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Poly(3,4-ethylenedioxythiophene): Dextran sulfate (PEDOT: DS) - A highly processable conductive organic biopolymer

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Abstract

A novel water-dispersible conducting polymer analogous to poly(3,4-dioxythiophene):polystyrene sulfonate (PEDOT:PSS) has been chemically synthesized in a single reaction in high yield. PEDOT:DS, a new member of the polythiophene family, is composed of a complex between PEDOT and the sulfonated polysaccharide polyanion dextran sulfate. Drop-cast films of aqueous suspensions of the material display a native conductivity of up to $7 \pm 1 \text{ S cm}^{-1}$, increasing to $20 \pm 2 \text{ S cm}^{-1}$ after treatment with ethylene glycol and thermal annealing. Mass ratios of the precursors NaDS and EDOT were varied from 5:1 to 2:1 and a decrease in the NaDS:EDOT ratio produces tougher, less hygroscopic films of higher conductivity. Ultraviolet-visible spectroelectrochemistry yields spectra typical of PEDOT complexes. Cyclic voltammetry reveals that PEDOT:DS is electrochemically active from -1.0 to 0.8V vs. Ag/Ag⁺ in acetonitrile, with similar characteristics to PEDOT:PSS. Water dispersions of PEDOT:DS are successfully processed by drop casting, spray coating, inkjet printing and extrusion printing. Furthermore, laser etching of dried films allows the creation of patterns with excellent definition. To assess the cytotoxicity of PEDOT:DS, L-929 cells were cultured with a polymer complex concentration range of 0.002 to 0.2 g l⁻¹ in cell culture medium. No significant difference is found between the proliferation rates of L-929 cells exposed to PEDOT:DS and those in plain medium after 96h. However, PEDOT:PSS shows around 25% less cell growth after 4days, even at the lowest concentration. Taken together, these results suggest PEDOT:DS has exceptional potential as an electromaterial for the biointerface.

Keywords

organic, conductive, processable, highly, ds, pedot, biopolymer, sulfate, poly, dextran, ethylenedioxythiophene, 4, 3

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Poly(3,4-ethylenedioxythiophene):dextran sulphate (PEDOT:DS) - a highly processable conductive organic biopolymer

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Abstract

A novel water-dispersible conducting polymer analogous to PEDOT:PSS has been chemically synthesized in a single reaction in high yield. PEDOT:DS, a new member of the polythiophene family, is composed of a complex between oxidized poly-3,4-dioxythiophene (PEDOT) and the sulfonated polysaccharide polyanion dextran sulfate (DS). Drop cast films of aqueous suspensions of the material display a native conductivity of up to $7 \pm 1 \text{ S cm}^{-1}$, increasing to $20 \pm 2 \text{ S cm}^{-1}$ after treatment with ethylene glycol and thermal annealing. Mass ratios of the precursors NaDS and EDOT were varied from 5:1 to 2:1 and a decrease in the NaDS:EDOT ratio produces tougher, less hygroscopic films of higher conductivity. UV-vis spectroelectrochemistry yields spectra typical of PEDOT complexes. Cyclic voltammetry reveals that PEDOT:DS is electrochemically active from -1.0 to 0.8V versus Ag/Ag⁺ in acetonitrile, with similar characteristics to PEDOT:PSS. Water dispersions of PEDOT:DS are successfully processed by drop casting, spray coating, inkjet printing and extrusion printing. Furthermore, laser etching of dried films allows the creation of patterns with excellent definition. To assess the cytotoxicity of PEDOT:DS, L-929 cells were cultured with a polymer complex concentration range of 0.002 to 0.2 gL⁻¹ in cell culture media. No significant difference is found between the proliferation rates of L-929 cells exposed to PEDOT:DS and those in plain media after 96 hours. However, PEDOT:PSS shows around 25% less cell growth after 4 days, even at the lowest concentration. Taken together, these results suggest PEDOT:DS has exceptional potential as a electromaterial for the biointerface.

Graphical abstract

Keywords

PEDOT, Dextran Sulfate, Electromaterial, Bioelectronics, Organic Electronics

Colour figures

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1. Introduction

Electrically conductive polymers are showing great promise as materials which can act as interfaces between electronics and biology in the emerging field of medical bionics [1]. Organic electromaterials have already found applications in devices such LEDs, transistors and solar cells [31]. More recently, the discovery that such materials exhibit ion transport properties [32] has seen the development of the delivery of charged molecules to exact locations in biological systems [33], and as ion-to-electron transducers in biosensors [34]. Furthermore, organic electromaterials are highly suited to biological systems because of their structural similarity to proteins, carbohydrates and nucleic acids [35]. The most suitable materials ideally possess a combination of properties that include high conductivity, low toxicity, ease of processing, and the capacity to be prepared and purified in a simple, inexpensive and scalable manner. Recently, a highly conductive PEDOT:tosylate complex prepared via vapour phase deposition was utilized successfully as an electrode material in a study of cell attachment and proliferation under electrical stimulation [2]. This investigation effectively demonstrates proof-of-principle, however vapour phase deposition places limits upon utility since electrode surfaces must be coated *in situ* and generally the amount of deposited polymer is very small. Therefore, we were prompted to undertake a search for conducting polymer which could be synthesized and isolated in reasonable quantity, processed in a straightforward way using non-toxic solvents, and subsequently used to manufacture electrode structures.

Commercially available PEDOT:PSS is easily processed and has high conductivity when treated with a secondary solvent such as ethylene glycol [3,4]. Pretreatment films made from this have been used to communicate with living cells [4]. We and others have shown that the dopant used with either PPy [5] or PEDOT [6] has a marked effect on the physical and chemical properties and hence cytocompatibility. Cytocompatibility of organic conducting polymers is known to be highly dependent on the molecular dopant used [7]. The dopant affects both the mechanical and electrical properties of the resultant organic conductor and furthermore, biologically active

dopants can induce specific cellular interactions [8,9]. This latter point is critically important. Studies with polypyrrole [36-39] and with PEDOT [40,41] clearly demonstrate the importance of dopant chemistry in the electrode performance and biocompatibility of these materials, allowing tailoring for specific applications. For example, these previous studies have shown that the ability to support nerve or muscle cell growth is clearly dependent on the dopant used. Thus, the capacity to tailor the composition and at the same time produce processable conducting polymers with bioactive dopant is critical to enabling fabrication of practical devices. Here we have sought to produce a PEDOT conducting polymer which incorporates a biomolecule as dopant.

