ELECTROCHEMICALLY POLYMERIZED
CONJUGATED POLYMER FILMS:
STABILITY IMPROVEMENT AND
SURFACE FUNCTIONALIZATION

by

Bin Wei

A dissertation submitted to the Faculty of the University of Delaware in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Materials Science and Engineering

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ABSTRACT

Conjugated polymers have been widely used in various applications including organic solar cells, electrochromic devices, chemical sensors, and biomedical devices. Poly(3,4-ethylenedioxythiophene) (PEDOT) and its derivatives have received considerable interest because of their low oxidation potential, relatively high chemical stability, and high conductivity. Electrochemical deposition is a convenient method for precisely fabricating conjugated polymer thin films. Here, we report the stability improvement and surface functionalization of electrochemically polymerized PEDOT films.

The long-term performance of PEDOT coatings is limited by their relatively poor stability on various inorganic substrates. Two different methods were used to improve the stability of PEDOT coatings, one involved using carboxylic acid functionalized EDOT (EDOT-acid) as adhesion promoter. EDOT-acid molecules were chemically bonded onto activated metal oxide substrates via chemisorption. PEDOT was then polymerized onto the EDOT-acid modified substrates, forming covalently bonded coatings. An aggressive ultrasonication test confirmed the significantly improved adhesion of the PEDOT films on electrodes with EDOT-acid treatment over those without treatment.

The other method was to use an octa-ProDOT-functionalized POSS derivative (POSSProDOT) as cross-linker. PEDOT copolymer films were electrochemically deposited with various concentrations of POSS-ProDOT. The optical, morphological and electrochemical properties of the copolymer films could be systematically tuned.
with the incorporation of POSS-ProDOT. Significantly enhanced electrochemical and mechanical stability of the copolymers were observed at intermediate levels of POSS-ProDOT content (3.1 wt%) via chronic stimulation tests.

Surface functionalization of conducting polymer films provides a potential means for systematically tailoring their chemical and physical properties. We have synthesized, polymerized and characterized a dialkene-functionalized variant of the ProDOT monomer. With the alkene side groups, highly efficient post-polymerization functionalization of the conducting film was successfully achieved via a radical-based thiol-ene “click” reaction with various terminal thiols, including alkanes, ethylene glycols, and ferrocenes. These surface modification led to dramatic changes in the charge transport and wetting behavior of the chemically functionalized films.
Chapter 1

INTRODUCTION

1.1 Conjugated Polymers and Electrochemical Polymerization – Background

1.1.1 Conjugated Polymers

Conjugated polymers have gained considerable interest in a wide range of applications, such as organic solar cells, light-emitting diodes, electrochromic devices, biosensors and neural interfaces because of their outstanding physical, chemical, and electrical properties. These polymers are organic macromolecules consisting of alternating single and double bonds along their chain backbones. The $p_z$ orbital left from the sp$^2$ hybridization of each carbon atom combines with the neighboring atom along the chain, resulting in a large delocalized $\pi$-conjugated system that facilitates intermolecular charge conduction as well as relatively easy lateral charge hopping between molecules. Like inorganic semiconductors, conjugated polymers can exist in either undoped (neutral) or doped (oxidized or reduced) states. Conjugated polymers in their undoped state are semiconductors or insulators with a low electrical conductivity of around $10^{-10}$ to $10^{-8}$ S/cm due to the relatively high energy gap (~2 eV) between HOMO and LUMO. Upon doping, the electrical conductivity can be increased by several orders of magnitude with values around $10^2$-$10^4$ S/cm. Since the discovery of highly conductive polyacetylene in 1977 by Heeger and coworkers, many other conjugated polymers have been designed and synthesized (Figure 1.1), including polyaniline (PANI), polyphenylene,
polyphenylenevinylene,\textsuperscript{17} polypyrrole (PPy),\textsuperscript{18} polythiophene (PTh)\textsuperscript{19} and poly(3,4-alkylenedioxythiophenes) (PEDOT and PProDOT).\textsuperscript{20}

\begin{center}
\begin{tabular}{c}
polyacetylene \\
polyphenylenevinylene \\
polypyrrole \\
polythiophene \\
poly(3,4-ethylenedioxythiophene) \\
poly(3,4-propylenedioxythiophene) \\
PEDOT \\
PProDOT
\end{tabular}
\end{center}

Figure 1.1 Monomer chemical structures of common conjugated polymers.

1.1.2 Electrochemical Polymerization

Conjugated polymers can be synthesized either chemically,\textsuperscript{21} by oxidative polymerization or organometallic condensation polymerization, or electrochemically \textsuperscript{22} by electrochemical polymerization. For chemical oxidative polymerization, an oxidant such as FeCl\textsubscript{3} or (NH\textsubscript{4})\textsubscript{2}S\textsubscript{2}O\textsubscript{8} is used to oxidize and polymerize the monomer.\textsuperscript{23,24} For organometallic condensation polymerization, a metal-based catalyst such as palladium (Pd) is used to catalyze the coupling reactions, e.g. Suzuki coupling, Heck coupling, and Sonogashira coupling.\textsuperscript{25} Since chemical polymerization is usually carried out in solution, a polymer solution or insoluble bulk solids will be obtained
depending on the solubility of the final polymer. Though chemical polymerization provides many different routes to synthesize a variety of conjugated polymers and permits the facile scale-up of these materials, electrochemical synthesis is a straightforward method that can be readily used to prepare conjugated polymer thin films with uniform surface and controllable thickness.\textsuperscript{20} During the electrochemical polymerization, a dilute monomer/electrolyte solution is placed in a three electrode deposition cell with a working electrode, a counter-electrode and a reference electrode. Upon applying an external electrical potential or current of sufficient energy to oxidize the monomer (usually around ~1 V), the monomers will form radical cations near the electrode surface. If the reaction conditions are maintained to favor the continued formation of polymers, the radical cations will react with each other to form dimers, trimers, tetramers and then long chain polymers until they eventually precipitate onto the electrode surface. Electrochemical polymerization has several advantages over conventional chemical polymerization: (1) the film thickness can be precisely controlled by delivering the right amount of charge to the deposition system, (32) different film morphologies can be obtained by selecting an appropriate combination of solvent and supporting electrolyte, (3) fast polymerization rate, the polymerization can be usually finished within half an hour.\textsuperscript{26}

Electropolymerization are usually carried out under one of three different conditions, (1) galvanostatic (constant current) mode, (2) potentiostatic (constant voltage) mode and (3) potentiodynamic (current and voltage cycling) mode. Conjugated polymers prepared by potentiostatic or galvanostatic polymerization are positively charged, well ordered and doped with counter ions from the electrolyte in order to make neutral, stable film. On the other hand, polymer films made from
potentiodynamic mode can be either in the charged (doped) state or neutral (undoped) state depending on the final potential that the reaction stops at. Potentiodynamic methods are also expected to produce films where the polymer chains are less ordered due to the continuous polymer chain conformation change and dopant exchange during the various oxidation and reduction cycles. Many different types of anions have been used as dopants including small molecules, such as perchlorates, chlorides and sulfonates, polymers with anionic pendant groups such as poly(styrenesulfonate) (PSS) and anionic biological molecules. The stability, morphology, conductivity and some other properties of the prepared polymer films rely largely on the dopant. For example, polymer films doped with PSS usually give smoother film morphologies but lower conductivities.

![Electrochemical polymerization mechanism of PEDOT](image-url)

Figure 1.2 Electrochemical polymerization mechanism of PEDOT
1.2 Conjugated Polymers for Interfacing Electronic Biomedical Devices with Neural Tissue

1.2.1 Neural Interfaces and Metallic Electrodes

There has been considerable continuing interest in interfacing electronic biomedical devices with neural tissue for restoring or supplementing the function of human nervous system.\textsuperscript{30,31} The term “neural interfaces” or “brain-machine interfaces” is usually used to describe this concept. The history of neural interfaces dates back to early 1920s when German physiologist and psychiatrist Hans Berger first recorded human brain activity by means of electroencephalography (EEG).\textsuperscript{32} Originally, neural interfaces were developed as a basic science tool, and have been used extensively to develop our understanding of how the nervous system works. After nearly a century of development, neural interfaces have made considerable progress in improving the quality of life for hundreds of thousands of individuals suffering from a variety of conditions including nerve damage,\textsuperscript{33,34} neurological disorders\textsuperscript{35} or limb loss.\textsuperscript{31} One major application of neural interfaces is for neural prostheses where patients can control robotic limbs to perform motor functions with their minds. Additionally, neural prostheses can also help people restore the function of sensory system. For example, cochlear implants can be used to restore some measure of hearing to the deaf and retinal prostheses can be used to help restore vision. Another important application of neural interfaces is to help manage and treat the debilitating tremor associated with Parkinson’s disease.

When Berger performed his initial experiments, he first used silver wires and then switched to silver foils that could be inserted under the scalps of his patients to record human brain activity. Since then, metallic electrodes, such as gold, platinum, stainless steel, and iridium oxide, have been widely used in neural interfaces to help
the communication between external biomedical devices and living tissues. Although metallic electrodes enjoy the advantage of being electrochemically stable or “inert”, significant drawbacks still exist. Metals are relatively stiff materials; their Young’s modulus is more than 4 orders of magnitude higher than that of neural tissues. Metals are non-biocompatible materials and they have limited if any specific interactions with surrounding tissues. The large mechanical mismatch and poor biocompatibility could trigger severe foreign body response once implanted, leading to scar tissue formation around the neural interface which would eventually block the charge transport from external devices to living tissues. In addition, biomedical devices are usually made from electronically conductive inorganic materials and thus electrical signals are controlled and transported via electrons. Living tissues are water-swollen electrolytes, and thus signals in tissues are dominated by ionic transport. High impedance would be obtained if only electronically conductive metals are used as electrodes. For neural signal recording, high electrode impedance means decreased signal-to-noise ratio and sensitivity. For stimulation purposes, higher voltages that well go beyond the limits necessary to cause local chemical reactions near the electrode are sometimes required to effectively stimulate neural tissues, and this could lead to potential tissue damage. In addition, there is an increasing need for smaller electrodes in order to improve the precision of recording or stimulation. Reducing the surface area of a metal electrode will result in a further increased electrical impedance.

1.2.2 Conjugated Polymers Coatings for Neural Interfacing Applications

To improve the long-term performance of neural interfacing devices, new materials that are soft and flexible, biocompatible with living tissues and highly conductive are highly desired. Recently, conjugated polymers have gained much
interest in a wide range of biomedical applications, such as biosensors, drug delivery, tissue engineering, actuators and neural interfaces. These polymers are particularly attractive for neural interface applications due to their relatively soft mechanical properties, high conductivity, excellent biocompatibility and tunable surface morphology. These soft materials usually have a typical Young’s modulus on the order of ~1 GPa. The modulus of conjugated polymer gels is even lower, on the order of kPa, and thus are expected to help reduce the mechanical properties mismatch between hard metal electrodes and soft living tissue. In addition, as mentioned previously, these polymers can be electrochemically doped and dedoped. During the doping and dedoping process, certain counter-ions can be incorporated into or released from the polymer matrix, thus allowing the simultaneous conduction of ions and electrons. This helps bridge the gap between the ionically-conductive living cells and electronically-conductive external biomedical devices, leading to decreased impedance and improved sensitivity. Electrochemical doping also opens a new means for improving the biocompatibility of these polymers by directly using biological molecules as dopants. For example biomolecules such as the neurotrophins Neural Growth Factor (NGF) and Brain-Derived Neurotrophic Factor (BDNF) can be incorporated into the polymer matrix during polymerization to promote neuron survival and neurite outgrowth and thus improve the long-term performance of the devices. Another advantage is that the surface morphologies of these polymers films can be tuned during the electrochemical polymerization by using monomers with different side groups, different substrates or doping with different counter ions, and films with high surface areas can usually be obtained. The high surface areas facilitate
ion exchange between the microelectrodes and living tissue, and therefore build more efficient pathways for electrode-tissue communication.

Among all the conjugated polymers, polypyrrole (PPy), polyaniline (PANI) and polythiophene (PTh) and its derivatives have been applied to neural interfacing applications. Particularly important derivatives of polythiophene are the alkoxy-functionalized poly(3,4 ethylenedioxythiophene) (PEDOT) and poly(3,4-propylenedioxythiophene) (PProDOT) that have become particularly promising candidates because of their low oxidation potential, relatively high chemical and thermal stability, and high conductivity. Results from studies focusing on PEDOT will be discussed in the following sections.

1.2.3 Polypyrrole (PPy) and Poly(3,4 ethylenedioxythiophene) (PEDOT)

The electrochemical polymerization of PPy and its chemical, electrical, mechanical properties have been extensively studied since the 1980’s. One major finding was that the dopant used in the electrochemical polymerization could affect the morphology of PPy films and, consequently, the electrical impedance of the material. Cui pioneered work using electrochemically deposited PPy films as coating materials for neural interfacing applications and showed that the impedance of PPy films were 1-2 orders of magnitude lower than bare gold at a frequency range from 10^-4 Hz. However, studies with living cells showed that PPy does not influence cell behavior, meaning that it can’t help mitigate the chronic foreign body response very much.

As mentioned above, the properties of conducting polymer coatings can be tailored through doping or chemical modification. In order to improve the interaction of PPy films with living cells, many biologically active molecules such as growth
factors, polymers with extracellular matrix protein fragments, peptides, enzymes and hyaluronic acid have been used as dopants or additives to the polymer matrix during electrochemical polymerization. It has been shown that the biological activity of these biological molecules could be retained after being chemically or physically incorporated into conducting polymer matrix, and the interaction with living cells was largely enhanced. For example, it was found that better PC-12 cell attachment was achieved with the neurotrophin Nerve Growth Factor (NGF) as dopant. PPy-coated cochlear electrodes showed decreased impedance as compared to bare platinum (Pt) electrodes.

The main problem of using PPy for neural interfacing applications is its poor chemical and electrical stability. Pyrrole has four available sites that can be oxidized, while only two α sites are needed to form an ideally linear chain polymer. The remaining two β sites is the main reason that makes PPy unstable. In an oxidative environment, the carbon at the β site can react with the carbon at the α site, which is called “α-β” coupling and water or other nucleophilic compounds can react with the β carbon, creating defects in the polymer backbone, leading to the degradation and decreased performance of the polymer. Under physiological conditions, this instability could be a concern for the long-term applications. These issues are also an issue for unsubstituted polythiophene (PTh).

