivity CPs can enable an ideal environment to engineer 3D tissue constructs especially for electrogenic cells, that can, for instance, be used to replace malfunctioning heart tissue.

Recent synthetic efforts focused on developing single component CP hydrogels that combine electrical conductivity with the mechanical properties of swollen hydrogels.⁴¹ Alternatively, pores were created inside a thick CP solid using an ice-templating method (Figure 5a, i).⁴ The redox state of such scaffolds, switched prior to cell culture, determined the conformation of adsorbed fibronectin of the ECM, and consequently the number of adhered cells, an effect pronounced more in the 3D environment compared to the planar case. Nevertheless, an optimized electrical stimulation protocol using the scaffolds that can lead to pronounced or specific effects on cell behavior is yet to be developed. Moreover, utilizing the CP scaffold as an electrode for sensing cellular signals in 3D has been only recently explored (Figure 5a, ii).⁴²

Neuromorphic Devices

Traditional computers are based on the von Neumann architecture, in which processing and storage of information take place at physically separated structures. This introduces the so-called von-Neumann bottleneck which sets an upper limit to the performance that can be achieved. An alternative computing architecture takes inspiration from biology, and in

particular from the way the brain works, and is hence called “neuromorphic”. According to this architecture, information is stored in the same “unit” that processes it, and this “unit” can be a circuit on a chip, or an individual device. The latter concept, in which the device itself acts as an artificial neuron or synapse and exhibits complex, history-dependent behaviour, is particularly useful because it can lead to very high integration density. Quite naturally, organic neuromorphic devices also became available, with an emphasis soon shifted to designs that leverage the coupling of ionic and electronic charges in CP films. Ion redistribution inside these layers (which corresponds to the “storage” function) affects their local doping state, and subsequently the electronic current that flows through the device (the “processing” function). The first example was an OECT based on a polyaniline channel and a solid electrolyte.⁴³ The injection of ions in the channel caused hysteretic behaviour that was dependent on bias history. Subsequent work built on this concept and explored the realization of neural networks using these devices.⁴⁴ Neuromorphic signal processing was demonstrated in PEDOT:PSS OECTs with liquid electrolytes,⁴⁵ and a vapour phase polymerized PEDOT composite demonstrated plasticity functions (Figure 5b, i).⁴⁶ An architecture combining design elements from a battery and an OECT showed very long memory retention time (Figure 5b, ii).¹⁰