A number of conducting polymer complexes incorporating biomolecular dopants have already been prepared, in a variety of ways. For example, polypyrrole:dextran sulfate (PPy:DS) has been prepared electrochemically by a number of groups since the mid-1990s [10-12]. Additionally, electrochemical syntheses of polypyrrole complexes of heparin, chondroitin sulfate and hyaluronic acid have been reported [13]. Polypyrrole:hyaluronic acid has also been prepared chemically [8]. Polyaniline complexes with dextran sulfate [14] and chondroitin sulfate [15] have been produced by chemical synthesis. Furthermore, various complexes of PEDOT with fibrinogen, hyaluronic acid and heparin have been synthesized and their electrochemical properties measured [16]. Surprisingly, PEDOT:DNA has been prepared chemically [17] to produce material with a conductivity of 1.0 S cm^{-1} ; the authors claim that the phosphate groups of the DNA are responsible for doping.

Here we have pursued development of PEDOT with dextran sulfate as dopant (PEDOT:DS). Dextran sulfate was used historically in medicine as an anticoagulant [18], but has found other uses, such as an antiviral agent shown to inhibit binding of HIV-1 to CD⁺ T-lymphocytes [19]. Furthermore, studies with PPy:DS composite polymers have demonstrated the material supports the adhesion of PC12 [20] and skeletal muscle [9] myoblasts. The sulfonated polysaccharide dextran sulfate has low toxicity, as indicated by its clinical use and its polyanionic structure suggests that it could effectively play the role of a dopant in conducting polymer complexes. Accordingly, we now report the first chemical synthesis

of PEDOT:dextran sulfate (PEDOT:DS) and describe its characterization, processability and cytocompatibility.

2. Materials and methods

2.1 Materials for synthesis and annealing procedure

Ethylene-3,4-dioxythiophene (EDOT) was obtained from Amsheng Chemical Company. Dextran sulfate sodium salt (NaDS) of MW 500,000 Da, poly(styrenesulfonic acid) sodium salt (NaPSS) of MW 70,000 Da, dialysis tubing of MWCO 12,400 Da and ethylene glycol were purchased from Sigma-Aldrich, Australia. Ammonium persulfate and iron(III) sulfate heptahydrate were obtained from Ajax Fine Chemicals, Australia. Tetrabutylammonium perchlorate was obtained from Sigma Aldrich and recrystallised from ethanol before use. Glass slides coated with indium tin oxide (ITO) (Delta Technologies). Ethylene glycol treatment of dried polymer films was accomplished by immersion of the coated glass slide into a shallow bath of the liquid in a Petri dish for approximately 20 seconds, then allowing the film to redry on a hotplate at 40°C or 65°C.

2.2 Synthesis of PEDOT complexes

Preparation of PEDOT:DS (1:2). A 25 mL screw top glass vial was charged with 3,4-ethylenedioxythiophene (141.1 mg, 0.9924 mmol), Milli-Q water (resistivity 18.2 M Ω cm) (10 mL) and a magnetic stirrer bar. To the stirred mixture was added dextran sulfate sodium salt of average MW 500,000 Da (287.3 mg, 0.6646 mmol monomer eq.). When dissolved, ammonium persulfate (275.0 mg, 1.205 mmol) was added in one portion. A stream of nitrogen was bubbled through the mixture for 5 min to remove dissolved oxygen, then iron (II) sulfate heptahydrate (0.5 mg, 1.8 μ mol) was added and the vial capped to exclude air. The mixture was placed in an ice/water bath and stirred at 0°C for 6 days, by which time a thick blue suspension was evident. The temperature was raised to 22°C and after a further 5 hours the reaction was quenched with the addition of 20mL of water. The resulting suspension was homogenised at 12,000 rpm for 10 minutes to reduce the particle size. The suspension

was transferred to dialysis tubing of MWCO 12,400 Da and dialysed in stirred water (1 L) for 2 days, changing the water twice during this time. A drop cast film of the PEDOT:DS product was created by placing 1 mL of the suspension on a microscope slide and drying at 40°C overnight. Water was removed from the dialyzed mixture by rotary evaporation at a bath temperature of 40°C to give the product (343.2 mg) as a deep blue solid with a yield of 86.7% of the expected mass balance.

PEDOT:PSS (1:1.8) was prepared by the following procedure. Poly(styrenesulfonic acid) sodium salt of MW 70,000 Da (4.242 g, 3.789 g of PSS anion, 20.54 mmol monomer eq.) was dissolved in 150 mL water. Ammonium persulfate (3.992 g, 17.49 mmol) was added and the mixture stirred until dissolved. Deoxygenation was performed by bubbling nitrogen gas through for 5 min. EDOT (1.5 mL, 2.114 g 14.87 mmol) was added by syringe in one shot, then the stirred suspension was cooled to 0°C in an ice/water bath. The mixture was stirred at 750 rpm and $\text{Fe}(\text{SO}_4)_3 \cdot 9\text{H}_2\text{O}$ (5 mg, 12 μmol) was added. A slow stream of nitrogen was bubbled through the mixture for the entirety of the reaction. After 24 hr, the resulting thick blue suspension was diluted with 100 mL water and centrifuged at 4100 rpm for 60 min. The supernatant was then poured off, 180 mL water added, and the mixture was shaken and then centrifuged for 60 min at 4100 rpm. Following centrifugation, the supernatant was poured off, 200 mL of water was added, and then the mixture was boiled with stirring for 2 hr. The mixture was then cooled to RT and further centrifuged for 60 min at 4100 rpm. Again the supernatant was removed, 180 mL of water was added, and the mixture was shaken and then centrifuged for 60 min at 4100 rpm, followed by an additional wash and centrifugation step. Evaporation under reduced pressure yielded 4.214 g of PEDOT:PSS (mass balance 71% of theoretical). Films were produced similarly as described above and conductivities were found to be $40.9 \pm 2.5 \text{ S cm}^{-1}$ from water alone and $231 \pm 15 \text{ S cm}^{-1}$ after treatment with ethylene glycol.

2.3 Conductivity determination

After synthesis, polymer films were prepared by drop casting an aqueous suspension onto glass slides for conductivity determination. Measurements of sheet resistance were obtained with a Jandel RM3 meter, employing a linear configuration four point probe of tip diameter 0.5 mm. For each film, measurements were taken at three different currents in three areas of the slide, each adjacent to a scratch down to the microscope slide surface made by a narrow spatula blade. Film thicknesses were measured with a Veeco Wyco NT9100 optical profilometer and were determined by averaging five measurements of the step height from the film surface to the microscope slide surface at the scratch boundary at each resistivity measurement site. Conductivity (σ , S cm⁻¹) was then calculated as a function of sheet resistance (R_s , Ω/sq) and film thickness (d , cm) according to Equation 1.

$$\sigma = \frac{1}{R_s \times d} \quad \text{Eq. 1}$$

2.4 Particle size determination by dynamic light scattering

The size of particles in aqueous suspensions of PEDOT:DS were determined by dynamic light scattering using a Malvern Zetasizer, Nano-ZS instrument.