To overcome the disadvantage of PPy or PTh and improve the long-term performance of neural electrodes, monomers and polymers that had higher electrochemical stability were investigated. The alkyl-functionalized polymer PEDOT was synthesized by scientists at the Bayer AG research laboratories in 1980’s. PEDOT was initially designed to give a soluble polymer that wouldn’t have any
undesired “α-β” or “β-β” couplings within the polymer chain backbone. However, it turned out that no matter how it was polymerized, pure PEDOT polymer was insoluble in every solvent investigated. Despite this insolubility, the polymer still exhibited some exciting and important properties, like high charge conductivity, high chemical and electrochemical stability, and low oxidation potential. These excellent properties have made PEDOT and its derivatives a promising candidate for neural interfacing applications. Martin pioneered the study of PEDOT films for neural interfacing applications in the 2000’s. and found that the electrochemical stability of PEDOT was significantly improved as compared to PPy. For example, during stability tests, PPy films lost their charge storage capacity after 400 CV cycles between -0.9~0.5 V, while PEDOT film maintained most of it. Similar to PPy, PEDOT has a high charge storage capacity and low electrochemical impedance. Typically, when coated onto microelectrodes, the impedance of PEDOT films is 2-3 orders of magnitude lower than that of the bare metal substrate.

Studies from both in vitro and in vivo experiments demonstrated that PEDOT coated electrodes increased the signal to noise ratio for neural signal recording. High quality unit recordings with a small peak-to-peak noise of 35.3 ± 5.3 μV were obtained from PEDOT coated microelectrodes, while bare electrodes gave low quality recordings with a peak-to-peak noise of 106.2 ± 8.2 μV. Recently, PEDOT-based EEG electrodes fabricated by the Malliaras group have shown better resolution than gold electrodes at 8~13 Hz. The SNR was 24.4 dB for PEDOT electrodes and 21.3 dB for gold electrodes. PEDOT coatings also help chronic neural stimulation. For effective stimulation, the electrode must transfer sufficient charge in order to exceed the threshold potential for neuronal depolarization. For retinal implants, the minimum
injection charge required for neuronal depolarization is 0.4–0.6 μC per phase of a biphasic stimulating pulse, and the size of the electrode is usually smaller than 100 μm in diameter.\textsuperscript{37} This corresponds to a minimum required electrode charge density of about 1 mC/cm\textsuperscript{2}. This value exceeds the safe charge-injection limit of many metals, such as platinum which has a safe limit of 0.1- 0.35 mC/cm\textsuperscript{2} and could induce tissue damage during the stimulation. Because of the substantially decrease impedance, the charge injection limit of the PEDOT-coated electrode was found to be 2.3 mC/cm\textsuperscript{2} leading to safer stimulation.

1.2.4 Improving the Stability of PEDOT Films

Though PEDOT has many advantages over metallic electrodes and it is much more stable than PPy, certain limitations still exist. One major challenge is its relatively low mechanical stability on certain inorganic substrates.\textsuperscript{65} Detachment and cracking of PEDOT coatings from various inorganic substrates under chronic neural recording or stimulation conditions have been reported by different groups and this film instability has been associated with the loss of device performance. Hence limiting the cracking and delamination of PEDOT coatings from substrates is necessary to improve their long-term performance.

Many efforts have been previously directed toward improving adhesion and cohesion strength of conjugated polymers on metallic substrates. Mekhalif et al. found that adhesion of polybithiophene to platinum was improved by thiol-modified phenyl monolayers.\textsuperscript{66} You and coworkers increased the stability of poly(3-methylthiophene) (P3MT) films on indium–tin oxide (ITO) surfaces using surface-initiated Kumada catalyst-transfer polycondensation\textsuperscript{67} (SI-KCTP) from surface-bound arylnickel(II) bromide initiators. Smela reported the use of thiol-modified pyrrole derivatives to
increase the adhesion of polypyrrole coatings on gold.\textsuperscript{68} Jerome et al. enhanced the adhesion of polypyrrole via copolymerizing polypyrrole with other polymers that could be grafted onto metal surfaces.\textsuperscript{69}

However, only a few studies have investigated the adhesion and mechanical stability of PEDOT coatings. Cui significantly improved the mechanical stability of PEDOT coatings on Pt electrodes via polymerizing PEDOT with carbon nanotubes (CNTs).\textsuperscript{65} Carli and coworkers made PEDOT films that are more mechanically robust using an EDOT substituted silane (APTES-EDOT) as adhesion promoter.\textsuperscript{70} These methods have provided thoughtful insights in optimizing mechanical stability of PEDOT coatings, but not yet a perfect protocol has been set for this problem. Therefore, new and more facile approaches for improving stability of PEDOT still remain an ongoing topic of interest.

1.2.5 Functionalization of Conjugated Polymers

The performance of conjugated polymers depends largely on the ability to optimize their properties for a given application. To improve conductivity, for example, the films are often annealed (either thermally or in solvent vapor) or small molecule additives are incorporated. However, the processability, surface chemistry, and biocompatibility of conjugated polymer films can only be tuned within a limited range without additional synthesis or functionalization. Fast and convenient chemical functionalization of conjugated polymers is still a challenge and of considerable continued interest for a wide variety of applications.

Conjugated polymers are often polymerized electrochemically instead of chemically due to their typically low solubility and the common requirement of a thin-film geometry. Electrochemical polymerization has many advantages over traditional
chemical polymerization such as its speed, reproducibility, and ability to create films with precisely controlled film thickness and morphology. Functionalized conducting polymers can be made by incorporating specific small molecules or even polymers of interest into the film as dopants during electropolymerization. However, since the dopants are only physically entrapped in the films, the desired functionality may be lost after dopant release or exchange during extended use. There still remains a need for reliable, stable film chemical functionalization strategies. Covalently incorporating functional groups onto the monomers themselves is an attractive strategy for the film functionalization. By doing so, it is ensured that the chemical functionality will remain in the film and not be lost upon electrochemical cycling. Various previous efforts have been directed toward the synthesis and electrochemical polymerization of polymers based on modified 3,4-alkylenedioxythiophenes. Balog et al. reported the synthesis of a functionalized EDOT derivative bearing a highly nucleophilic thiolate group as the side chain. Guittard synthesized and characterized a fluorinated EDOT derivative and made superhydrophobic films by electrochemically polymerizing this new monomer. Povlich successfully introduced a carboxylic acid side group to EDOT and created peptide-functionalized PEDOT films.

Despite the simplicity and success of using functionalized thiophene monomers to make copolymers, it is not applicable when the introduced side groups are too bulky or have competing redox reactions under the same conditions with the monomer polymerization. Side groups with low oxidation potentials may interfere with, or even inhibit, the thiophene polymerization reaction.

Post-polymerization functionalization of appropriately designed precursor conjugated polymers is a possible means to overcome this problem. Post-
polymerization functionalization has been widely used in conventional polymer surface modifications, and has also been applied to conjugated polymers. However, in macromolecular reactions, the low reaction rate and the formation of byproducts can often be drawbacks. Therefore, the use of a clean, efficient reaction that could be carried out under mild conditions with high yield and easy separation would be even more advantageous. In this respect, the radical based thiol–ene “click” reaction is a particularly attractive candidate for polymer functionalization. This reaction has received considerable attention in recent years due to its many advantages over other available coupling reactions. Thiol–ene “click” reactions usually tolerate a variety of solvents in the presence of oxygen. They give high, often quantitative yields, and produce limited byproducts, leading to straightforward purification. They have been shown to be particularly useful in polymer surface functionalization and macromolecular synthesis including block copolymers and dendrimers, as well as in more traditional applications ranging from crosslinked networks to functionalized biomaterials. Thiol–ene “click” chemistry also provides an additional advantage over other “click” methods that various cysteine-containing peptides or proteins (i.e., with terminal thiols) could be easily introduced to the polymer without extra chemical modification or toxic catalysts. This would be especially beneficial for biofunctionalizing conjugated polymers on biomedical devices such as neural electrodes.

1.3 Outline of the Thesis

This dissertation focuses on the stability improvement, surface functionalization, nucleation and growth studies of electrochemical polymerized poly(3,4-alkenylenedioxythiophenes) coatings for biomedical applications. The whole
thesis can be divided into three major topics: improving the film stability of PEDOT coatings using different EDOT derivatives, functionalizing the surface of PProDOT films via thiol-ene “click” chemistry and some early work about the nucleation and growth mechanism of PEDOT film using in-situ TEM.

Chapter 2 and 3 describe an approach that uses EDOT derivative, EDOT-COOH and EDOT-NH₂, respectively, to create covalently bonded PEDOT coatings on conducting substrates. The two EDOT derivatives could be chemically bonded onto metal oxides surfaces via chemical adsorption and formed a strong bonding layer for the following PEDOT polymerization. The adhesion of PEDOT was significantly improved via this method.

Chapter 4 describes the synthesis of an octa-ProDOT-functionalized polyhedral oligomeric silsesquioxane (POSS) derivative (POSS-ProDOT) and its copolymerization with EDOT monomer to improve the stability of PEDOT coatings. The optical, morphological and electrochemical properties of the PEDOT-co-POSS-ProDOT copolymer films were studied. Largely enhanced electrochemical and mechanical stability of the copolymers was observed at intermediate levels of POSS-ProDOT content (3.1 wt%) via chronic stimulation tests.

Chapter 5 describes the post-polymerization modification of PProDOT surfaces. A dialkene functionalized ProDOT derivative (ProDOT-diene) was synthesized and electrochemical polymerization of this new monomer was studied. The surface of the P(ProDOT-diene) film was modified by various functional thiols via thiol-ene “click” reaction. The surface chemistry, wetting angles and electrical properties of the films could be tuned via this method.
Chapter 6 provides the summary of results from each chapter and also some suggestions for future work.
Chapter 2

SIGNIFICANT ENHANCEMENT OF PEDOT THIN FILM ADHESION TO INORGANIC SOLID SUBSTRATES WITH EDOT-ACID

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2.1 Introduction

Conjugated polymers have been widely investigated for applications in bioelectronics\cite{79,80} and biomedical devices\cite{81}, especially neural electrodes.\cite{8,65,82,83} These conjugated polymeric materials can play an important role in bridging between neurons and electrodes due to their high electronic and ionic conductivity. Among the currently available conjugated polymers, poly(3,4-ethylenedioxythiophene) (PEDOT) has received considerable interest because of its low oxidation potential, relatively high chemical and thermal stability, and high conductivity.\cite{26,84} PEDOT has been shown to significantly lower the impedance and increase the charge-injection capacity of metallic neural microelectrodes.\cite{44,85} Despite these advantages, certain limitations still exist. One major challenge is the relatively low adhesion of PEDOT polymer on various inorganic substrates. Detachment of PEDOT coatings from the inorganic substrate under chronic neural recording or stimulation conditions has been associated with the loss of device performance.\cite{37,45,86} Limiting the cracking and delamination of PEDOT coatings from substrates is necessary to improve their long-term performance.\cite{87}
Many efforts have been previously directed toward improving adhesion of conjugated polymers on metallic substrates. Mekhalif et al. found that adhesion of polybithiophene to platinum was improved by thiol-modified phenyl monolayers.\textsuperscript{66} You and coworkers increased the stability of poly(3-methylthiophene) (P3MT) films on indium–tin oxide (ITO) surfaces using surface-initiated Kumada catalyst-transfer polycondensation (SI-KCTP) from surface-bound arylnickel(II) bromide initiators.\textsuperscript{88} Smela reported the use of thiol-modified pyrrole derivatives to increase the adhesion of polypyrrole coatings on gold.\textsuperscript{89,90} Jerome et al. enhanced the adhesion of polypyrrole via copolymerizing polypyrrole with other polymers that can be grafted onto metal surfaces.\textsuperscript{69}

However, only a few studies have investigated the adhesion and mechanical stability of PEDOT coatings.\textsuperscript{65,70} Cui significantly improved the mechanical stability of PEDOT coatings on Pt electrodes via polymerizing PEDOT with carbon nanotubes (CNTs). Carli and coworkers made PEDOT films that are more mechanically robust using an EDOT substituted silane (APTES-EDOT) as adhesion promoter. These methods have provided thoughtful insights in optimizing adhesion and mechanical stability of PEDOT coatings, but not yet a perfect protocol has been set for this problem. Therefore, new and more facile approaches for improving stability of PEDOT still remain an ongoing topic of interest.

In this chapter, EDOT carboxylic acid (EDOT-acid) self-assembled monolayers were used to improve the adhesion between PEDOT coatings and metallic substrates. EDOT-acid\textsuperscript{28} was designed to create functional conducting polymer films that could be covalently modified with biomolecules such as peptides through the carboxylic acid side group. Employing the carboxylic acid chemistry, this molecule can also act as an
adhesion promoter. Carboxylic acids have long been studied and used to tune the surface properties of metals and metal oxides via chemisorption. For example, ferrocene dicarboxylic acid and 3-thiophene acetic acid were used to modify ITO electrodes. Although many different reagents have been developed to modify metals and metal oxides, EDOT-acid is a particularly attractive option as its EDOT moiety allows convenient copolymerization with PEDOT. Furthermore, EDOT-acid is more chemically and thermally stable than its pyrrole-acid and thiophene-acid counterparts. We hypothesized that PEDOT coatings on EDOT-acid modified electrodes might preserve the established advantages of PEDOT, and would also exhibit enhanced long-term mechanical stability and adhesion to substrates. In this work, PEDOT films were electrochemically coated on EDOT-acid modified ITO and stainless steel electrodes, and their morphology and electrochemical properties were characterized. The mechanical stability and adhesion of the coatings were investigated by ultrasonication tests.

2.2 Materials and Methods

2.2.1 Materials

Tetrabutyl ammonium perchlorate (TBAP), 3,4-ethylenedioxythiophene (EDOT) and 2,3-dihydrothieno(3,4-b)(1,4)dioxine-2-carboxylic acid (EDOT-acid) were purchased from Sigma-Aldrich. All other chemicals were of analytical grade, and Milli-Q water from a Millipore Q water purification system was used throughout. All reagents and solvents were used without further purification, unless otherwise noted. ITO-coated glass slides were purchased from Delta Technologies with a surface resistivity of 4-8 Ω/sq.
2.2.2 Cleaning, Activation and Surface Modification of ITO Coated Glass Slides

The ITO-coated glass slides (with 0.15-0.20 μm thick ITO coatings on 0.7 mm thick glass substrates) were ultrasonically cleaned (Kendal HB-23, 220 W) in acetone, 2-propanol and deionized water, each for 15 minutes. After drying in a stream of N₂, the substrates were then treated in UV Ozone (Novascan PSD UV Ozone cleaner) for 30 min to activate the ITO surface. The ITO coated glass substrates were dipped into a 10 mM ethanol solution of EDOT-acid at room temperature for 12 h in order to ensure the formation of a densely packed monolayer on ITO surface. The substrates were then rinsed with acetonitrile to remove any residual EDOT-acid molecules from the ITO surface and finally dried in a stream of N₂.