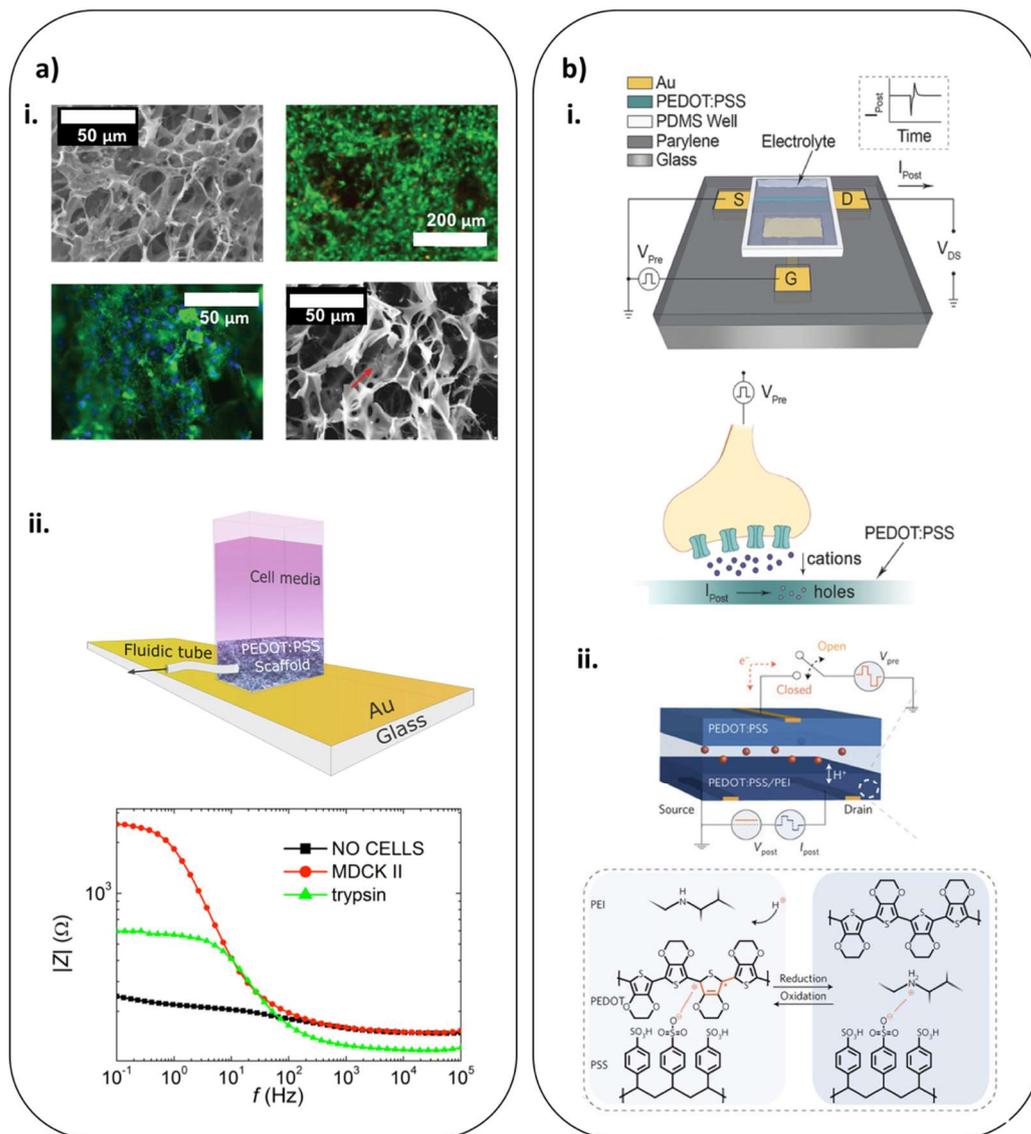


Figure 5. (a) a CP macroporous scaffold hosts mammalian cell culture in 3D (i),⁴ and can be used as an impedance sensor of cell growth (ii).⁴² (b) short-term synaptic plasticity with OECTs (i),⁴⁵ an OECT as a low-voltage artificial synapse for neuromorphic computing (ii).¹⁰

Conclusions and perspectives

Given the broad range of applications, there is a great variety of figures of merit that can help guide materials development. In neural electrodes, for example, a low electrochemical impedance is sought, and this can be achieved using highly doped (conducting) polymers that offer high electronic and ionic conductivity. In field-effect transistors on the other hand, a high

ON/OFF ratio plays a key role in signal transduction, and this can be achieved with semiconducting small molecules that form crystalline films with a high hole mobility and low doping concentrations. In addition to electronic properties, mechanical and biological properties must also be considered. Moreover, bioelectronics implies the use of devices as opposed to just materials, meaning that appropriate substrates, contacts, interconnects need to be considered and the “active” organic electronic material must be compatible with the constraints introduced by these. By definition, the environment in which bioelectronic device operate is radically different than that encountered in applications such as displays and energy harvesting. The devices will come in contact with aqueous solutions with a high salt concentration, which are corrosive to traditional electronic materials. Some applications will only require transient operation (cutaneous monitoring), while others might require several years of lifetime *in vivo* (implantable stimulators). Long-term operational and shelf stability are particularly relevant to organic bioelectronics materials, as the devices need to maintain their performance for a sustained period and successfully face the challenge of interfacing with complex biological systems. For example, from a synthetic point of view, the morphological stability of organic materials can be improved by post deposition cross-linking or by the introduction of non-covalent intermolecular interactions. Synthetic approaches to polymerisation of bioelectronic polymers also need to include tolerance to either biological functionality incorporated in the monomers or include a reactive group capable of efficient functionalisation with biological functionality in a post polymerisation reaction. The challenge of purification and employment of soft, hygroscopic, ethylene glycol oligomers, typically used as polymer side chains, in catalytic reactions, where they often chelate and suppress catalytic function must also be solved. Finally, the regulatory framework, which makes it difficult to introduce new materials to the clinic, should also be considered. All these factors need to be

taken into account before designing a new material and will pave the way for new CP structures for high performance devices for biology.

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