2.5 Scanning electron microscopy

SEM images were obtained using a JEOL JSM7500FA cold Field Emission Gun Scanning Electron Microscope (FEGSEM) at an accelerating voltage of 5 kV and a spot size setting of 8. Secondary electron images were collected via a semi in-lens detector at a working distance (WD) of 7 mm.

2.6 Cyclic voltammetry

The electrochemical measurements were carried out on polymer films with an eDAQ system controlled by EChem software. A platinum mesh counter electrode was employed, with a reference electrode of Ag/Ag⁺ and an electrolyte of 0.1 M tetrabutylammonium perchlorate (TBAP) in deoxygenated CH₃CN at a scan rate of 100 mV/s. A dilute aqueous suspension of each polymeric

complex was spray coated onto glass slides coated with ITO to create a working electrode, masked to an area of 0.8 cm².

2.7 Spectroelectrochemistry

An indium tin oxide (ITO) glass slide coated in the polymer complex of choice was placed in a quartz cuvette containing 0.1 M TBAP in acetonitrile, installed in the beam path of a UV-Vis spectrophotometer (Shimadzu UV-1800). Spectroelectrochemistry data was recorded vs an Ag wire reference electrode and a Pt counter electrode. Applied voltages for the Ag wire were rescaled vs Ag/Ag⁺ using ferrocene as a standard. Controlled-potential measurements were carried out with an eDAQ system running EChem software.

2.8 Thin film deposition and etching

In order to prepare polymer films for characterization and to demonstrate processing capabilities a range of scalable deposition methods were examined, including spray coating, inkjet printing and extrusion printing. For electrochemistry and spectrophotometry experiments, spray coating was utilized, where glass slides coated with ITO were cut to size (~ 10 x 50 mm) and both ends were taped to aluminum foil covering a hotplate heated to 65°C. A dilute suspension of PEDOT:DS in 5% aqueous ethylene glycol was loaded into an airbrush and the mixture was sprayed carefully onto the glass slides using an air pressure of 50 psi at a distance of 15-20 cm. Spraying was deemed complete when the transparency was approximately 80%.

Micro-patterns of PEDOT:DS were created using a piezoelectric Dimatix Materials Printer (DMP-2800, Fujifilm, USA) at room temperature. An inkjet printable formulation was prepared by horn ultrasonication (20 min, 30% power) of an ice-cooled aqueous dispersion (10 mg/mL) of PEDOT:DS (1:5), followed by passage through a syringe tip filter of pore size 450 nm. Micro-patterns were printed

by syringe-loading the PEDOT:DS formulation into a custom designed 10 pL cartridge equipped with a 16 nozzle print head. The whole cartridge was then positioned in the printer and subsequently controlled by Dimatix software to transfer pre-designed patterns onto the glass slide. The formulation was typically printed using a jet voltage of 25.0V, a frequency of 5.0 kHz, and a customized waveform.

Extrusion printing of a viscous aqueous suspension of PEDOT:DS was performed using a custom printer based on a modified computer numerically controlled (CNC) milling machine [21] (Sherline Products, CA). In brief, the system was equipped with a three-axis positioning platform and was controlled by the manufacturer's EMC2 software interface. An attachment to permit syringe pressurization for deposition was constructed and gas pressure was adjusted via a regulator (1-100 psi). Approximately 0.5 mL of a concentrated (~ 10%) aqueous suspension of PEDOT:DS was loaded into a 2 mL plastic syringe barrel using a small spatula. Up to five layers of PEDOT:DS were deposited onto a glass microscope slide at a feed rate of 100 mm/min, using strand spacing of 1.0 mm, feed pressure of 2.5 psi, to final dimensions of 10 x 10 mm.

A laser ablation technique for etching thin films was additionally examined. For the experiments, glass slides spray coated with PEDOT:DS (1:2) were placed in a multi-wavelength laser engraver (PLS6MW from Universal Laser Systems). Using the 1.06 μm fiber laser, an image was selectively etched from the surface of the glass slides without affecting the bulk substrate.

2.9 Biological Testing Methods

The proliferation of a fibroblast cell line (L-929 cells) was observed over 4 days in the presence of three different concentrations of PEDOT:PSS or PEDOT:DS. The final concentrations of the polymer complexes in media were 0.2 mg/mL, 0.02 mg/mL and 0.002 mg/mL. L-929 cells were plated at 2500 cells/cm² in a 96-well plate, and allowed to grow for 24 hours, before the media was completely removed and replaced by cell media containing PEDOT dispersions. The dispersions were added to the cell media in Phosphate Buffered Saline (PBS), with 100 μL of PBS and PEDOT dispersion added to 5

mL of Dulbecco's Modified Eagle Medium (DMEM) + 10% Fetal Bovine Serum (FBS) with 1% penicillin/streptomycin. 100 μ L of plain PBS was added to untreated controls. After addition of the media, cells were imaged and lysed in preparation for Pico Green Assay at 2, 24, 48, 72 and 96 hours. A Quant-iT PicoGreen dsDNA assay (Invitrogen) was used to assess cell number at each of the above time points, with each point run in triplicate.

3. Results

3.1 Synthesis of PEDOT:DS

PEDOT:DS was prepared in a single reaction by the oxidative polymerization of 3,4-ethylenedioxythiophene in an aqueous solution of high molecular weight dextran sulfate sodium salt, as illustrated in Figure 1. When complete, the reaction mixture is deep blue in colour – indicative of the presence of PEDOT. After dilution with water, the mixture is briefly homogenized, then dialysis is performed in order to remove inorganic byproducts. Removal of water by rotary evaporation yields PEDOT:DS as a dark blue solid.

Figure 1. Preparation of PEDOT:DS by catalysed persulfate oxidation of EDOT in the presence of dextran sulfate sodium salt.