2.2.3 Surface Characterization

Static water contact angles were measured by applying a 5 µL drop of deionized water to a film set on a leveled base. Photographs were taken of the drops and their contact angles were measured using NIH ImageJ software with a Drop Shape Analysis plug-in and DropSnake method.

X-ray Photoelectron Spectroscopic (XPS) characterization of both the bare electrodes and EDOT-acid modified electrodes were performed using a Kratos Axis Ultra 165 XPS system equipped with a hemispherical analyzer.

Scanning electron microscopy images of PEDOT films deposited on both unmodified and modified ITO substrates were acquired using a Zeiss Auriga 60 Focused Ion Beam-Scanning Electron Microscope (FIB-SEM) operating at 3 kV.

The surface morphologies of unmodified ITO and EDOT-acid modified ITO substrates were investigated using a Bruker BioScope Catalyst atomic force microscope (AFM) in air in tapping mode. Silicon cantilevers with a spring constant
of 5 N/m were used. The heights and root-mean-squared roughnesses of features were calculated from image sections with a size of 5×5 \( \mu \text{m}^2 \) using the Gwyddion software.

The surface coverage and adsorption kinetics were studied by quartz crystal microbalance with dissipation (QCM-D) from Q-sense using a stainless steel coated sensor. The fundamental resonant frequency of the crystal was 5 MHz. The crystal was mounted in a fluid cell with a flow rate of 50 µl/min and a solution concentration of 2 mM.

### 2.2.4 Electrochemical Polymerization and Characterization

The electrochemical polymerization and characterization were performed with an Autolab PGstat12 Potentiostat/Galvanostat (EcoChemie) using the Nova 1.8 electrochemical software in a three-electrode cell. PEDOT was electrochemically polymerized on both unmodified and modified ITO glass slides (~0.5 cm\(^2\)) under galvanostatic conditions (0.075 mA) from a dilute (5 mM) acetonitrile solution containing 0.1 M tetrabutyl ammonium perchlorate (TBAP) as supporting electrolyte. For CV, the EDOT-acid monomer (5 mM) and EDOT-acid modified ITO or stainless steel substrates were scanned between -0.6 V and +1.4 V in acetonitrile solution (0.1 M TBAP) with a Ag/AgNO\(_3\) reference electrode. The PEDOT films were scanned between -0.9 V and +0.5 V in a phosphate buffered saline (PBS) buffer solution free of monomer. For EIS, the sample acted as the working electrode, a platinum plate was the counter electrode, a saturated Ag/AgCl electrode was the reference electrode, and PBS was the electrolyte. A 5 mV sinusoidal AC signal was applied over a frequency range of 1-10\(^5\) Hz. Both impedance and phase angle data were collected over the entire frequency range.
2.2.5 Ultrasonic Testing

To test the adhesion of PEDOT on both modified and unmodified electrodes, the PEDOT coated electrodes were immersed in a 20 ml glass vial that was filled with DI water. The vials were put in a Kendal HB-23 ultrasonic cleaner with a power of 220 W for specified periods of time (from a few seconds to several minutes).

2.3 Results and Discussion

2.3.1 Chemisorption of EDOT-Acid on Activated ITO

The ITO glass slides were first ultrasonically cleaned and then activated in UV Ozone for 30 minutes since the as-received ITO slides are expected to be contaminated with ambient organic species and the density of surface hydroxyl group is low. The EDOT carboxylic acid (EDOT-acid) is commercially available (now available from Tractus-chemistry) and can be directly synthesized as well. The
chemisorption of EDOT-acid and subsequent electropolymerization of PEDOT are shown in Figure 2.1. After UV ozone activation, the ITO glass slides were immediately immersed into vials containing fresh 10 mM EDOT-acid ethanol solution for up to 12 hours to ensure that a closely packed monolayer was formed during the chemisorption. It has been previously reported that carboxylic acid derivatives are readily chemisorbed onto ITO surfaces and other conducting substrates, such as stainless steel, without significantly changing the surface roughness of the substrates. Figure 2.2a shows the cyclic voltammogram of EDOT-acid monomer solution (5 mM in acetonitrile) and the voltammograms for both modified and unmodified ITO surfaces are shown in Figure 2.2b. A sharp anodic peak corresponding to the oxidation of the EDOT-acid was observed at +1.25 V in Figure 2.2a, and an oxidation peak with similar potential was also found for the EDOT-acid modified substrates as shown in Figure 2.2b. In contrast to the sharp peak of the EDOT-acid monomer solution, the oxidation peak of modified substrates was rather broad even after a full day of immersion. The broad peak was also irreversible; it only occurred in the first cycle with no oxidation peaks found in the following cycles. In addition, no reduction or oxidation peaks associated with polymerization of the thin layer of EDOT were ever observed. The surface coverage of the adsorbed molecule was estimated to be $1.7 \times 10^{-10}$ mol/cm$^2$ as determined coulometrically, and is only one third of the expected saturated monolayer coverage ($4 \times 10^{-10}$ mol/cm$^2$). Presumably, the reason that the electrochemically determined coverage is so low is that only a fraction of the ITO surface is capable of supporting electron transfer to the adsorbed molecule. The successful adsorption of EDOT-acid on metal or metal oxide was also confirmed via QCM measurement with a stainless steel coated sensor and the adsorption kinetics was
studied as well. The frequency change and corresponding mass change calculated via Sauerbrey equation were shown in Figure 2.3. After the initial equilibration step with pure ethanol, introduction of the EDOT-acid solution (point A in Figure 2.3) caused a sudden drop in the resonant frequency signal, followed by a slower frequency decrease. The whole adsorption lasted for 15 minutes until it reached a steady state. No obvious frequency change was found after rinsing with PBS buffer solution, indicating that the EDOT-acid molecules were strongly adhered to the metal oxide surface.

Figure 2.2 CV of EDOT-acid monomer (a) and CV of bare (green curve) and modified electrodes (red curve) (b).
Figure 2.3  Quartz crystal microbalance plot (a) and estimated mass deposited (b) over time.

2.3.2 Surface Characterization of EDOT-Acid Modified ITO Electrodes

The formation of the adsorbed EDOT-acid thin layer could also be confirmed via static contact angle measurements. Figure 2.4 shows the static contact angles of UV Ozone cleaned ITO, ITO exposed to ethanol and EDOT-acid modified ITO. The UV Ozone treated ITO was extremely polar and had a water contact angle less than 5°.
The water contact angle of ITO increased to 32° after 12 h ethanol exposure and the EDOT-acid modified ITO had a contact angle of 54°. The topographies of both clean ITO substrates and EDOT-acid modified ITO substrates were characterized by AFM, as shown in Figure 2.5. Polycrystalline grains with an average diameter of ~36 nm and a root-mean-square roughness on a 5×5 μm² regions of ~4.1 nm could be found on the clean, unmodified ITO substrates as reflected in Figure 2.5a. The EDOT-acid modified surface still showed the same polycrystalline nature of the unmodified ITO substrate with only a small decrease in the surface roughness (rms ~3.9 nm), indicating that the chemisorbed EDOT-acid thin film was smooth and homogeneous. These results show that the thin EDOT-acid layer did not significantly change the surface morphology and texture of the ITO films. XPS analysis was used to study the composition of the adsorbed EDOT-acid thin layer. Figure 2.5 presents the high resolution XPS data of the carbon (a) and sulfur (b) regions from both unmodified ITO and EDOT-acid modified ITO electrodes. The presence of carboxylic acid groups in the EDOT-acid coated films was clearly demonstrated by a strong peak at 288.5 ev (Figure 2.6a). The major peak at 285.8 ev corresponds well with the C(1s) peak from PEDOT. S(2p) peaks were also detected near 164 eV, as shown in Figure 2.6b. No sulfur signal was observed from the unmodified ITO electrodes. The C(1s) peaks in the unmodified ITO are from contaminants and can be easily distinguished from the chemisorbed EDOT-acid thin layer with carboxylic acid side groups.
Figure 2.4  Contact angle measurements of (a) UV Ozone cleaned ITO slides; (b) ITO slides after 12 h EtOH exposure; (c) EDOT-acid modified ITO slides.

Figure 2.5  Representative AFM images of (a) UV Ozone cleaned ITO electrodes and (b) EDOT-carboxylic acid modified ITO electrodes
2.3.3 Electrochemical Properties of PEDOT on EDOT-Acid Modified ITO

PEDOT was electrochemically polymerized onto unmodified and EDOT-acid modified ITO slides under constant current (0.15 mA/cm\(^2\)) with tetrabutylammonium perchlorate (TBAP, 0.1 M) as electrolyte in a standard three-electrode cell. The electrochemical behavior of PEDOT coated electrodes and bare ITO glass slides were studied using cyclic voltammetry, as shown in Figure 2.7. PEDOT coatings on both electrodes showed reversible oxidation and reduction peaks during electrochemical scanning between -0.9 V and +0.5 V (vs Ag/AgNO\(_3\)). One benefit of using PEDOT as coating is the greatly improved charge storage capacity (CSC) as compared with the bare electrode. It is clear from Figure 2.7 that depositing PEDOT on bare ITO and EDOT-acid modified ITO dramatically increased the CSC of the electrodes. The magnitude of the increase of CSC was similar for both substrates. The shapes of the CV curves of PEDOT on EDOT-acid modified ITO were nearly identical to those on unmodified ITO. This indicated that the EDOT-acid thin layer did not have a
significant effect on the redox behaviors and charge storage capacity of the PEDOT-coated electrodes.

Figure 2.7 Cyclic voltammetry of bare ITO, PEDOT on ITO and PEDOT and EDOT-acid modified ITO. (Both PEDOT films were electrodeposited under constant current (0.075 mA) for 12 min).

The electrochemical properties of PEDOT-coated electrodes were further investigated by using EIS in 0.1 M PBS buffer solution. After PEDOT deposition, the amplitude of the impedance of the electrodes decreased by 2-3 orders of magnitude at frequencies between 1 Hz and 1000 Hz as seen in Figure 2.8. This dramatic drop in impedance has been associated with the increase in effective surface area and ability
of the PEDOT to facilitate both electronic and ionic transport. It was found that the low frequency impedance of PEDOT coated onto the EDOT-acid modified electrode was only just slightly higher than that of PEDOT coated unmodified ITO (Figure 2.8), again indicating that the thin EDOT-acid adhesion promoter layer did not significantly block charge transport through the PEDOT-ITO interface.

![Electrochemical impedance spectroscopy of bare ITO, unmodified and modified ITO electrodeposited with PEDOT.](image)

**Figure 2.8** Electrochemical impedance spectroscopy of bare ITO, unmodified and modified ITO electrodeposited with PEDOT.

### 2.3.4 Adhesion Testing

The adhesion strength of the PEDOT coatings on both EDOT-acid modified and unmodified substrates were investigated by a simple but effective ultrasonic tests. The
PEDOT coated electrodes were first immersed into a 20 mL vial that was filled with DI water. The vials were put in a Kendal HB-23 ultrasonic cleaner with a power of 220 W for a specified time during the test. Optical images of the electrodes before and after the sonication test are shown in Figure 2.9. The PEDOT films on unmodified ITO electrodes could only sustain up to 5 s of sonication. After sonication, these PEDOT films were fragmented into many small pieces and the nearly the whole film was dispersed into the solvent. However the PEDOT films coated onto EDOT-acid modified ITO remained intact even after 2 minutes of sonication. The excellent mechanical stability of the PEDOT films on EDOT-acid modified ITO indicates that there are significantly stronger interactions between the polymer and the ITO electrodes. The substantially improved adhesion of PEDOT on metals and metal oxides with EDOT-acid coatings suggests that this modification may be important for optimizing performance in long-term recording or stimulation applications.

![Optical images of PEDOT films on ITO and modified ITO before and after ultrasonication adhesion test. PEDOT on ITO was tested for 5 seconds and PEDOT on modified ITO was tested for 2 minutes.](image)

Figure 2.9 Optical images of PEDOT films on ITO and modified ITO before and after ultrasonication adhesion test. PEDOT on ITO was tested for 5 seconds and PEDOT on modified ITO was tested for 2 minutes.
2.3.5 Surface Morphology of PEDOT Films

The morphologies of the PEDOT thin films electrochemically deposited onto bare ITO and EDOT-acid modified ITO electrodes were studied using SEM as shown in Figure 2.10. For SEM studies, PEDOT films were grown in acetonitrile under a constant current (0.075 mA) with varying deposition times (9 min and 12 min). Clearly, the morphologies of the films were affected by the interfacing interactions with the underlying substrates. When coated onto bare ITO, which has no specific interactions with PEDOT, the PEDOT film showed a bumpy and rough surface where star shaped patterns formed by buckling were found (Figure 2.10a and 2.10c).20,98

Buckling delamination is a common phenomenon in thin film materials. Delamination of a weakly bonded thin film from its substrate can occur spontaneously when the strain energy in the film exceeds the interfacial energy resisting separation.99-100 It has been reported that acetonitrile can cause modest swelling of PEDOT.101 During swelling, the internal strain energy that built up in the PEDOT film during electropolymerization was evidently larger than the interfacial energy with the bare substrate, thus leading to the observed buckling delamination. When the substrate was modified with EDOT-acid, the stronger interactions between the film and the substrate suppressed the formation of buckling. This observation is similar to previous studies showing less film buckling when crosslinking agents were introduced into electrochemically deposited PEDOT copolymers.45 As the film became thicker, the buckling pattern became denser and closer together. The size of the bulking ridges also increased. The bulking effect is consistent with PEDOT having limited adhesion on unmodified ITO. However, only flat and uniform films with no such buckling features were formed on EDOT-acid modified ITO substrates (Figure 2.10b and 2.10d). At the smallest length scales (~100 nm), both films showed the bumpy surface
structure commonly observed in electrochemically deposited PEDOT. Evidently the thin adhesion layer of EDOT-acid increases the interactions between the film and inorganic electrode, eliminating the mechanical buckling seen on the unmodified substrates.

Figure 2.10   SEM images of PEDOT films on pure ITO electrode (a,c) and EDOT acid modified ITO electrode (b,d) in acetonitrile for 9 min (a,b) and 12 min (c,d) at constant current mode (0.15 mA/cm²). (Scale bar represents 10 µm)
2.4 Conclusions

ITO electrodes were successfully modified by EDOT-acid via chemisorption. PEDOT thin films could be electrodeposited onto the EDOT-acid modified electrodes. The electrochemical impedance spectra showed that the impedance of PEDOT coated EDOT-acid modified ITO electrodes was much lower than that of bare ITO electrode. The charge storage capacity of PEDOT coated modified electrode were much higher than that of bare ITO characterized by CV. The mechanical stability and adhesion of the PEDOT coatings on modified ITO was tested by aggressive sonication test. The morphologies were characterized by SEM, and verified the elimination of mechanical buckling of the films on EDOT-modified substrates. These characteristics demonstrate that EDOT-acid has the ability to serve as an adhesion promoter from improving the performance of PEDOT, and presumably other conjugated polymers, as electrochemically deposited coatings on inorganic biomedical devices.
Chapter 3

IMPROVING PEDOT ADHESION TO INORGANIC SUBSTRATES WITH EDOT-AMINE

3.1 Introduction

Conjugated polymers have attracted considerable attention in a wide range of biomedical applications, such as biosensor, drug delivery, tissue engineering, actuators, and neural interfaces over the past few decades. These polymers are particularly attractive for neural interface applications as they can provide a relatively soft, high surface area and highly conductive interface between the typically metallic electrodes and the tissue. Among the currently available conjugated polymers, poly(3,4-ethylenedioxythiophene) (PEDOT) has gained much interest because of its low oxidation potential, relatively high chemical and thermal stability, and high conductivity. PEDOT has been shown to significantly lower the impedance and increase the charge injection capacity of metallic neural microelectrodes, yielding electrodes with superior signal to noise ratio. Bioactive molecules such as peptides and nerve growth factors could be incorporated into the polymer matrix during the electrochemical polymerization to improve the chronic stability and biocompatibility of the electrode and encourage growth of neurons towards the electrode. To apply the PEDOT coated electrodes for various biomedical applications, one of the major challenges is the relatively poor adhesion of PEDOT coatings to inorganic metallic and semiconducting substrates. It has been reported that cracking and delamination of PEDOT coatings from the inorganic substrate under
chronic neural recording or stimulation conditions could lead to the loss of device performance. Limiting the cracking and delamination of PEDOT coatings from substrates is necessary to improve their long-term performance.

Efforts have been previously directed toward improving adhesion of conjugated polymers on metallic substrates. You and coworkers increased the stability of poly(3-methylthiophene) (P3MT) films on indium–tin oxide (ITO) surfaces using surface-initiated Kumada catalyst-transfer polycondensation (SI-KCTP) from surface-bound arylnickel(II) bromide initiators. Smela reported the use of thiol-modified pyrrole derivatives to increase the adhesion of polypyrrole coatings on gold.

However, only a few studies have investigated the adhesion and mechanical stability of PEDOT coatings. Cui significantly improved the mechanical stability of PEDOT coatings on Pt electrodes via polymerizing PEDOT with carbon nanotubes (CNTs). Carli and coworkers made PEDOT films that are more mechanically robust using an EDOT substituted silane (APTES-EDOT) as adhesion promoter. These methods have provided thoughtful insights in optimizing adhesion and mechanical stability of PEDOT coatings, but not yet a perfect protocol has been set for this problem. Therefore, new and more facile approaches for improving stability of PEDOT still remain an ongoing topic of interest. Here, we demonstrate a facile approach to use EDOT methyl amine (EDOT-amine) as adhesion promoter to improve the adhesion between PEDOT coatings and metallic substrates. Amines could also chemically adsorbed onto metallic substrates, and have been studied and used to tune the surface properties of metals before. For example, 1,12-diaminododecane and n-hexylamine were used to modify ITO electrodes. Although different reagents have been developed to modify metal and metal oxides, EDOT-amine is a particularly
attractive option as its EDOT moiety allows convenient copolymerization with PEDOT and EDOT is more chemically and thermally stable than its pyrrole and thiophene counterparts. We expected that with EDOT-amine as adhesion promoter, PEDOT films may keep the established advantages, and would also exhibit enhanced long-term mechanical stability and adhesion to substrates. In this work, PEDOT films were electrochemically coated on EDOT-amine modified ITO electrodes, and their morphology and electrochemical properties were characterized. The mechanical stability and adhesion of the coatings were investigated by ultrasonication tests.

3.2 Materials and Methods

3.2.1 Materials

Tetrabutyl ammonium perchlorate (TBAP), 3,4-ethylenedioxythiophene (EDOT), 3, 4-dimethoxythiophene, p-toluenesulfonic acid monohydrate and 3-bromo-1,2-propanediol were purchased from Sigma-Aldrich. All other chemicals were of analytical grade, and Milli-Q water from a Millipore Q water purification system was used throughout. All reagents and solvents were used without further purification, unless otherwise noted. ITO-coated glass slides were purchased from Delta Technologies with a surface resistivity of 4-8 Ω/sq.

3.2.2 Cleaning, Activation and Surface Modification of ITO Coated Glass Slides

The ITO-coated glass slides (with 0.15-0.20 μm thick ITO coatings on 0.7 mm thick glass substrates) were ultrasonically cleaned (Kendal HB-23, 220 W) in acetone, 2-propanol and deionized water, each for 15 minutes. After drying in a stream of N₂, the substrates were then treated in UV Ozone (Novascan PSD UV Ozone cleaner) for 30 min to activate the ITO surface. The ITO coated glass substrates were dipped into a
10 mM ethanol solution of EDOT-NH$_2$ at room temperature for 12 h in order to ensure the formation of a densely packed monolayer on ITO surface. The substrates were then rinsed with acetonitrile to remove any residual EDOT-NH$_2$ molecules from the ITO surface and finally dried in a stream of N$_2$.

3.2.3 Surface Characterization

Static water contact angles were measured by applying a 5 µL drop of deionized water to a film set on a leveled base. Photographs were taken of the drops and their contact angles were measured using NIH ImageJ software with a Drop Shape Analysis plug-in and DropSnake method.

Scanning electron microscopy images of PEDOT films deposited on both unmodified and modified ITO substrates were acquired using a Zeiss Auriga 60 Focused Ion Beam-Scanning Electron Microscope (FIB-SEM) operating at 3 kV.

3.2.4 Electrochemical Polymerization and Characterization

The electrochemical polymerization and characterization were performed with an Autolab PGstat12 Potentiostat/Galvanostat (EcoChemie) using the Nova 1.8 electrochemical software in a three-electrode cell. PEDOT was electrochemically polymerized on both unmodified and modified ITO glass slides (~0.5 cm$^2$) under galvanostatic conditions (0.075 mA) from a dilute (5 mM) acetonitrile solution containing 0.1 M tetrabutyl ammonium perchlorate (TBAP) as supporting electrolyte. For CV, the EDOT-NH$_2$ monomer (5 mM) and EDOT-NH$_2$ modified ITO substrates were scanned between -0.6 V and +1.4 V in acetonitrile solution (0.1 M TBAP) with a Ag/AgNO$_3$ reference electrode. The PEDOT films were scanned between -0.9 V and +0.5 V in a phosphate buffered saline (PBS) buffer solution free of monomer. For
EIS, the sample acted as the working electrode, a platinum plate was the counter electrode, a saturated Ag/AgCl electrode was the reference electrode, and PBS was the electrolyte. A 5 mV sinusoidal AC signal was applied over a frequency range of $1-10^5$ Hz. Both impedance and phase angle data were collected over the entire frequency range.

3.2.5 Ultrasonic Testing

To test the adhesion of PEDOT on both modified and unmodified electrodes, the PEDOT coated electrodes were immersed in a 20 ml glass vial that was filled with DI water. The vials were put in a Kendal HB-23 ultrasonic cleaner with a power of 220 W for specified periods of time (from a few seconds to several minutes).

3.3 Results and Discussions

3.3.1 Chemisorption and Surface Characterization of EDOT-NH$_2$ on Activated ITO

![Chemisorption and Surface Characterization of EDOT-NH$_2$ on Activated ITO](image)

Figure 3.1 The chemisorption of EDOT-amine (red) onto ITO slides (blue) and electrodeposition of PEDOT (black).
EDOT methyl amine was synthesized from hydroxymethyl functionalized EDOT (EDOT-OH) based on previous procedures.\textsuperscript{105}

Figure 3.1 shows the chemisorption of EDOT-amine and subsequent electropolymerization of PEDOT films. To prepare the adsorbed EDOT-amine thin layers, the ITO glass slides were first ultrasonically cleaned and then activated in UV Ozone for 30 minutes since the as-received ITO slides are expected to be contaminated with ambient organic species.\textsuperscript{91} After UV ozone activation, the ITO glass slides were immediately immersed into vials containing freshly made 10 mM EDOT-amine ethanol solution for up to 12 hours to ensure the formation of closely packed EDOT-amine layers.\textsuperscript{94} It has been previously reported that amino derivatives are readily chemisorbed onto ITO surfaces and other conducting substrates, such as gold, without significantly changing the surface roughness of the substrates. The resulting EDOT-amine thin layers were characterized by cyclic voltammetry (CV) and contact angle measurement. The cyclic voltammograms of EDOT-amine monomer solution (5 mM in acetonitrile), both modified and unmodified ITO surfaces are shown in Figure 3.2. In Figure 3.2a, two sharp anodic peaks corresponding to the oxidation of the amine side group and EDOT were observed at +1.00 V and +1.25 V, respectively, and two broad oxidation peaks were also found at similar potentials for the EDOT-amine modified substrates as shown in Figure 3.2b. The broad peaks were irreversible and only occurred in the first cycle with no oxidation peaks found in the following cycles. In addition, no reduction or oxidation peaks associated with EDOT oligomers or PEDOT were ever observed, indicating that the adsorbed EDOT-amine was not polymerized. The successful chemisorption of EDOT-amine on inorganic substrates was also confirmed by static contact angle measurements as shown in Figure 3.3. The
initial UV ozone treated ITO surface was extremely polar and had a static contact angle less than 5 ± 0.5° and the contact angle increased to 52 ± 1.4° after being immersed into EDOT-amine solution for several hours. The change in the surface free energy indicated that ITO surface was successfully modified.

Figure 3.2 CV of EDOT-amine monomer (a) and CV of bare (green curve) and modified electrodes (red curve) (b).

Figure 3.3 Contact angle measurements of (a) UV Ozone cleaned ITO slides; (b) EDOT-amine modified ITO slides.
3.3.2 Electrochemical Properties of PEDOT on EDOT-NH$_2$ Modified ITO

PEDOT was subsequently electrochemically deposited onto both unmodified and EDOT-amine modified ITO glass slides under constant current (0.15 mA/cm$^2$) with tetrabutylammonium perchlorate (TBAP, 0.1 M) as electrolyte in a standard three-electrode cell. The electrochemical properties of PEDOT coated electrodes and bare ITO glass slides were first investigated using cyclic voltammetry, as shown in Figure 3.4a. Reversible oxidation and reduction peaks of PEDOT films on bare and modified ITO slides were observed during electrochemical scanning between -0.9 V and +0.5 V (vs Ag/AgNO$_3$). It has been well reported that using PEDOT as coating materials could significantly enhance the charge storage capacity (CSC) of the metal electrodes and thus improve the signal to noise ratio of neural electrodes. It is clearly seen from Figure 3.4a that the CSC of the electrodes were dramatically improved upon depositing PEDOT films, and no obvious difference was observed for bare ITO and modified ITO. The redox behaviors of PEDOT on modified ITO were nearly identical to those on bare ITO, indicating that the EDOT-amine thin layer did not have a significant effect on the redox behaviors.

One major advantage of using PEDOT coatings for neural interfaces is that they can significantly lower the impedance of the electrodes mostly due to their intrinsic electronic and ionic conductivities, and thus improve the signal to noise ratio. The electrochemical properties of the PEDOT coated electrodes were further characterized with EIS in 0.1 M PBS buffer solution at the frequency range of 1-100 kHz. It was shown in Figure 3.4b that the amplitude of the impedance of the PEDOT coated electrodes decreased by 2-3 orders of magnitude at frequencies between 1 Hz and 1000 Hz, the frequency range that is relevant to neural recordings. This dramatic drop in impedance value has been associated with the increase in effective surface area.
and ability of PEDOT to facilitate both electronic and ionic transport. It was found that the impedance of PEDOT coated modified electrode was only slightly higher than that of coated bare ITO (Figure 3.3b), again indicating that the adhesion promoter layer did not significantly impair charge transport through the PEDOT-ITO interface.

![Figure 3.4](image)

**Figure 3.4** Cyclic voltammetry of bare ITO, PEDOT on ITO and PEDOT and EDOT-amine modified ITO (a) and electrochemical impedance spectroscopy of bare ITO, unmodified and modified ITO electrodeposited with PEDOT (b).

### 3.3.3 Adhesion Testing

The adhesion strength of the PEDOT coatings on both EDOT-NH₂ modified and unmodified substrates were investigated by a simple but effective ultrasonic test. The PEDOT coated electrodes were first immersed into a 20 mL vial that was filled with DI water. The vials were put in a Kendal HB-23 ultrasonic cleaner with a power of 220 W for a specified time during the test. Figure 3.5 shows the optical images of
the PEDOT coated electrodes before and after the sonication tests. It is clearly seen that PEDOT coatings on modified electrodes displayed a higher adhesion strength compared to that of the coatings on unmodified electrodes. The PEDOT films on the unmodified ITO electrodes was quickly destroyed (around 3 s) by the ultra-sonication. These PEDOT films fell into pieces after the test and nearly the whole film was dispersed into the PBS solution. However the PEDOT films coated onto EDOT-amine modified ITO remained almost intact even after 1 minute of sonication. The excellent mechanical stability of the PEDOT coatings on EDOT-amine modified ITO indicates that there are significantly stronger interactions between the polymer and the ITO electrodes. The substantially improved adhesion of PEDOT on metals and metal oxides with EDOT-NH₂ coatings suggests that this modification may be important for optimizing performance in long-term recording or stimulation applications.