3.2 Investigation of factors affecting properties of PEDOT:DS

Experiments were conducted to investigate the factors which affect the conductivity and other physical properties of PEDOT:DS. Several variables were studied: a) the ratio of NaDS to EDOT during synthesis; b) the reaction temperature; c) the temperature for thermal annealing; and d) effect of treatment with ethylene glycol. Results are summarized in Table 1. For these experiments, drop cast films of the polymer were prepared on glass microscope slides from each aqueous suspension of PEDOT:DS and left to evaporate or dry overnight at 40°C. Conductivities were determined for the films and following treatment with ethylene glycol. The film was thermally annealed for 4 hr at 65°C, which resulted in a native conductivity of $19.2 \pm 0.7 \text{ S cm}^{-1}$.

Table 1. Conductivity, particle size and physical property data for PEDOT:DS films as a function of synthesis conditions and annealing temperature. *Annealed overnight at 65°C.

Mass ratio NaDS:EDOT	Reaction temperature °C	Z average particle size (nm)	Film conductivity S cm^{-1}	Conductivity after EG treatment S cm^{-1}	Dried film characteristics
5.07:1	22	690.7 ± 3.2	0.11 ± 0.03	0.10 ± 0.02	Weak, tacky
2.52:1	22	457.5 ± 2.1	1.45 ± 0.03	$14.8 \pm 0.7^*$	Stronger, slightly tacky
2.04:1	22	394 ± 2.6	3.9 ± 0.2	5.3 ± 0.09	Strong, not tacky
1.99:1	0	433.6 ± 4.1	7.5 ± 0.6	10.4 ± 1	Strongest, not tacky
2.04:1	0	575.7 ± 1.4	$19.2 \pm 0.7^*$	$19.6 \pm 2.7^*$	Tough, dry

Scanning electron micrographs were obtained of the dried PEDOT:DS films, in order to measure particle size. A typical micrograph is displayed in Figure 2.

Figure 2. SEM images of PEDOT:DS drop cast film.

3.3 Electrochemical and spectroelectrochemical properties of PEDOT:DS

The electrochemical behavior of a PEDOT:DS (1:2) film with native conductivity 19.2 S cm^{-1} (Fig. 3A, black line) was measured using cyclic voltammetry and compared with that for PEDOT:PSS of native conductivity 40.9 S cm^{-1} (Fig. 3A, grey line). Figure 3B illustrates the electrochromic nature of PEDOT:DS films.

Figure 3. A) Cyclic voltammograms for PEDOT:DS (black line) and PEDOT:PSS (grey line) in CH₃CN containing 0.1 M TBAP from -1.3 to 0.8V at a scan rate of 100mV/s. Fifth scans are shown. B) Photos showing electrochromic behavior of PEDOT:DS - top is sky blue oxidised state and bottom is dark blue reduced state. C) Spectroelectrochemistry data for PEDOT:DS and for D) PEDOT:PSS.

3.4 Processing

Processability of PEDOT:DS was evaluated by subjecting the material to a number of established film deposition and patterning techniques. Both drop casting and spray coating of aqueous suspensions were effective at coating significant areas of substrate, in much the same way that roll-to-roll processing is used industrially. Intricate microstructures could successfully be deposited onto glass by inkjet printing and extrusion printing. Additionally, an etching method was examined, where laser machining was used to ablate dried films.

Aqueous suspensions of PEDOT:DS can be successfully spray coated onto heated ITO glass surfaces using an inexpensive airbrush. Samples with a higher proportion of DS tended to crack when drying due to shrinkage upon dehydration. To minimize this effect, approximately 100 coats of a dilute suspension were applied. Samples with a lower proportion of DS shrank to a smaller degree upon

drying, as expected, permitting relatively smooth films to be produced. These latter samples also produced tougher, less hygroscopic films.

PEDOT:DS also makes excellent inks for inkjet printing. An ink was prepared by taking an approximately 1% (w/v) aqueous suspension of PEDOT:DS (1:5), subjecting it to horn ultrasonication, and then passing it through a 0.45 μm filter to remove larger particles. Viscosity and surface tension measurements, critical parameters for assessing the viability of inkjet printing,³⁰ were then taken and determined to be 16.8 cP and 35.3 dyn/cm respectively. A Dimatix materials printer was then used to deposit five layers of the suspension onto a glass microscope slide without surface modification. A parallel line pattern was chosen, consisting of line width 50 μm with 500 μm line spacing. Microscope images of the printing results are displayed in Figure 4A and 4B. The printed lines were visibly parallel, relatively even in colour, with well-defined boundaries. We conclude that this formulation provides good inkjet printability and thus holds potential for the creation of electrically conductive microstructures.

Extrusion printing requires a more viscous ink formulation [21]. As such, an aqueous suspension of PEDOT:DS (1:2) of approximate concentration 2% (w/v) was concentrated slowly under rotary evaporation until the consistency resembled that of thick paint. The concentration at this point was estimated to be approximately 10% (w/v). The resulting mixture was loaded into the barrel of a 2 mL syringe atop a custom built 3-axis extrusion printer [21]. A hatched pattern was deposited onto a glass microscope slide, with successive layers being printed in an orthogonal direction to the previous. A square matrix consisting of 10 horizontal lines overlapped with 10 vertical lines of dimensions 10 x 10 mm was then built up by printing five layers (Figure 4C). Single layer printed lines had an average width of approximately 265 μm (Figure 4D). The images show that multi-layer, sub-centimetre scale structures can be extrusion printed whilst maintaining a reasonable level of definition and detail. We anticipate that refinement of the PEDOT:DS ink formulation and the extrusion printing procedure

would allow a significant increase in printing resolution. In summary, initial results indicate that water suspensions of PEDOT:DS can be successfully extrusion printed.

Figure 4. PEDOT:DS processability studies. A) 5X microscope image of 50µm inkjet printed lines of an aqueous PEDOT:DS suspension onto untreated glass. B) 20X images of inkjet printed line. C) Image of 5 layer extrusion printed PEDOT:DS. D) Single printed layer from extrusion printing. E) Spray coated PEDOT:DS slide which has been laser machined to selectively remove the polymer layer.

Laser machining was undertaken in order to demonstrate that PEDOT:DS can be successfully and accurately patterned not only by deposition, but by an etching technique. Films of PEDOT:DS were produced by spray coating an aqueous suspension of the polymer onto glass slides and then allowing to

fully dry. The spray coated slides were then placed in a specialized laser engraver system. The machine is adaptable to multiple lasers of different wavelengths, permitting optimal excitation and evaporation of a range of materials. A 1.06 μm fibre laser was utilized in this case, a wavelength which will selectively ablate the polymer layer without affecting the glass below. As shown in Figure 4E coating areas have been selectively removed to produce a predefined pattern.

3.5 Cytocompatibility studies

The cytocompatibility of PEDOT:DS was assessed by culturing populations of the attachment dependent L-929 fibroblast cell line in the presence of PEDOT:DS, PEDOT:PSS and DMEM media controls. Light microscopy images taken during the course of L-929 cell proliferation (Figure 5) demonstrate that the cells remain viable with extended exposure to either PEDOT:PSS or PEDOT:DS. Cell populations exhibited a typical L-929 morphology, were observed to proliferate, and produced few apoptotic cells despite intimate contact with the PEDOT materials.

Figure 5. Optical microscopy of the growth of L-929 cells in the presence of (A-E) PEDOT:DS and (F-J) PEDOT:PSS. Images were obtained after 2 (A,F), 24 (B,G), 48 (C,H), 72 (D,I) and 96 (E,J) hours of culture. All scale bars represent 100 μ m.

Quantitative analysis of proliferation by Pico Green Assay (Figure 6) revealed that the growth rates of L-929 cells were minimally perturbed by the presence of DS and PSS doped PEDOT across the tested concentration range.

Figure 6. L-929 cell proliferation in culture conditions when exposed to PEDOT:DS and PEDOT:PSS in concentrations ranging from 0.002 - 0.2% (w/v), as determined by Pico Green Assay. Cell number represents the average number of cells/mL in a 96-well plate well.

4. Discussion

4.1 Synthesis of PEDOT:DS

Preparation of PEDOT:DS (Figure 1) involves the oxidative polymerization of 3,4-ethylenedioxythiophene in the presence of the dextran sulfate polyanion, a surfactant and an anticoagulant. Water was chosen as the solvent since this is the best medium for bioactive molecules. Dextran sulfate sodium salt (NaDS) is very soluble in water and despite the poor water solubility of

EDOT (2.1 mg/mL at 20°C) [3], the steady-state concentration is sufficient for the reaction to run to completion. The preparation of PEDOT:DS requires a single reaction, as illustrated in Figure 1.

Initially a mixture of EDOT, dextran sulfate sodium salt of average molecular weight 500,000 Da and ammonium persulfate in water is stirred at room temperature. The first stage of the reaction is the one electron oxidation of EDOT, which has an oxidation potential of 1.50V. Persulfate ion ($E_0 = 2.01\text{V}$ vs NHE) is a powerful oxidant and each mole will consume 2 moles of electrons, with concomitant production of two moles of sulfate ion, as per Equation 2,

Although the reaction between EDOT and persulfate is favoured according to the relative electrode potentials, the observed formation of PEDOT:DS in uncatalysed reactions is slow. This is consistent with the slow reaction kinetics observed for reactions between persulfate and organic substrates. For example, a study of the kinetics of the oxidation of 1,4-dioxane in water by persulfate ion yielded a pseudo first-order rate constant of $1.8 \times 10^{-4} \text{ s}^{-1}$ at 25°C and a large activation energy of 87.9 kJmol^{-1} [22].

Therefore, following deoxygenation, a catalytic amount of iron (II) sulfate is added to initiate the reaction. The Fe^{2+} ion reacts with persulfate producing Fe^{3+} , sulfate anion and the sulfate radical anion - a reactive species with a high oxidation potential ($E_0 = 2.6\text{V}$ vs NHE) [23], as shown in Equation 3.

The oxidation potential of EDOT is 1.50V vs NHE, and sulfate radical anion easily removes an electron from EDOT to commence the polymerization process. Each oligomerisation event involves the transfer of two electrons and liberates two protons, and as a consequence the pH of the reaction mixture decreases over time. The molar ratio of potassium persulfate to EDOT required to achieve polymerization is theoretically 1:1. In practice, slightly more than 1.15 moles is added in order to also oxidize the PEDOT backbone, forming charge-propagating bipolarons. Polysaccharides are known to

undergo oxidative cleavage and decomposition in the presence of oxidants [24,25] but dextran sulfate appears not to have suffered this fate to a significant extent in the presence of persulfate.

The predominant dopant is dextran sulfate polyanion. While there is precedent for sulfate anion to significantly improve conductivity through its action as a dopant [42], sulfate groups on the dextran polymer are covalently bound and thus do not exist as free sulfate ions. It is clear from the conductivity vs composition data in Table 1 that an increased proportion of dextran sulfate in the formulation results in lower electrical conductivity. This indicates that the dopant is having a partly insulating effect and is thus mainly organic in nature. Furthermore, when films of PEDOT:DS are heated to temperatures in excess of 120°C overnight irreversible decomposition is observed. This low decomposition temperature is indicative that the dopant is a polysaccharide. It is likely that some sulfate anions (introduced via iron sulfate catalyst) may be incorporated as dopant during synthesis, but these should be removed by the dialysis purification step.

4.2 Factors affecting physical properties of PEDOT:DS

A study was undertaken to determine how the physical properties of PEDOT:DS are affected by reagent proportions, reaction temperature and annealing temperature. Table 1 summarizes the effects of these parameters upon particle size and conductivity of PEDOT:DS films. The mass ratio of EDOT to NaDS exerts the largest effect upon the properties of PEDOT:DS. A comparison of PEDOT:DS from reactions performed at 22°C and whose films were both annealed at 40°C indicates that conductivity increased from 0.11 S cm⁻¹ for the 5:1 formulation, up to 3.9 S cm⁻¹ for the 2:1 sample. This represents a conductivity increase of 35 times as the NaDS:EDOT ratio decreases to a modest 40% of its original value. The corresponding behavior can be explained by the fact that dextran sulfate is not electrically conductive and that its reduced ratio results in more facile charge conduction between adjacent PEDOT chains in the three dimensional PEDOT:DS structure.

As the ratio of NaDS:EDOT decreases, a second effect is evident. PEDOT:DS films with a smaller proportion of DS become tougher and less tacky, as assessed by scratching the films with a spatula and touching them with a gloved finger. Despite the qualitative nature of this analysis, useful information on bulk properties was obtained. Films with the highest proportion of DS (5:1) would not fully dry at 40°C and were sticky to the touch. However, the 2:1 formulation produced films which were dry to the touch, adhered well to the glass slide and were resistant to scratching. This phenomenon can be understood simply by recognizing that polysaccharides such as dextran sulfate are hygroscopic: the smaller the proportion of DS, the less hygroscopic is the product.