Figure 3.5 Optical images of PEDOT films on ITO and modified ITO before and after ultrasonication adhesion test. PEDOT on ITO was tested for 3 seconds and PEDOT on modified ITO was tested for 1 minutes.
3.3.4 Surface Morphology of PEDOT films

The morphologies of the PEDOT thin films electrochemically deposited onto bare ITO and EDOT-NH\textsubscript{2} modified ITO electrodes were studied using SEM as shown in Figure 3.5. For SEM studies, PEDOT films were grown in acetonitrile under a constant current mode (0.075 mA) with varying deposition times (9 min and 12 min). It can be observed that the morphologies of the films was largely affected by the interfacing interactions with the underlying substrates. PEDOT films coated on bare ITO showed a bumpy and rough surface where star shaped patterns formed by buckling were found, indicating that there is only little or even no specific interactions between the film and substrate (Figure. 3.6a and 3.6c). As the thickness of the film increased, the size of the buckling ridges also increased and the buckling pattern became denser and closer together. Buckling delamination is a common phenomenon in thin film materials. Delamination of a weakly bonded thin film from its substrate can occur spontaneously when the strain energy in the film exceeds the interfacial energy resisting separation\textsuperscript{99,100,106}. This buckling delamination was presumably resulted from the swelling and partial delamination of the as-formed PEDOT film in the solvent. The thick and more cohesive PEDOT film tended to detach from ITO substrate due to its limited adhesion. It has been reported that acetonitrile can cause modest swelling of PEDOT\textsuperscript{101}. During swelling, the internal strain energy that built up in the PEDOT film during electropolymerization was evidently larger than the interfacial energy with the bare substrate, thus leading to the observed buckling delamination. However, with EDOT-amine modification, the PEDOT film on ITO showed no such buckling. (Figure. 3.6b and 3.6d). Under higher magnification, both films showed the characteristic bumpy surface morphology that consisted ~100 nm grains. This morphology is commonly observed in electrochemically deposited
PEDOT. It is evident that the EDOT-amine adhesion promoting thin layer increases the interactions between the film and inorganic electrode, eliminating the mechanical buckling seen on the unmodified substrates.

Figure 3.6 SEM images of PEDOT films on pure ITO electrode (a,c) and EDOT-amine modified ITO electrode (b,d) in acetonitrile for 9 min (a,b) and 12 min (c,d) at constant current mode (0.15 mA/cm²). Scale bar represents 20 µm.

3.4 Conclusions

In conclusion, ITO electrodes were successfully modified by EDOT methyl amine via chemisorption and PEDOT films were subsequently electrochemically deposited onto the modified electrodes. The PEDOT coated electrodes exhibited higher charge storage capacity and much lower impedance than bare electrodes. The
PEDOT coatings on EDOT-amine modified electrodes showed significantly enhanced mechanical stability and adhesion under aggressive sonication tests. The morphologies were characterized by SEM, and showed that no mechanical buckling was formed on the films coated on EDOT-amine modified substrates. These characteristics demonstrate that EDOT-amine is able to serve as an adhesion promoter for improving the performance of PEDOT, and presumably other conjugated polymers, as electrochemically deposited coatings on inorganic biomedical devices.
Chapter 4

ENHANCED ELECTROCHEMICAL PERFORMANCE OF PEDOT FILMS WITH POSS-PRODOT AS CROSS LINKER

4.1 Introduction

Conjugated polymers have gained much interest in a wide range of biomedical applications, such as biosensors, drug delivery, tissue engineering, actuators, and neural interfaces over the past few decades. These polymers are particularly attractive for neural interface applications due to their relatively soft mechanical properties, tunable surface morphology, high conductivity and excellent biocompatibility. These soft materials usually have a typical young’s modulus on the order of ~1 Gpa and thus could help reduce the mechanical properties mismatch between hard metal electrodes and soft living tissue. In addition, they usually provide a high surface area which can facilitate the ion exchange between the microelectrodes and living tissues, therefore build a more efficient pathway for the electrode-tissue communication. And due to their good electronic and ionic conductivities, the impedance is usually reduced and charge storage capacity is improved. Among the currently available conjugated polymers, alkoxy-functionalized polythiophene such as poly(3,4 ethylenedioxythiophene) (PEDOT) and poly(3,4-propylenedioxythiophene) (PProDOT) has become one of the most promising candidate because of its low oxidation potential, relatively high chemical and thermal stability, and high conductivity. PEDOT coated electrodes have been studied and used for neural interfaces, and their advantages and improvements over conventional
metal electrodes were reported. Though conjugated polymers do have many advantages over other materials, these polymers are normally fragile and are easy to crack and delaminate from the metal electrodes. One major challenge of these polymers is the low electrochemical stability for long-term neural recording or stimulation. Loss of device performance such as decreased charge carrying capacity and increased impedance of PEDOT coated neural electrodes under chronic neural recording or stimulation conditions were reported by different groups. Not only do these delaminations potentially decrease the performance of the devices, but could also leave behind fractions of the film in the tissue. It is therefore of interest to make an electrochemically and mechanically stable PEDOT film to improve the long-term performance of PEDOT coatings and minimize the uncertainties that posed to biological systems.

Several strategies have been directed toward improving electrochemical stability of conjugated polymers on metallic substrates. Cui found that stability of PEDOT films was improved by using carbon nanotubes as dopant during the electrochemical polymerization. Inganas and coworkers chemically cross linked the polyelectrolyte dopant PSS and found that the stability of PEDOT:PSS was substantially improved. Ouyang reported the use of a conjugated 3-armed EDOT derivative, 1,3,5-tri[2-(3,4-ethylenedioxythienyl)]-benzene (EPh) as cross linker to increase the mechanical stability of PEDOT coatings. Despite these developments, the search for conducting polymer materials that are more electrochemically and mechanically robust remains an ongoing topic of interest.

Here, we introduce the use of a ProDOT functionalized cage-like inorganic core material, polyhedral oligomeric silsesquioxane (POSS), to increase the
electrochemical and mechanical stability of PEDOT films. Polyhedral oligomeric silsesquioxane (POSS), which has a cage-like structure with a stable inorganic Si-O core of dimensions from 1 to 3 nm surrounded by organic substituents that can form organic–inorganic hybrid framework when incorporated into other polymer matrixes\textsuperscript{110,111}. POSS nanoclusters are known to enhance the temperature and oxidation resistance, surface hardening and mechanical integrity of polymers upon incorporation. In recent reports, the incorporation of POSS units into polyaniline has enhanced the electrochemical performance of polyaniline, the electrodes of PANI/POSS nanocomposites possess better cyclic stability than pure PANI due to the support effect of the SOPS nanoparticles which restricts the change of the nanostructure at the cycle-life test.

In this work, we synthesized functionalized POSS-ProDOT cross linker via hydrosilylation and thiol-ene “click” chemistry, and subsequently prepared PEDOT/POSS-ProDOT copolymers by electrochemical polymerization. The POSS core can strengthens the interaction between the PEDOT chains. We felt that this cross linker would enhance the long-term stability of PEDOT coatings and preserved the excellent electrical properties of PEDOT.

4.2 Materials and Methods

4.2.1 Materials

3,4-dimethoxythiophene, diethyl allylmalonate, lithium aluminum hydride, p-toluene sulfonic acid (p-TSA), tetrabutyl ammonium perchlorate (TBAP), 3-Mercaptopropyl trimethoxysilane (MTS), 2,2-dimethoxy-2- phenylacetophenone (DMPA) and 3,4-ethylenedioxythiophene (EDOT) were purchased from Sigma-
Aldrich. Stainless steel electrodes (E363/76/SPC) were purchased from Plastics One. ITO-coated glass slides were purchased from Delta Technologies with a surface resistivity of 4-8 Ω/sq. All other chemicals were of analytical grade, and Milli-Q water from a Millipore Q water purification system was used throughout. All reagents and solvents were used without further purification, unless otherwise noted. Samples were irradiated using a UVP Black Ray UV Bench Lamp XX-15L, emitting 365 nm light at 15 W.

4.2.2 Syntheses of ProDOT-ene and POSS-SH

ProDOT-ene was synthesized via the p-TSA catalyzed transetherification route from 3,4-dimethoxythiophene and 2-allyl-1,3-propanediol (Scheme 4.1) as previously described.\textsuperscript{21} The synthesis of POSS-SH was shown in Scheme 4.2 according to literature\textsuperscript{112,113}. 5 mL MTS, 10 mL concentrated hydrochloric acid and 120 mL methanol were added into a 500 mL round bottom flask. The reaction mixture was refluxed at 90 °C for 30 h under agitation to ensure the completed hydrosilylation. The white viscous precipitate was first washed with methanol for three times and then dissolved in 2mL THF. The THF solution was added to 100 mL acetonitrile drop-wise and then allowed to crystallize at -20 °C for overnight. The final product was dried in a vacuum oven at room temperature for 12 h.

4.2.3 Preparation of POSS-ProDOT via thiol-ene “click” chemistry

POSS-SH (30 mg, 0.03mmol) and a minimum of THF were added to a vial and heated to dissolve the thiol. ProDOT-ene (70 mg, 0.35 mmol) and 0.1 wt% of 2,2-dimethoxy-2-phenylacetophenone (DMPA) were added, and the mixture was sparged with argon for five minutes. The vial was placed under a UV lamp and irradiated for
one hour (Scheme 4. 3). A small amount of methanol was added, and the product was ultrasonicated for 2 min. The supernatant was decanted and the product redissolved in chloroform, and concentrated by evaporation to give a viscous oil.

4.2.4 Electrochemical polymerization and characterization

All the electrochemical polymerization and characterization were performed with a Gamry Potentiostatic Reference 600TM in a three electrode cell. Stainless steel electrode (Plastics One) or ITO-coated glass (Delta Technologies) served as the working electrode, a platinum plate of 1 cm² surface area was the counter electrode, with Ag/AgNO₃ as the reference electrode. The electrochemical characterization of POSS-ProDOT was studied in a dilute (2 mM) dichloromethane solution containing 0.1 M tetrabutyl ammonium perchlorate (TBAP) as supporting electrolyte. PEDOT homopolymer and PEDOT/POSS-ProDOT copolymer with various contents of POSS-ProDOT were prepared under constant voltage (+ 1.1 V) with a total electrodeposition charge of 27 mC. For CV, the polymer films were scanned between -1.0 V and +0.8 V in a phosphate buffered saline (PBS) buffer solution free of monomer with an Ag/AgCl reference electrode. For EIS, the sample acted as the working electrode, a platinum plate as the counter electrode and PBS as the electrolyte. A sinusoidal AC signal with 10 mV amplitude was applied over a frequency range of 1-10⁵ Hz. Both impedance and phase angle data were collected over the frequency range.

4.2.5 Characterization

NMR spectra (¹H, ¹³C and ²⁹Si) were acquired on either a Bruke DRX-400 or Bruker DRX-600 spectrometer. Chemical shifts are reported in parts per million,
referenced to chloroform solvent as internal standard (CHCl$_3$: 7.24 ppm for $^1$H and 77.2 for $^{13}$C).

Optical microscopy was performed on a Nikon Eclipse LV100 POL microscope. The images were collected via a Nikon DS-Ri1 camera.

FTIR spectra were collected on a Perkin Elmer Spectrum 100 spectrometer fitted with a Universal ATR accessory.

UV-visible spectra of the polymer films were collected on a Shimadzu UV-2550 spectrophotometer (Shimadzu, Japan).

Scanning electron microscopy images analysis of polymer films were acquired using a Zeiss Auriga 60 Focused Ion Beam-Scanning Electron Microscope (FIB-SEM) operating at 3 kV.

X-ray Photoelectron Spectroscopic Characterization was performed using a Kratos Axis Ultra 165 XPS system equipped with a hemispherical analyzer.

4.3 Results and Discussion

4.3.1 Syntheses and Characterization of ProDOT, POSS-SH and POSS-ProDOT

Thiol functionalized polyhedral oligomeric silsesquioxane (POSS) was synthesized via the direct hydrosilylation of 3-mercaptopropyl trimethoxysilane (MTS) in methanol as shown in Fig. 4.2, and its structure was confirmed by both NMR and FTIR spectra. The thiol functional side groups is critical for the following thiol-ene reaction to make a core material that can act as cross linker during the electrodeposition, thus the existence of the thiol groups need to be checked first. The $^1$H NMR spectrum of POSS-SH with assigned peaks is shown in Figure 4.4a, the thiol side group was clearly confirmed by the triplet centered at 1.38 ppm. The thiol group
can also be confirmed by the absorption peak located at 2550 cm$^{-1}$ ascribing to the characteristic absorption of $\text{–SH}$ stretching vibration in FTIR (Fig. 4.5). The 3D structure of POSS-based hybrid material which is vital to improve the mechanical properties of the PEDOT films was confirmed by both NMR and FTIR spectra. The sharp peak located at -67.12 ppm in $^{29}$Si NMR spectrum (Fig. 4.6) indicated that the silicon atoms were all magnetically equivalent, and this T-type silanol silicon peak confirmed that each silicon atom was covalently bonded with three oxygen atoms and one carbon atom, suggesting that the POSS–SH with cage-like structure was successfully synthesized. The asymmetric stretching vibration of Si–O–Si at 1082 cm$^{-1}$ and 1000 cm$^{-1}$ in FTIR confirmed the cage-like structure as well (Fig. 4.5). As shown in Fig. 4.1, ProDOT-ene was synthesized via the p-TSA catalyzed transetherification route from 3,4-dimethioxythiophene and 2-allyl-1,3-propanediol. The ProDOT-ene was purified as a light yellow viscous liquid and the chemical structure was confirmed by NMR and FTIR. In Figure 4.4b, all the chemical shifts corresponding to each proton on ProDOT-ene are clearly assigned. The two peaks located at 5.2 ppm and 5.8 ppm in $^1$H NMR correspond to the protons on the ene-moiety. The electroactive cross linker, POSS-ProDOT, was prepared from POSS-SH and ProDOT-ene via thiol-ene “click” chemistry with 0.1w% DMPA as radical initiator. As was confirmed by both $^1$H NMR (Fig. 4.4c) and FTIR (Fig. 4.5), the disappearance of the three peaks located at 1.38 ppm, 5.2 ppm and 5.8 ppm in $^1$H NMR and changes of the characteristic peaks associated with the alkene group on the ProDOT-ene ( =C-H bend at 916 and 994 cm$^{-1}$ and C=C stretch around 1639 cm$^{-1}$ ) and the –SH group on the POSS-SH ( -SH bend at 2550 cm$^{-1}$) indicated the success of the thiol-ene reaction.
Figure 4.1 Synthesis of ProDOT-ene

Figure 4.2 Synthesis of POSS-SH
Figure 4.3  Synthesis of POSS-ProDOT via thiol-ene “click” chemistry

Figure 4.4  Chemical structure and 1H NMR spectra in CDCl3 of  (a) POSS-SH, (b) ProDOT-ene and (c) POSS-ProDOT
Figure 4.5 FTIR spectra of ProDOT-ene (green), POSS-SH (red) and POSS-ProDOT (purple).
Figure 4.6  Chemical structure and 13C and 29Si NMR spectra in CDCl3 of POSS-SH
4.3.2 Electrochemical Study of POSS-ProDOT, EDOT and EDOT/POSS-ProDOT Mixed Solutions

The electrochemical behavior of POSS-ProDOT cross linker was investigated via Cyclic Voltammetry by potentiodynamically scanning the solution between -0.6 V and +1.5 V (vs. Ag/AgNO₃). Cyclic Voltammograms from a typical experiment are shown in Figure 4.8. An irreversible oxidation corresponding to ProDOT that occurred at +1.20 V was seen in the first anodic scan (red curve) and the similar oxidation potential value of the cross linker to that of EDOT indicated that it would be relatively easy to get POSS-ProDOT incorporated into PEDOT films. In the subsequent scans, unlike the electrochemical polymerization of ProDOT derivatives, no obvious peaks associated with the formation of PProDOT polymers were found at lower potentials.
during both anodic and cathodic scans. This low polymerizability of POSS-ProDOT is presumably due to the large steric hindrance coming from the bulky POSS core, and it is generally thought and has been reported by several groups that monomers with bulky side groups cannot form corresponding polymers via direct electrochemical polymerization. The electrochemical behaviors of pure EDOT and EDOT/POSS-ProDOT mixed solutions were also studied via cyclic voltammetry and no obvious difference was observed among these solutions.

Figure 4.8 Electrochemical polymerization of ProDOT-diene (5mM) in ACN/TBAP (0.1 M). 1st scan (red), subsequent scans, 2nd to 4th (purple).
4.3.3 Optical Properties

PEDOT/POSS-ProDOT copolymer films were obtained by applying a potentiodynamic scan with potential cycling between -0.6 V and +1.2 V (vs. Ag/AgNO₃) for 8 cycles in a series mixed monomer solutions. The optical properties of the films prepared in mixed monomer solutions didn’t change significantly with increasing POSS-ProDOT feed ratio. The electrochemically deposited PEDOT had a blue color due to its partially oxidized state, and the copolymers showed similar color as PEDOT thin films. The UV-Vis-NIR spectra of the polymer films under neutral states were shown in Figure 4.9. It was found that the copolymerization shifted the absorption maximum to shorter wavelength. As shown in Table 4.1, for pure PEDOT thin films, the absorption maximum was 576 nm, while with more and more cross linker added to the solution, the absorption maximum shifted from 576 nm to 543 nm. The 33 nm difference in absorption maximum also well explained the similar color of pure PEDOT and copolymer films. It was previously reported by our group that the absorption maximum of PEDOT films can be significantly tuned by adding a conjugated cross linker, EPh. Absorption maximum shifts of hundreds of nanometers were observed with EPh as cross linker, however, in our system, much smaller shifts were observed. This difference may lie in the fact that conjugated cross linker had a high impact on the electrochemistry of the EDOT and PEDOT, once the conjugated cross linker got incorporated into PEDOT chains, it significantly reduced the polymerizability of polymer chains and thus lead to a shorter chain length. On the contrary, in our system, the polymer chain length was presumably only affected by the steric hindrance from the bulky POSS core. And the slightly shortened chain length may probably result from the similar reactivity of ProDOT to that of EDOT and the relatively high degree of freedom of the pendant ProDOT molecule.
<table>
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<td>PEDOT-1.7% wt P-P</td>
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<tr>
<td>PEDOT-3.1% wt P-P</td>
<td>549</td>
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<tr>
<td>PEDOT-8.0% wt P-P</td>
<td>543</td>
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Table 4.1  UV-vis absorption maximum of PEDOT and copolymer films

![Figure 4.9](image)

Figure 4.9  UV-vis absorption of PEDOT films with various POSS-ProDOT contents.

4.3.4  Electrochemical Properties

PEDOT and PEDOT/POSS-ProDOT copolymers were electrochemically polymerized onto stainless steel electrodes under constant voltage (+ 1.1 V, a total
deposition charge of 27 mC) with tetrabutylammonium perchlorate (TBAP, 0.1 M) as electrolyte in a standard three-electrode cell. In order to serve as a good electrode for neural interface, it is necessary that this PEDOT film is more electrically active and more sensitive than its metal counterparts while in a physically and biochemically dynamic environment. To assess these issues, we performed both cyclic voltammetry (CV) to determine the charge storage capacity and electrical impedance spectroscopy (EIS) to determine electrode impedance. Cyclic voltammetry of stainless steel electrodes, PEDOT and its copolymers coated electrodes were shown in Figure 4.10. Both PEDOT and its copolymers showed reversible oxidation and reduction reactions as indicated by the anodic and cathodic current peak on the CV curve. The peak potential indicates the voltage at which the reaction takes place and the enclosed area of the curve is proportional to the charge storage capacity. Clearly the PEDOT and its copolymer films has significantly higher charge storage capacity (CSC) than the the stainless steel electrode. Such higher CSC associated with the high effective surface area is a result of both PEDOT’s unique faradic reaction and higher capacitance current. The CV curves of PEDOT and copolymers were of similar shape, while the oxidation peaks shifted to the positive direction with more cross linker added in. This shifted oxidation peaks indicated that the cross linker changed the conjugation length of PEDOT.

The electrochemical properties of coated electrodes were further investigated using electrical impedance spectroscopy (EIS) in 0.1 M PBS buffer solution. After PEDOT deposition, the amplitude of the impedance of the coated electrodes decreased by 2-3 orders of magnitude at frequencies between 1 Hz and 1000 Hz as seen in Figure 4.11. This dramatic drop in impedance has been associated with the increase in
effective surface area and ability of the PEDOT to facilitate both electronic and ionic transport. It was also found that at low POSS-ProDOT concentration (< 3.1wt%), the impedance of PEDOT copolymer coated electrodes were similar to that of PEDOT coated electrodes. While the impedance was slightly increased for PEDOT films with higher POSS-ProDOT concentration. The increased impedance at higher cross linker concentration may come from two major factors. Firstly, POSS nanoparticles are insulating and the excess POSS raised the internal impedance of the PEDOT-8.0 wt% POSS-ProDOT. Secondly, the cross linker changed the morphology of the polymer film during the electrochemical deposition, with more and more cross linkers added, the morphology gradually changed from an open structure to a closed structure. It has been reported that films with an open structure usually have lower impedance in comparison to the films with a closed structure. The 8.0 wt% POSS-ProDOT feed ratio has the most cross linker in the film and thus has the highest impedance.
Figure 4.10  Cyclic voltammetry of PEDOT and copolymer films

Figure 4.11  Electrochemical impedance spectroscopy of stainless steel, PEDOT and copolymer films deposited on stainless steel
4.3.5 Morphology

The morphologies of the electrochemically deposited PEDOT homopolymer and PEDOT/POSS-ProDOT copolymer thin films were studied using SEM shown in Figure 4.12. For PEDOT homopolymer films, two layers of both fuzzy, network-like structure composed of small fibers and interfibrillar pores were found. The bottom layer is relatively flat while the top layer is bumpy and with flower-like clusters covering the whole surface. The diameters of the small fibers and clusters are usually around 50 nm and 2 µm, respectively. The pore sizes are typically smaller than 1 µm in diameter. As POSS-ProDOT are introduced into the PEDOT/POSS-ProDOT films, their morphologies show an interesting evolution from a rough structure to a dense structure upon increasing the POSS-ProDOT loading. With more and more POSS-ProDOT in the mixed solutions, less and less clusters were found on the top layer of the films. For example, with 8.0 wt% POSS-ProDOT added, the pore sizes decreased, the flower-like clusters almost completely disappeared and some of the clusters were even collapsed into dense flakes. This is presumably due to the decreased solubility of copolymer chains in the solution since POSS-ProDOT could cross link PEDOT chains during the polymerization, and with more POSS-ProDOT added, more dense and insoluble precipitates were formed on the films due to the cross linking effect.
Figure 4.12  SEM images of PEDOT and copolymer films on stainless steel electrodes: (a) PEDOT; (b) PEDOT-1.7 wt% PP; (c) PEDOT-3.1 wt% PP; (d) PEDOT-8.0 wt% PP. Scale bar represents 10 µm

4.3.6 Electrochemical stability

For long-term electrochemical stability, conjugated polymer coatings were first studied by repeating CV tests in PBS buffer solution at a scan rate of 100 mV/s for 1000 consecutive cycles. After the CV cycling, all the polymer films were then subjected to an EIS test. It was clearly shown in Figure 4.13 that the copolymerization significantly affected the electrochemical stability of PEDOT films. With 1.7 wt% POSS-ProDOT in the feed, the copolymer film showed similar impedance spectra as the PEDOT film at the same deposition charge density. By increasing the POSS-ProDOT feed ratio to 3.1 wt%, a significant decrease in impedance magnitude was observed in comparison to the pure PEDOT film. When the POSS-ProDOT feed ratio was further increased to 8.0 wt%, the impedance benefit from the conjugated polymer
coatings was almost diminished. At 8.0 wt% POSS-ProDOT feed ratio, the impedance magnitude of the coated electrode after the stability test was at the same magnitude as stainless steel electrode. The results are presumably resulted from the continuous swelling and shrinkage during the long-term charge/discharge process. The POSS-ProDOT is mechanically more stable than PEDOT and can act as a cross linker in the polymer matrix and thus can restrict the change of the polymer films during the oxidation and reduction process. For 1.7 wt% POSS-ProDOT feed ratio, only few cross linker was incorporated into the polymer and thus the copolymer showed similar stability as PEDOT. By increasing the feed ratio to 3.1 wt%, an appropriate amount of POSS-ProDOT is incorporated into the polymer and the strengthening effect coming from the cross linker can help increase the stability of PEDOT coatings. While with further increased feed ratio, the possibly substantially changed mechanical properties of PEDOT films made themselves unstable under CV stimulations. The stability change of copolymer films can also be confirmed by evaluating the morphology of the coatings after CV cycling. A comparison of the electrochemical impedance of stainless steel, PEDOT and copolymers at 1 Hz before and after stability tests was shown in Figure 4.14. The SEM images of the PEDOT and copolymer with various POSS-ProDOT contents were shown in Figure 4.15. After the stability test, PEDOT film showed cracks and delamination which is consistent with literature. By adding 1.7 wt% POSS-ProDOT, only macro crack was observed. Films with 3.1 wt% POSS-ProDOT showed the most intact morphology with no crack or delamination. Polymer coating with 8.0 wt% showed similar crack and delamination as pure PEDOT films. The trend of the effect of cross linker on the morphologies of PEDOT films correlated well with the EIS spectra.
Figure 4.13  Electrochemical impedance spectroscopy of PEDOT and copolymer films after stability test.

Figure 4.14  Electrochemical impedance spectroscopy of Stainless steel, PEDOT and copolymer films at 1 Hz before and after stability tests.
4.4 Conclusions

In summary, we have synthesized an octa-ProDOT functionalized polyhedral oligomeric silsesquioxane (POSS-ProDOT) cross linker via hydrosilylation and thiol-ene “click” chemistry, and its structure was confirmed by both nuclear magnetic resonance (NMR) ($^1$H, $^{13}$C, $^{29}$Si) and Fourier transform infrared (FT-IR) spectroscopies. The cross linker was electrochemically copolymerized with EDOT in mixed monomer solutions to create cross-linked PEDOT/POSS-ProDOT copolymer composite films on metal electrodes. The optical, electrical and morphological...
properties of the copolymer films can be tuned by adjusting the feeding ratio of the cross linker. With more POSS-ProDOT incorporated into the films, the optical absorption shifted towards shorter wavelength direction, the impedance slightly increased and the morphology gradually changed from an open structure to a closed structure. The electrical stability of PEDOT films were studied via chronic stimulation tests and significantly enhanced stability at low POSS-ProDOT content were observed with 3.1 wt% POSS-ProDOT exhibiting the best result. It is expected that this highly stable PEDOT-co-POSS-ProDOT material will be an excellent candidate for use in biomedical devices such as neural electrodes.
Chapter 5

POST-POLYMERIZATION FUNCTIONALIZATION OF POLY(3,4-PROPYLENEDIOXYTHIOPHENE) (PProDOT) VIA THIOL-ENE “CLICK” CHEMISTRY

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5.1 Introduction

Poly(3,4-alkylenedioxythiophenes) such as poly(3,4-ethylenedioxythiophene) (PEDOT) and poly(3,4-propylenedioxythiophene) (PProDOT) and their derivatives have been widely used in organic solar cells,\textsuperscript{114,115} electrochromic devices,\textsuperscript{116,117} biosensors\textsuperscript{118} and neural electrodes.\textsuperscript{7,43} The interest in using polydioxythiophenes for these applications is related to their low oxidation potential, relatively high chemical and thermal stability, and high conductivity. For example, electrochemically deposited PEDOT films on metal electrodes have shown to dramatically decrease the impedance of the microfabricated neural probes.\textsuperscript{37} Polythiophenes are also of interest for energy storage and conversion devices. Liu and coworkers designed and characterized an electrochemical supercapacitor based on PProDOT-Me\textsubscript{2}.\textsuperscript{119}

The performance of conjugated polymers depends largely on the ability to optimize their properties for a given application. To improve conductivity, for example, the films are often annealed (either thermally or in solvent vapor)\textsuperscript{27} or small molecule additives are incorporated.\textsuperscript{120} However, the processability, surface chemistry, and biocompatibility of conjugated polymer films can only be tuned within
a limited range without additional synthesis or functionalization. Fast and convenient chemical functionalization of conjugated polymers is still a challenge and of considerable continued interest for a wide variety of applications.

Conjugated polymers are often polymerized electrochemically instead of chemically due to their typically low solubility and the common requirement of a thin-film geometry. Electrochemical polymerization has many advantages over traditional chemical polymerization such as its speed, reproducibility, and ability to create films with precisely controlled film thickness and morphology. Functionalized conducting polymers can be made by incorporating specific small molecules or even polymers of interest into the film as dopants during electropolymerization. However, since the dopants are only physically entrapped in the films, the desired functionality may be lost after dopant release or exchange during extended use. There still remains a need for reliable, stable film chemical functionalization strategies. Covalently incorporating functional groups onto the monomers themselves is an attractive strategy for the film functionalization. By doing so, it is ensured that the chemical functionality will remain in the film and not be lost upon electrochemical cycling. Various previous efforts have been directed toward the synthesis and electrochemical polymerization of polymers based on modified 3,4-alkylenedioxythiophenes. Balog et al. reported the synthesis of a functionalized EDOT derivative bearing a highly nucleophilic thiolate group as the side chain. Guittard synthesized and characterized a fluorinated EDOT derivative and made superhydrophobic films by electrochemically polymerizing this new monomer. Malmstrom synthesized a new EDOT derivative with an ATRP-initiating side group and grafted poly(acrylic acid) (PAA) brushes on PEDOT films via ATRP.
Povlich successfully introduced a carboxylic acid side group to EDOT and created peptide-functionalized PEDOT films.\textsuperscript{28} Despite the simplicity and success of using functionalized thiophene monomers to make copolymers, it is not applicable when the introduced side groups are too bulky or have competing redox reactions under the same conditions with the monomer polymerization.\textsuperscript{73,74,123,124} Side groups with low oxidation potentials may interfere with, or even inhibit, the thiophene polymerization reaction.