A lowering of the DS ratio clearly achieved both an increase in conductivity and handle of the product. However, if the DS proportion is lowered much further the resultant PEDOT:DS does not remain suspended in water but slowly agglomerates. Dextran sulfate is required not only as a dopant, but to help form micelles which permit hydrophobic PEDOT to enter the aqueous phase. Lower amounts of DS therefore compromise the propensity to form micelles. Furthermore, it was discovered that if an aqueous suspension of 2:1 PEDOT:DS is evaporated under vacuum to dryness, the resulting blue solid can be difficult to resuspend in water. For this reason, it is advised to store PEDOT:DS as an aqueous suspension.

The temperature of annealing of the PEDOT:DS films also exhibited a significant effect upon conductivity. A sample of the 2:1 formulation displayed a conductivity of 7.5 S cm^{-1} when annealed at 40°C. However, when annealed at 65°C, the resulting conductivity increased to 19.2 S cm^{-1} , 2.5 times that of the sample annealed at the lower temperature. In an attempt to further increase conductivity, a drop cast film of PEDOT:DS was heated overnight at 120°C, however the sample decomposed illustrating that PEDOT:DS is less thermally stable than PEDOT:PSS. This is consistent with the low decomposition temperature of many sugars.

The temperature of reaction also exerted a significant effect upon conductivity. For the 2:1 formulation, conductivity almost doubles from 3.9 to 7.5 S cm^{-1} as the reaction temperature is

decreased from 22 to 0°C. This is consistent with lower temperatures favouring the formation of longer and better ordered PEDOT chains.

Treatment of dried PEDOT:DS films with ethylene glycol has a variable effect upon the conductivity. A 2:1 formulation synthesized at 0°C displays a native conductivity of 7.5 S cm^{-1} when annealed at 40°C, and 10.4 S cm^{-1} after treatment with ethylene glycol and annealing at the same temperature. It is clear therefore that ethylene glycol increases conductivity at this annealing temperature. However, the same formulation when annealed at 65°C results in no significant difference between pre- and post-ethylene glycol conductivities (19.2 and 19.6 S cm^{-1} respectively). This is in contrast to PEDOT:PSS, which when treated with ethylene glycol (or a number of other secondary solvents such as DMSO or DMF) will increase in conductivity by 2-3 orders of magnitude. Secondary solvent treatment [26] of PEDOT:PSS is believed to increase conductivity by removal of an insulating PSS layer, and by morphological and conformational change promoted by stabilization of separation between PEDOT and PSS portions of the molecule. It is possible that the mechanism of secondary solvent conductivity increase is the same for both PEDOT:PSS and PEDOT:DS. Furthermore, thermal annealing may accomplish the same phase separation as that promoted by solvents such as ethylene glycol. The observation that thermal annealing of PEDOT:DS requires lower temperatures (less energy) than for PEDOT:PSS is consistent with weak electrostatic interactions between the PEDOT and DS fragments of the molecule. This is supported by the fact that aqueous dispersions of PEDOT:DS are less stable than those of PEDOT:PSS. The well-established phenomenon of thermal annealing in PEDOT:PSS is itself not completely understood [27].

The ratio of NaDS:EDOT and reaction temperature also affected the average particle size and particle size distribution (Table 1) of PEDOT: DS dispersions. The average particle size and distribution was detected by Dynamic Light Scattering (DLS) as synthesized and the results showed that the average particle size of PEDOT:DS increase with the ratio of NaDS salt. The sample obtained using a

NaDS:EDOT ratio of 5.07 had the largest average particle size. In addition, when the NaDS: EDOT ratio was constant the use of a lower synthesis temperature resulted in larger particles.

The data obtained using DLS reflects the particle size distribution. The size of individual PEDOT:DS particles was then characterized using high resolution SEM. Images of drop cast PEDOT:DS samples (NaDS: EDOT = 2.04, 0 °C) (Fig. 2) illustrated particle size typically between 60-80nm. Presumably the DLS data reflects agglomeration in solution and/or the presence of some (rogue) larger particles.

4.3 Electrochemistry and spectroelectrochemistry of PEDOT:DS

A comparative study of the electrochemistry and spectroelectrochemistry of PEDOT:DS and PEDOT:PSS revealed significant similarities in behaviour. Both cyclic voltammograms (Figure 3) showed similar shapes, typical for polythiophenes undergoing the complex charging-discharging processes associated with reverse cycling [28]. The capacitance current for a PEDOT:DS coated ITO electrode was found to be only slightly less than that for the PEDOT:PSS coated ITO electrode, which might be accounted for by differences in the conductivity of the two materials.

It was noted that PEDOT:DS, like PEDOT:PSS, is visibly electrochromic. Reduced PEDOT:DS is dark blue but on oxidation to 0.8V the colour changes to a highly transmissive sky blue. Images of the oxidized and reduced PEDOT:DS films on ITO glass are displayed in Figure 3B. To further investigate the electrochromic properties of those films, spectroelectrochemistry experiments were performed. The UV-Vis spectra of the polymer coatings were recorded as a function of applied voltage, over the range -1.0 to 0.8V vs Ag/Ag⁺ for PEDOT:DS (Figure 3C) and for PEDOT:PSS (Figure 3D). At a potential of -1.0V, the PEDOT:DS appears to be fully reduced, with the maximum absorption peak at 593 nm. Maxima at ca. 600 nm are characteristic of PEDOT complexes and are a result of the π - π^* transition [29]. The reduced spectrum for PEDOT:PSS exhibits a 30 nm ($\lambda_{\text{max}} = 623$ nm) bathochromic shift of the absorption maximum, indicating an extension of the conjugation length along the polymer chains compared with PEDOT:DS [28]. Upon oxidation, the electrochemically polymerized PEDOT:DS

developed a free carrier tail as well as exhibited a decrease in absorbance at 593 nm, as expected for an oxidized electroactive polythiophene [29].

In summary, electrochemical and spectroelectrochemical experiments demonstrate that the electroactivity and the spectral properties of the newly synthesized polymer PEDOT:DS are comparable to those for PEDOT:PSS.

4.4 Processing of PEDOT:DS

An investigation into methods by which PEDOT:DS can be applied to glass revealed that the material can be processed very much like PEDOT:PSS. Aqueous suspensions of the polymer complex are easily prepared and manipulated. Spray coating allows significant areas to be coated with thin, even films, particularly so for PEDOT:DS formulations lower in DS. Inkjet printing allows deposition of material with a resolution suitable for the creation of microstructures. Extrusion printing does not share the resolution of inkjet printing, but allows for the rapid deposition of larger quantities of material and may be suitable for the production of three dimensional structures. Laser ablation from PEDOT:DS films provides a method for the rapid fabrication of accurate patterns by the removal of material and is highly suited to the production of microscale devices.

4.5 Cytocompatibility of PEDOT:DS

An investigation into the cytotoxicity of PEDOT:DS and PEDOT:PSS towards attachment dependent L-929 fibroblast cells revealed that neither material is significantly toxic. Cells were exposed to a concentration range of 0.002-0.2% (w/v) of each polymer complex in aqueous DMEM media over a time period of 0-96 hours. Light microscopy images (Figure 5) indicated that cells exposed to either material remained viable and continued to exhibit typical L-929 morphology. One clear difference was that PEDOT:DS was gradually internalized into the L-929 cells, whereas PEDOT:PSS was not.

Quantitative analysis of proliferation was performed using a Pico Green assay (Figure 6) and revealed that growth rates of L-929 cells were largely unaffected by exposure to PEDOT:DS or

PEDOT:PSS, even at the highest concentrations. During the initial days of culture, unaltered media and the lower concentrations of PEDOT were observed to outperform those with 0.2% (w/v) PEDOT:DS in the media. However, by 96 hours all concentrations of PEDOT:DS were comparable to the control within experimental error. At the same time point, cells exposed to PEDOT:PSS had proliferated less quickly, yielding cell counts between 15-25 % lower than the control across all concentrations (see Supplementary Information, Figure S1).

In summary, our results indicate that the L-929 cell line is able to proliferate naturally in the presence of PEDOT:DS, slightly outperforming PEDOT:PSS under the test conditions. These results providing encouraging signs towards the potential biological application of PEDOT:DS.

5. Conclusions

PEDOT:DS has been chemically synthesized in high yield by a one-step reaction, resulting in a product conductivity of up to 19.6 S cm^{-1} . Conductivity of the product can be maximized by: using a low ratio of NaDS to EDOT during preparation; conducting synthesis at low temperature; performing thermal annealing of dried films at higher temperature; and by treatment of aqueous suspensions or dried films with ethylene glycol. Low DS ratios also result in tougher, less hygroscopic material.

Electroactivity and capacitance behavior of PEDOT:DS are typical of polythiophenes. Comparison of the spectroelectrochemistry of PEDOT:DS with that of PEDOT:PSS indicated that PEDOT:DS has the shorter conjugation length, but similar absorption changes throughout the potential range -1.0 to 0.8V.

Water based suspensions of PEDOT:DS can be deposited onto glass successfully by spray coating, inkjet printing and extrusion printing. High resolution etching of PEDOT:DS films is possible by laser ablation. Such processing techniques offer much promise for the production of microscale devices.

The growth of L-929 cells in media containing PEDOT:DS dispersion was not different to cell media alone over 4 days (despite an initial decrease in proliferation), while PEDOT:PSS showed decreased

cell number after this period in culture, indicating that the PEDOT:DS dispersions show greater potential for biological applications than the PSS-doped polymers. Interestingly, PEDOT:DS is gradually absorbed into the PC12 cell body, whereas PEDOT:PSS is not. The reasons for this are not clear and will be investigated in future studies. This effect may however provide a novel avenue for utilizing PEDOT:DS as a mechanism for delivery of therapeutic agents within cells. Overall, early data indicates that PEDOT:DS may be a suitable material for use in biological applications such as the electrostimulation of cells.

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References

- [1] Wallace GG, Moulton SE, Kapsa RMI, Higgins MJ. Organic Bionics. Weinheim:Wiley-VCH Verlag GmbH; 2012.
- [2] Stewart EM, Fabretto M, Mueller M, Molino PJ, Griesser HJ, Short RD, Wallace GG. Cell attachment and proliferation on high conductivity PEDOT–glycol composites produced by vapour phase polymerisation. *Biomater Sci* 2013;1:368-378.
- [3] Elshchner A, Kirchmeyer S, Lovenich W, Merker U, Reuter K. PEDOT: Principles and Applications of an Intrinsically Conductive Polymer. Boca Raton: CRC Press; 2010. p 118.

- [4] Yang SY, Kim BN, Zakhidov AA, Taylor PG, Lee J-K, Ober CK, Lindau M, Malliaras GG. Detection of Transmitter Release from Single Living Cells Using Conducting Polymer Microelectrodes. *Adv Healthcare Mater* 2011;23:H184-H188.
- [5] Gelmi A, Higgins MJ, Wallace GG. Physical surface and electromechanical properties of doped polypyrrole biomaterials. *Biomaterials* 2010;31:1974-83.
- [6] Cui X, Martin DC. Electrochemical deposition and characterization of poly (3 ,4-ethylenedioxythiophene) on neural microelectrode arrays. *Sens Actuators B* 2003;89:92-102.
- [7] Asplund M, Thaning E, Lundberg J, Sandberg-Nordqvist AC, Kostyszyn B, Inganäs O, von Holst H. Toxicity evaluation of PEDOT/biomolecular composites intended for neural communication electrodes. *Biomed Mater* 2009;4:045009.
- [8] Collier JH, Camp JP, Hudson TW, Schmidt CE. Synthesis and characterization of polypyrrole-hyaluronic acid composite biomaterials for tissue engineering applications. *J Biomed Mater Res* 2000;50:574-84.
- [9] Gilmore KJ, Kita M, Han Y, Gelmi A, Higgins MJ, Moulton SE, Clark GM, Kapsa R, Wallace GG. Skeletal muscle cell proliferation and differentiation on polypyrrole substrates doped with extracellular matrix components. *Biomaterials* 2009;30:5292-304.
- [10] Hodgson AJ, Gilmore K, Small C, Wallace GG, Mackenzie IL, Aoki T, Ogata N. Reactive supramolecular assemblies of mucopolysaccharide , polypyrrole and protein as controllable biocomposites for a new generation of 'intelligent biomaterials'. *Supramol Sci*. 1994;1:77-83.
- [11] Knob R, Maier V, Ranc V, Znaleziona J, Sevcik J. Dopa and tyrosine enantiomers migration order reversal using uncoated and polypyrrole coated capillaries. *Global J Anal Chem* 2010;1:228-232.
- [12] Molino PJ, Higgins MJ, Innis PC, Kapsa RM, Wallace GG. Fibronectin and bovine serum albumin adsorption and conformational dynamics on inherently conducting polymers: a QCM-D study. *Langmuir* 2010;28:8433-45.