Post-polymerization functionalization of appropriately designed precursor conjugated polymers is a possible means to overcome this problem. Post-polymerization functionalization has been widely used in conventional polymer surface modifications, and has also been applied to conjugated polymers.\textsuperscript{75,125} However, in macromolecular reactions, the low reaction rate and the formation of byproducts can often be drawbacks. Therefore, the use of a clean, efficient reaction that could be carried out under mild conditions with high yield and easy separation would be even more advantageous. In this respect, the radical based thiol–ene “click” reaction is a particularly attractive candidate for polymer functionalization. This reaction has received considerable attention in recent years due to its many advantages over other available coupling reactions.\textsuperscript{76,77,126,127} Thiol–ene “click” reactions usually tolerate a variety of solvents in the presence of oxygen. They give high, often quantitative yields, and produce limited byproducts, leading to straightforward purification. They have been shown to be particularly useful in polymer surface functionalization and macromolecular synthesis including block copolymers and dendrimers, as well as in more traditional applications ranging from crosslinked networks to functionalized biomaterials. Thiol–ene “click” chemistry also provides an
additional advantage over other “click” methods that various cysteine-containing peptides or proteins (i.e., with terminal thiols) could be easily introduced to the polymer without extra chemical modification or toxic catalysts. This would be especially beneficial for biofunctionalizing conjugated polymers on biomedical devices such as neural electrodes.\textsuperscript{28,78,128}

In this chapter, we report the post-polymerization functionalization of poly(3,4-propylenedioxythiophene) (PProDOT) via thiol–ene “click” chemistry. Various terminal thiols were surface immobilized onto PProDOT-diene films under mild reaction conditions with high conversion efficiencies. The resulting functionalized PProDOT polymers were examined by a variety of analytical techniques.

![Synthesis of ProDOT-diene (1), electrochemical polymerization of (1) to form poly(ProDOT-diene) (P1) and “click” reaction of P1 with various thiols 2a-c to form P2a-c. (i) pTSA in Toluene at 100 °C for 2 days (ii) ACN/TBAP; (iii) 0.1% DMAP, UV 365 nm, room temperature.]

\textbf{Figure 5.1} Synthesis of ProDOT-diene (1), electrochemical polymerization of (1) to form poly(ProDOT-diene) (P1) and “click” reaction of P1 with various thiols 2a-c to form P2a-c. (i) pTSA in Toluene at 100 °C for 2 days (ii) ACN/TBAP; (iii) 0.1% DMAP, UV 365 nm, room temperature.
5.2 Materials and Methods

5.2.1 Materials

3,4-Dimethoxythiophene, diethyl diallylmalonate, lithium aluminum hydride, tetrahydrofuran (THF), toluene, p-toluene sulfonic acid (p-TSA), acetonitrile (ACN), tetrabutyl ammonium perchlorate (TBAP), 2-ethylhexanethiol, o-(2-mercaptoethyl)-o’-methyl-hexa(ethylene glycol), 6-(ferrocenyl) hexanethiol were purchased from Sigma-Aldrich. All reagents and solvents were used without further purification, unless otherwise noted. ITO coated glass slides were purchased from Delta Technologies.

5.2.2 Chemical and Electrochemical Polymerization

For oxidative chemical polymerization, FeCl₃ (112 mg, 0.69 mmol) was suspended in 2 mL of CHCl₃ with stirring. A solution of ProDOT-diene (55 mg, 0.23 mmol) dissolved in 1 mL of CHCl₃ was added dropwise, upon which the solution immediately turned dark purple. After stirring for 18 h at room temperature, excess methanol was added to precipitate the polymer and wash away any remaining FeCl₃. The resulting solid was filtered and washed with methanol, then dried under vacuum to give 30 mg (55% yield) of a purple powder. The electrochemical polymerization of ProDOT-diene and characterization of the resulting PProDOT-diene polymer films were performed with an Autolab PGstat12 Potentiostat/Galvanostat (EcoChemie) controlled by a personal computer using the Nova 1.8 electrochemical software in a three-electrode cell. ITO-coated glass (Delta Technologies) served as the working electrode, a platinum plate of 1 cm² surface area was the counter electrode, with Ag/AgNO₃ as the reference electrode. The electrochemical polymerization of ProDOT-diene was studied in a dilute (5 mM) acetonitrile solution containing 0.1 M
tetrabutyl ammonium perchlorate (TBAP) as supporting electrolyte. The electrodeposited and surface modified polymer films were investigated in neat electrolyte solution free of monomer.

5.2.3 Thiol-Ene “Click” Reaction

ITO electrodes coated with PProDOT-diene (P1) thin films with thickness ranging from 0.5 mm to 1.5 mm were immersed into vials containing appropriate thiols (2 mmol) in acetonitrile and 0.1 wt% DMPA as catalyst. Samples were irradiated using a UVP Black Ray UV Bench Lamp XX-15L, emitting 365 nm light at 15 W. After 1 hours of UV (365 nm) exposure at room temperature, the functionalized films were rinsed with copious amounts of acetonitrile and dried in vacuum.

5.2.4 Characterization

NMR spectra (\(^1\)H and \(^{13}\)C) were acquired on a Bruker DRX-400 spectrometer. Chemical shifts were reported in parts per million, referenced to chloroform solvent as internal standard (CHCl\(_3\): 7.24 ppm for \(^1\)H and 77.2 for \(^{13}\)C). FTIR spectra were collected on a Perkin Elmer Spectrum 100 spectrometer fitted with a Universal ATR accessory. Scanning Electron Microscopy (SEM) images and Energy-dispersive X-ray Spectroscopy (EDS) analysis were acquired using a Zeiss Auriga 60 Focused Ion Beam-Scanning Electron Microscope (FIB-SEM) operating at 3 kV (SEM) and 10 kV (EDS), respectively. Static water contact angles measurements were performed by applying a 5 mL drop of deionized water to a film set on a levelled base.Photographs were taken of the drops and their contact angles measured using ImageJ software with a Drop Shape Analysis plug-in and the DropSnake method.
5.3 Results and Discussion

5.3.1 Synthesis and Chemical Polymerization of ProDOT-diene

Figure 5.2 Chemical structure and 1H NMR spectra in CDCl₃ of (a) ProDOT-diene and (b) ProDOT-diEH
Figure 5.3 $^{13}$C NMR spectra of ProDOT-diene in CDCl$_3$
Figure 5.4 FTIR spectra of ProDOT-diene and ProDOT-diEH. Characteristic absorption bands are labelled with their corresponding wavenumbers.

The bi-functional precursor monomer ProDOT-diene was synthesized via the p-TSA catalyzed transesterification route from 3,4-dimethoxythiophene and 2,2-diallyl-1,3-propanediol (Figure 5.1) as previously described.\textsuperscript{21} The dialkene functionalized monomer offers a number advantages over the monofunctional monomer with either alkene, alkyne or azide as the side group. Compared to the mono-functional monomer we previously reported, the bi-functional derivative would largely increase the graft density of the surface modification and thus the properties of the conjugated polymers could be more widely tuned. In addition, functional polymers with pendant electroactive side groups could be produced via either thiol–ene “click” or azide–alkyne “click” step growth polymerization with a bi-functional precursor monomer.
The dialkene functionalized monomer also opens the possibility of directly polymerization via ADMET polymerization.

The ProDOT-diene was purified as a light yellow viscous liquid and the chemical structure was confirmed by $^1$H NMR, $^{13}$C NMR and FTIR. In Fig. 5.2 A, all the chemical shifts corresponding to each proton on the monomer are clearly assigned. The two peaks located at 5.2 ppm and 5.8 ppm in $^1$H NMR correspond to the protons on the ene-moiety. Fig. 5.4 A displays the FTIR spectrum of ProDOT-diene. The peaks around 1374 and 1451 cm$^{-1}$ are the characteristic C=C and C–C stretches of the thiophene ring. The stretching absorption of the alkylenedioxy group and the C–S stretch of the thiophene ring are found at 1189 and 847 cm$^{-1}$, respectively.

To verify that the thiol–ene “click” chemistry was feasible for this molecule, ProDOT-diene was subjected to various terminal thiols in the presence of a radical initiator. As confirmed by both $^1$H NMR (Fig. 5.2 B) and FTIR (Fig. 5.4 B), the disappearance of the two peaks located at 5.2 ppm and 5.8 ppm in $^1$H NMR and changes of the characteristic peaks associated with the alkene group on the ProDOT-diene (≈C–H bend at 916 and 994 cm$^{-1}$ and C=C stretch around 1639 cm$^{-1}$) indicated that the alkene side groups were consumed during the thiol–ene addition. This clearly shows that the ProDOT-diene derivative structure allows various functionalized monomers to be attached through this highly efficient chemistry. The synthesis, polymerization and post-polymerization functionalization process of ProDOT-diene are shown in Fig. 5.1.

We previously reported the polymerization of various monofunctionalized ProDOTs including ProDOT-ethylhexane and ProDOT-SO$_3$H.$^{21}$ We also successfully polymerized difunctionalized ProDOT with different small alkyl side groups, for
example butanethiol. However, it is not possible to polymerize monomers with electroactive side groups that have lower oxidation potentials than the monomer backbone. Bulky, sterically hindered side groups can also interfere with thiophene Polymerization.\textsuperscript{73,74,124,130} In these cases, the direct modification of the conducting polymer products, instead of the monomer precursors, allows for fine-tuning of the ultimate materials surface chemistry without compromising the polymerization and fabrication processes.

PProDOT-diene was chemically polymerized in chloroform with ferric chloride as oxidant, precipitated and then rinsed with copious amounts of methanol to give a dark purple powder. The unmodified polymer had limited solubility in all kinds of organic solvents, however, after modification with alkyl thiols using “click” chemistry the final product showed solubility in tetrahydrofuran, chloroform and toluene. This successfully proved that the thiol–ene “click” chemistry could also be performed on solid polymers as well as the liquid monomers.

5.3.2 Electrochemical Polymerization and Characterization

The ProDOT-diene monomer was electrochemically polymerized with a potentiodynamic method, scanning between -0.60 V and +1.30 V (vs. Ag/AgNO\textsubscript{3}). Cyclic voltammograms from a typical experiment are shown in Fig. 5.5. The irreversible oxidation of ProDOT-diene at +1.20 V is seen in the first anodic scan (red curve). In the subsequent scans, new electroactive species appeared at lower potentials with two small peaks at +0.05 V and +0.35 V corresponding to the formation of polarons and bipolarons\textsuperscript{131,132} during the anodic scan and two reduction peaks at +0.10 V and -0.28 V during the cathodic scan. The two anodic peaks gradually merged into one broad anodic peak after further electrochemical scans, probably due to the post-
polymerization of the polymer. These peaks demonstrated the formation and growth of the PProDOT-diene conjugated polymer film. The thickness of the polymer film steadily increased and could be precisely controlled by the number of scans (Fig. 5.6). The resulting polymer thin films were well adhered to the ITO substrate.

Figure 5.5 Electrochemical polymerization of ProDOT-diene (5mM) in ACN/TBAP (0.1 M). 1st scan (red), subsequent scans, 2nd to 6th (purple).
Figure 5.6  Relationship between scan cycles and film thickness.

In order to study the redox behavior of the polymer, the films (0.6 mm thick) were rinsed with acetonitrile to eliminate any residual monomer and then cyclic voltammetric studies were performed with the electrodeposited polymer in 0.1 M solution of TBAP in monomer-free acetonitrile by cycling the potential between -0.60 V and +0.80 V at scan rates of 50, 100, 150, 200, 250, 300 and 350 mV/s (Fig. 5.7a). The polymer oxidation and reduction current increased linearly as a function of voltage scan rate\(^{133,134}\) indicating that the coating was electroactive (Fig. 5.7b). For subsequent surface modification of conducting polymers, electrochemically stable films are a prerequisite. The electrochemical stability of the polymer film P2 was examined by continuous redox cycling. The CV curves of the 1st scan and 100th scan are plotted in Fig. 5.8. By comparing the charge storage capacity (CSC) of the two curves, it was found that 93% of the CSC was retained after 100 electrochemical
scans, indicating that the polymer film is indeed electrochemically stable and would be an excellent platform for post-polymerization functionalization.

Figure 5.7  (a) Scan rate dependence of P(ProDOT-diene) film on a ITO electrode in 0.1 M TBAP/ACN at different scan rates. (b) Relationship of anodic and cathodic current peaks as a function of scan rate of P(ProDOT-diene) in 0.1 M TBAP/ACN.
5.3.3 Post-Polymerization Functionalization and Electrochemical Characterization

Based on the high yield of the “click” reaction at the monomer stage and the highly stable thin polymer films that were generated by electrodeposition, it was possible for us to modify the surface of the poly(ProDOT-diene) with various terminal thiols. The protocol for post polymerization functionalization of PProDOT-diene (P1) by thiol–ene “click” chemistry was as follows: ITO electrodes coated with PProDOT-diene thin films were immersed in vials containing various thiols (a–c in Fig. 5.1)
in acetonitrile as solvent and 2,2'-dimethyl-2-phenyl-acetophenone (DMPA) as photo-initiator. After being exposed to UV 365 nm for 3 hours at room temperature with gentle swirling, the films were rinsed with copious amounts of acetonitrile to remove excess thiols \(^{135}\) and then dried in vacuum.

![FTIR spectra](image)

Figure 5.9 FTIR spectra of P(ProDOT-diene) and EH-thiol modified P(ProDOT-diene). Part of the characteristic absorption bands are labelled with wavenumbers.

Fig. 5.9 compares the FTIR spectra of the polymer films before and after surface immobilization from 1900 cm\(^{-1}\) to 600 cm\(^{-1}\),\(^{20,136,137}\) By comparing the FTIR spectrum of P1 with that of P2a, characteristic changes in the spectral features can be found. The
stretching band of the –C=C backbone at 1638 cm⁻¹ and =C–H stretch at 916 cm⁻¹ were found in P1, but almost completely disappeared in the FTIR spectrum of P1a. This observation indicates that the attachment of the EH-thiol onto the P1 side chain is associated with the consumption of the –CH=CH₂ moieties of P1, which can be ascribed to the thiol–ene addition in the present case.