- [13] Serra Moreno J, Panero S. Evaluation of the interface aging process of polypyrrole–polysaccharide electrodes in a simulated physiological fluid. *Electrochim Acta* 2012;68:1-8.
- [14] Yuan G-L, Kuramoto N. Water-Processable Chiral Polyaniline Derivatives Doped and Intertwined with Dextran Sulfate: Synthesis and Chiroptical Properties. *Macromolecules* 2002;35:9773-9779.
- [15] Yuan G-L, Kuramoto N. Synthesis of Helical Polyanilines Using Chondroitin Sulfate as a Molecular Template. *Macromol Chem Phys* 2004;205:1744-1751.
- [16] Asplund M, von Holst, H, Inganäs, O. Composite biomolecule/PEDOT materials for neural electrodes. *Biointerphases* 2008;3:83-93.
- [17] Ner Y, Invernale MA, Grote JG, Stuart JA, Sotzing, GA. Facile chemical synthesis of DNA-doped PEDOT. *Synth Met* 2010;160:351-353.
- [18] Hall M, Ricketts CR. The use of dextran sulfate as a blood anticoagulant in biological research. *J Clin Pathol* 1952;5:366.
- [19] Baba M, Pauwels R, Balzarini J, Arnout J, Desmyter J, De Clercq E. Mechanism of inhibitory effect of dextran sulfate and heparin on replication of human immunodeficiency virus in vitro. *Proc Natl Acad Sci USA* 1988;85:6132-6.
- [20] Hodgson AJ, John MJ, Campbell T, Georgevich A, Woodhouse S, Aoki T, Ogata N, Wallace GG. Integration of biocomponents with synthetic structures: Use of conducting polymer polyelectrolyte composites. *Proc SPIE—Int Soc Opt Eng* 1996;2716:164-176.
- [21] Mire CA, Agrawal A, Wallace GG, Calvert P, in het Panhuis, M. Inkjet and extrusion printing of conducting poly(3,4-ethylenedioxythiophene) tracks on and embedded in biopolymer materials. *J Mater Chem* 2011;21:2671.
- [22] Félix-Navarro RM, Lin-Ho SW, Barrera-Diaz N, Pérez-Sicairos S. Kinetics of the Degradation of 1,4-Dioxane Using Persulfate. *J Mex Chem Soc* 2007;51:67-71.
- [23] Huie RE, Clifton CL, Neta P. Electron transfer reaction rates and equilibria of the carbonate and sulfate radical anions. *Radiat Phys Chem* 1991;38:477-481.

- [24] Balakrishnan B, Lesieur S, Labarre D, Jayakrishnan A. Periodate oxidation of sodium alginate in water and in ethanol-water mixture: a comparative study. *Carbohydr Res* 2005;340:1425-9.
- [25] Duan J, Kasper DL. Oxidative depolymerization of polysaccharides by reactive oxygen/nitrogen species. *Glycobiology* 2011;21:401-9.
- [26] Alemu D, Wei H-Y, Ho K-C, Chu C-W. Highly conductive PEDOT:PSS electrode by simple film treatment with methanol for ITO-free polymer solar cells. *Energy Environ Sci* 2012;5:9662-9671.
- [27] Dimitriev OP, Grinko DA, Noskov YV, Ogurtsov NA, Pud AA. PEDOT:PSS films—Effect of organic solvent additives and annealing on the film conductivity. *Synth Met* 2009;159:2237-2239.
- [28] Roncali J. Conjugated Poly(thiophenes): Synthesis, Functionalization, and Applications. *Chem Rev* 1992;92:711-738.
- [29] Groenendaal L, Zotti G, Aubert P-H, Waybright SM, Reynolds JR. Electrochemistry of Poly(3,4-alkylenedioxythiophene) Derivatives. *Adv Mater* 2003;15:855-879.
- [30] Weng B, Shepherd RL, Crowley K, Killard AJ, Wallace GG. Printing conducting polymers. *Analyst* 2010;135:2779-89.
- [31] Malliaras G, Friend R. An organic electronics primer. *Phys Today* 2005;58:53–58.
- [32] Leger JM. Organic electronics: the ions have it. *Adv Mater* 2008;20:837–841.
- [33] Simon DT, et al., Organic electronics for precise delivery of neurotransmitters to modulate mammalian sensory function. *Nat Mater* 2009;8:742–746.
- [34] Lin P, Yan F. Organic thin-film transistors for chemical and biological sensing. *Adv Mater* 2012;24:34–51.
- [35] Lanzani G. Materials for bioelectronics: Organic electronics meets biology. *Nat Mater* 2014;13:775-776.
- [36] Ateh DD, Navsaria HA, Vadgama P. Polypyrrole-based conducting polymers and interactions with biological tissues. *J Roy Soc Interface* 2006;3:741–752.

- [37] Gilmore KJ, Kita M, Han Y, Gelmi A, Higgins MJ, Moulton SE, Clark GM, Kapsa R, Wallace GG. Skeletal Muscle Cell Proliferation and Differentiation on Polypyrrole Substrates Doped with Extracellular Matrix Components. *Biomaterials* 2009;30:5292-5304.
- [38] Liu X, Gilmore KJ, Moulton SE, Wallace GG. Electrical Stimulation Promotes Nerve Cell Differentiation on Polypyrrole/Poly (2-Methoxy-5 Aniline Sulfonic Acid) Composites. *J Neural Eng* 2009;6:065002(10pp).
- [39] Gelmi A, Higgins MJ, Wallace GG. Physical Surface and Electromechanical Properties of Doped Polypyrrole Biomaterials. *Biomaterials* 2010;31:1974-1983.
- [40] Molino PJ, Tibbens A, Kapsa RMI, Wallace GG. Incorporating biodopants into PEDOT conducting polymers: impact of biodopant on polymer properties and biocompatibility. *MRS Proc* 2013;1569:225-230
- [41] Molino PJ, Yue Z, Zhang B, Tibbens A, Liu X, Kapsa RMI, Higgins MJ, Wallace GG. Influence of Biodopants on PEDOT Biomaterial Polymers: Using QCM-D to Characterize Polymer Interactions with Proteins and Living Cells. *Adv Mater Interfaces* 2014;1:1300122
- [42] Reyes-Reyes M, Cruz-Cruz I, López-Sandoval R. Enhancement of the Electrical Conductivity in PEDOT:PSS Films by the Addition of Dimethyl Sulfate *J Phys Chem C* 2010;114:20220–20224

Supplementary Figures

Figure S1- Comparison of L-929 cell numbers after exposure to PEDOT:DS and PEDOT:PSS dispersions for 96 hours. Overall, PEDOT:PSS dispersions showed consistently lower cell numbers than the PEDOT:DS treated cells (15-25% lower cell densities), however the trend was not statistically significant.