Figure 5.10  Cyclic Voltammograms of P(ProDOT-diene) films after post-polymerization functionalization with various terminal thiols a-c via thiol-ene “click” chemistry in acetonitrile containing 0.1M TBAP as electrolyte.
In order to demonstrate the broad scope of our synthetic strategy, three moieties with different conductivities and functionalities were chosen. The ethyl-hexyl moiety has alkyl side groups (a) that are charge blocking, so we expected that this group would create an electrically insulating layer, leading to a dramatic decrease in the charge transport properties. While not useful for devices, it would demonstrate that the chemistry was proceeding as anticipated. For the PEG thiol (b) we expected to form a thin, uniform, hydrophilic surface layer. Such layers are known to be useful for functionalizing biomedical devices. Ferrocene (c) is an electroactive substituent that can easily change its oxidation state. Attaching a moiety such as this to the polymer films, and showing that the modified material responds dramatically to the electrical activity of the environment, would show the potential of similar chemistries for making chemical sensors based on these materials. The electrochemical behavior of the resulting polymer films was investigated by CV. The comparison of the CV curves of the pristine and modified films is shown in Fig. 5.10. It is clear that the redox behavior of the PProDOT films was considerably altered by grafting the functional moieties onto their surfaces. The disappearance of the broad redox peaks located at +0.1 V that were observed in the pristine polymer film P1 and the significantly reduced charge storage capacity of the modified film P2a (Fig. 5.10a) are evidently due to the relatively insulating nature of the 2-ethylhexane thiol (a). The electroactivity of the PProDOT was maintained when modified with a relatively short alkane chain, whereas longer alkyl side groups block charge transport more effectively. In our experiment, the bi-functionality of the side chain presumably allowed a high surface density of grafted alkyl chains. Fig. 5.10b showed that both the redox peak potentials and the oxidation onset potentials in the o-(2-mercaptoethyl)-o’-
methyl-hexa(ethylene glycol) (b) modified polymer film P2b shifted in the positive direction. The oxidation peak potential shifted from +0.1 V to +0.5 V and the oxidation onset potential shift from -0.35 V to +0.15 V. The higher charge storage capacity of polymer film P2b as compared to polymer film P2a is evidently due to the enhanced ion transport enabled by thiol (b) considering the almost tripled chain length of thiol (b) than that of thiol (a). The CV of polymer P2c which was modified by electroactive 6-(ferrocenyl) hexanethiol (c) clearly showed the reversible redox behavior of the ferrocene overlaid with the broad peaks of the PProDOT conducting polymer backbone. The potential of the reduction peak in polymer film P2c was the same as for thiol (c) while the potential of the oxidation peak of the modified polymer film P2c (Epox = +0.22 V) was slightly higher than that of thiol (c) (Epox = +0.15 V). This may be due to interference with the conducting polymer itself. Similar to P2b, the oxidation onset potential also shifted to the positive direction moving from 0.35 V to 0 V.

5.3.4 Surface Characterization

The successful surface immobilization on the PProDOT-diene thin films was also confirmed by static contact angle measurements as shown in Figure 5.11. The pristine PProDOT-diene films were quite hydrophobic, with a water contact angle of 130°. This high contact angle value is likely due to both the intrinsic hydrophobicity of PProDOT polymer films, as well as the rough surface structure of the polymer films as shown in Fig. 5.12. Due to the similarly non-polar EH-thiol and ferrocene thiol groups, not much difference was found between the corresponding modified and unmodified PProDOT films. However, when highly hydrophilic PEG was grafted onto the surface, the contact angle of the polymer films decreased to 50°, confirming the
ability to dramatically tune the surface wettability of these conjugated polymer coatings through surface chemistry.

Figure 5.11 Contact angle measurement of P(ProDOT-diene) film (a), Ethylhexane thiol modified film (b), PEO6 thiol modified film (c) and Ferrocene thiol modified film (d).
Figure 5.12 SEM images of (a) P(ProDOT-diene); (b) EH-thiolmodified PProDOT-diene; (c) PEO-thiol modified P(ProDOT-diene); (d) Ferrocene-thiol modified PProDOT-diene. (Scale bar represents 2 µm)
The morphologies of the polymers before and after modification were examined using SEM as shown in Fig. 5.12. Similar to the PProDOT films as shown in Fig. 5.13, the PProDOT-diene films also showed a rough, network-like structure composed of small fibers and interfibrillar pores. In these networks, the diameter of the pores was between 100 and 300 nm and the diameter of these fibers was around 100 nm. Morphological studies of PProDOT-diene films prepared with different numbers of
deposition scans revealed an initially dense surface layer followed by a more articulated, rough surface structure. The effective surface area is significantly increased by this open, rough morphology, and this facilitates charge transport.  

Another potential advantage is that rough surfaces may enhance cell adhesion strength and thus promote growth and proliferation. The rough surface morphology of the PProDOT-diene films investigated were all well retained even after the modification with various thiols, as seen in Fig. 5.12. This makes it feasible for us to consider immobilizing other moieties of interest such as catalysts or biologically active molecules that could find potential applications in novel biosensors or biomedical devices, while retaining the advantages of the rough, articulated surface morphology.

![Figure 5.14 EDS analysis of ferrocene thiol modified P(ProDOT-diene).](image)

5.4 Conclusions

We have synthesized and characterized a dialkene-functionalized variant of the ProDOT monomer (ProDOT-diene). The corresponding polymer PProDOT-diene was successfully synthesized via both oxidative chemical polymerization and potentiodynamic electrochemical polymerization. Various terminal thiols were readily attached to the PProDOT-diene films by using thiol–ene “click” reactions under mild
conditions. Systematic variations in cyclic voltammetry were observed in the functionalized polymer films, clearly showing how these surface modifications could be used to dramatically alter the charge transport and wetting behavior of the resulting polymer films. This synthetic route also allows the incorporation of pendant electronically active groups such as ferrocene to be covalently attached to the conducting polymer films, which is usually not possible by direct polymerization of the corresponding monomers. This synthetic strategy provides a straightforward means for immobilizing other moieties of interest for conjugated polymer films, such as catalysts or biologically active molecules that could find potential applications in novel biosensors or biomedical devices.
Chapter 6

CONCLUSIONS AND FUTURE DIRECTIONS

6.1 Conclusions

In this thesis, we presented the stability improvement, surface functionalization, and nucleation and growth mechanism studies of electrochemically polymerized poly(3,4-alkylenedioxythiophenes) coatings for biomedical applications.

The second and third chapters described using EDOT-COOH (Chapter 2) and EDOT-NH$_2$ (Chapter 3) as adhesion promoters for improving the adhesion strength of PEDOT films. It was found that ITO electrodes were successfully modified by either EDOT-COOH or EDOT-NH$_2$ via chemisorption and PEDOT thin films could be electrodeposited onto the modified electrodes. Neither adhesion promoter sacrificed the electrochemical properties of the films, and the mechanical stability and adhesion of the PEDOT coatings were significantly improved in both cases.

The fourth chapter described another method to improve the mechanical and electrochemical stability of PEDOT films using an octa-ProDOT functionalized polyhedral oligomeric silsesquioxane (POSS-ProDOT) as crosslinker. The crosslinker was synthesized via hydrosilylation and thiol-ene “click” chemistry, and its structure was confirmed by both Nuclear Magnetic Resonance (NMR) ($^1$H, $^{13}$C, $^{29}$Si) and Fourier Transform Infrared (FT-IR) spectroscopies. The crosslinker was electrochemically copolymerized with EDOT in mixed monomer solutions to create cross-linked PEDOT/POSS-ProDOT copolymer films on metal electrodes. The optical, electrical and morphological properties of the copolymer films can be tuned
by adjusting the feed ratio of the crosslinker. With more POSS-ProDOT incorporated into the films, the optical absorption shifted towards shorter wavelengths, the impedance slightly increased and the morphology gradually changed from an open structure to a closed structure. The electrical stability of PEDOT films were studied via chronic stimulation tests and significantly enhanced stability at low POSS-ProDOT content were observed with 3.1 wt% POSS-ProDOT exhibiting the best result. It is expected that this highly stable PEDOT-co-POSS-ProDOT material will be an excellent candidate for use in biomedical devices such as neural electrodes.

The fifth chapter described the surface functionalization of PProDOT films via thiol-ene “click” chemistry. A dialkene-functionalized variant of the ProDOT monomer (ProDOT-diene) was synthesized and characterized. The corresponding polymer PProDOT-diene was successfully polymerized via both oxidative chemical polymerization and potentiodynamic electrochemical polymerization. Various terminal thiols were readily attached to the PProDOT-diene films by using thiol–ene “click” reactions under mild conditions. Systematic variations in cyclic voltammetry were observed in the functionalized polymer films, clearly showing how these surface modifications could be used to dramatically alter the charge transport and wetting behavior of the resulting polymer films. This synthetic strategy provides a straightforward means for immobilizing other moieties of interest for conjugated polymer films, such as catalysts or biologically active molecules that could find potential applications in novel biosensors or biomedical devices.
6.2 Future Directions

6.2.1 Adhesion Promoter

As stated previously in this chapter, two different molecules (EDOT-COOH and EDOT-NH\(_2\)) were used in this thesis. The mechanical stability of the polymer films was significantly improved while the electrochemical stability almost stayed the same. It is of interest to know whether the poor electrochemical stability is from the adhesion promoter or the bulk film. By studying the performance of the chemisorbed thin layer, we can get a better understanding of the adsorption/desorption process under electrochemical stimulus. If these two molecules desorb or decompose severely under electrochemical stimulus, a more stable side group such as silane or alkene will be needed to make a better adhesion promoter. Another interesting possibility would be to study the nucleation and growth of the deposition on modified substrate. On unmodified substrates, polymerization can only take place in the solution, and polymer films are formed via precipitation. If modified substrates are used, polymer chains can either grow from the substrate or precipitate out from the solution. It would be interesting to know at what stages during the polymerization these two different routes take place. The “grow-from” approach is more likely to take place at the beginning while the “precipitate out” mechanism would probably go on through the whole deposition process. Adhesion and electrochemical properties of these films at their early stages should be studied and compared, and detailed knowledge about the nucleation and growth-performance relationship would be obtained. With this better understanding of the nucleation and growth mechanisms, new molecular designs and electrochemical deposition methods for better device performance are expected.
6.2.2 PEDOT Crosslinkers

As mentioned in the first chapter the electrochemical stability of PEDOT films was improved using a medium concentration of cross linker while the modulus also increased. It is advantageous to lower the modulus of coatings on stiff electrodes to mitigate the foreign body reaction when implanted into soft tissue. A crosslinker that doesn’t so significantly increase the Young’s modulus of the films would be an interesting future development. Figure 6.1 shows one potential molecular design consisting of a long chain polymer containing alternating ProDOT and poly(ethylene glycol) (PEG) oligomer units. Pendant ProDOT moieties are linked to the main chain via thiol-ene chemistry, so that during the polymerization the PEG units would not interfere with the conjugated polymer chain. PEG oligomers are chosen because of the following reasons: 1, PEG is more biocompatible than POSS or PEDOT, so using PEG should improve the biocompatibility of the whole films and thus might help mitigate the foreign body reaction; 2, PEG oligomers are softer materials with a Young’s modulus less than 100 MPa and it can help decrease the Young’s modulus of the bulk film. Other molecular designs, such as replacing the PEG oligomers using various thiol functionalized peptides or other biomolecules could be used to further improve the biocompatibility.

If this long chain crosslinker was chemically polymerized through its EDOT monomers, then a soft conducting polymer gel should be obtained. Systematic studies on the mechanical, morphological and electrochemical properties of these gels should be performed.

Besides its potential use as a crosslinker, this ProDOT-PEG copolymer could also be electrospun into fibers because of its high solubility in various kinds of solvents. By tuning the molecular weights of the ProDOT segment and the PEG
segment, polymer fibers with different compositions could be made. Systematic studies about the polymer chain orientation within the single fiber, mechanical property and conductivity of single fiber can then be performed.

Another interesting molecular design, a ProDOT end capped PEG monomer, is shown in Figure 6.2. This simple molecule itself can be used as a cross linker as well. By tuning the chain length of the PEG segment, polymers with different ionic/electronic conductivity could be obtained. If the PEG segment is relatively long and the two ProDOT ends are replaced with ProDOT oligomers or polymers, as shown in Figure 6.3, then the new polymer maybe can self-assemble and have some interesting properties.

![Figure 6.1 Structure of the ProDOT and PEG oligomer copolymer.](image1)

![Figure 6.2 Structure of ProDOT-PEG-ProDOT monomer.](image2)
6.2.3 Surface Modification

As discussed earlier in this chapter, the P(ProDOT-diene) synthetic strategy can be applied to almost any peptide or other biomolecules that reacts with the alkene side groups with a very high yield. The effect of peptide or other biomolecules modified surfaces on the growth and differentiation of neuronal cells needs to be investigated in vitro using a mixture of neuronal and non-neuronal primary cells.

It would also be interesting to electrochemically polymerize the P(ProDOT-diene) with peptides as co-dopant in gels and a peptide rich soft conjugated polymer gel should be obtained. This gel could undergo further thiol-ene reactions and the polymers inside the gel could be further functionalized with peptides. In vitro and in vivo studies regarding the growth and differentiation of neuronal cells also need to be investigated.

6.2.4 PEDOT Cubic Phase

Recently, Jeong and coworkers reported the highly stretchable PEDOT:PSS and surfactant mixtures that can be potentially used as deformable electronics, but the structure of these mixtures are not well understood. Our group previously reported
the characterization of bicontinuous cubic PEDOT gels prepared within lyotropic cubic poly(oxyethylene)$_{10}$ nonylphenol ether (NP-10) templates$^{146}$. The chemical composition of the two systems seem similar and it is suspicious that there’s some ordered structure inside mixtures. A simple diffusion couple experiment could be carried out, and optical microscope can be used to roughly study the structure of the mixtures at different compositions. Different phases, such as lamellar, hexagonal and cubic phases, may be seen from the diffusion couple, and SAXS or TEM can be used to study the crystal structure of the mixtures.

Another interesting experiment that can be done with PEDOT:PSS is to blend it with PEG and glycidoxypropyltrimethoxysilane (GOPS). PEG can improve the toughness of PEDOT:PSS aGOPS can cross link the mixtures. By blending with these two reagents, the new soft, tough and highly conductive will be interesting for some potential applications, such as implantable devices.
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Appendix

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