Flexible Nanowire Conductive Elastomers for Applications in Fully Polymeric Bioelectronic Devices*

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Abstract— **Soft, flexible polymer-based bioelectronics are a promising approach to minimize the chronic inflammatory reactions associated with metallic devices, impairing long-term device reliability and functionality. This work demonstrates the fabrication of conductive elastomers (CEs) consisting of chemically synthesized poly(3,4-ethylenedioxythiophene) (PEDOT) nanowires embedded within a polyurethane (PU) elastomeric matrix, resulting in soft and flexible, fully polymeric electrode materials. Increasing PEDOT nanowire loadings resulted in an improvement in electrochemical properties and conductivity, an increased Young's modulus and reduced strain at failure. Nanowire CEs were also found to have significantly improved electrochemical performance compared to one of the standard electrode materials, platinum (Pt). Indirect *in vitro* cytocompatibility test was carried out to investigate the effect of leachable substances from the CE on primary rodent cells. Nanowire CEs provide a promising alternative to metals for the fabrication of soft bioelectronics.**

I. INTRODUCTION

Bioelectronic devices have proven to be effective therapies to alleviate neurological disorders and diseases such as Parkinson's or epilepsy by stimulating the nervous tissues [1]. One key to sustained device performance is the formation of a close interface between cells and electronics. Ideally, interfacing electrode materials should display compliant and stretchable mechanics to conform to soft dynamic tissues while safely transferring charge to electroactive cells, allowing a seamless integration of the electronics within the implanted tissues[2]. While conventional bioelectronic devices employ metals such as platinum (Pt) as electrode materials, they face issues providing efficient and stable functionality over chronic timescales. This is in part due to the severe mechanical mismatch at the interface between the stiff metals and the soft tissues inducing a chronic inflammatory response. This biological reaction results in scar tissue encapsulation of the device, further insulating the device from any recordable tissue activity and compromising neural stimulation at safe injection levels. This ultimately limits long term device efficacy. Furthermore, metals are limited in their capacity to stimulate surrounding tissues at safe therapeutic levels, without causing tissue or electrode damage. The low charge injection abilities of metals hinder their ability to function at small geometrical areas as needed in high resolution electrode arrays.

Flexible and soft polymer-based bioelectronics have emerged as one approach to address the drawbacks of metal-based devices[3]. Conductive polymers (CPs) have gained popularity as electrode materials due to their desirable electrical functionality, flexibility in processing and biocompatibility[4]. Of particular interest is their mixed ionic/electronic conductivities, facilitating charge delivery to tissues where charge transport rely entirely on ionic fluxes. However, CPs are also associated to poor mechanical durability. Incorporation of CPs into softer matrices such as elastomers has been demonstrated as a way to produce robust electroactive biomaterials, able to conform to tissue surfaces during continuous physiological motion. While many composites of CPs and elastomers have been reported to combine both electroactivity and mechanical compliance, many suffer from limited conductivities exhibiting values lower than 10^{-4} S.cm^{-1} for materials used for tissue engineering purposes[5]–[7]. Other CP-elastomer composites reported conductivities within the range of 2 to 120 S.cm^{-1} for applications in wearable electronics [8]–[10] where material cytocompatibility has not yet been assessed. Several works have shown the development of these materials into polymeric electrode arrays for neural recording[11] and into soft wires capable of intramuscular stimulation[12].The use of additives resulted in stretchable freestanding CP-elastomer composites of conductivities up to 600 S.cm^{-1}[13]. However these additives have been reported to be prone to leaching, raising concerns on their toxic impact on their environment[13]. One strategy to increase conductivity without additives could be the use of nanostructured CPs, where the large aspect ratios confer high conductivity[14].

This work describes the fabrication of nanowires of doped PEDOT and their subsequent incorporation into a PU elastomeric matrix to produce fully polymeric, soft and flexible conductive elastomers (CE). To obtain a functional electrode material, the effect of PEDOT nanowire content on the electrochemical and mechanical properties of the CE composites were investigated and compared to conventional Pt, prior to assessing the indirect *in vitro* cytocompatibility of the materials.

II. METHODS

A. Fabrication of PEDOT nanowire CE

PEDOT nanowires were synthesized by oxidative polymerization via a self-assembled micellar soft-template route previously reported[15], [16]. Briefly, an aqueous

solution of 0.3M sodium dodecyl sulfate (SDS) was prepared. An aqueous solution of 6.9986 M iron chloride (III) was added to the SDS solution and stirred at 50°C for 1h. Next, 21 mmol of 3,4-ethylenedioxythiophene monomer was slowly introduced into the solution under stirring and the polymerization reaction was allowed to proceed for 6h at 50°C. The resulting product was washed using acetone and methanol to remove excess surfactant and unreacted chemicals and dried under vacuum filtration. Morphology of the nanowires were imaged using a scanning electron microscopy (SEM) (Zeiss LEO Gemini). PEDOT nanowires were dispersed by ultrasonication in dimethylacetamide (DMAC) at 4.6 mg.mL^{-1}. The dispersion was then mixed via ultrasonication and stirring to 3 mL of a 10 wt% (w/v) PU-DMAC solution across different PEDOT loadings, ranging from 10 wt% to 40 wt%. The resulting solutions were directly solvent cast onto glass plates and cured at 60 °C for 36h to obtain thin CE sheets.

B. Electrochemical properties

Electrochemical properties were characterized by electrical impedance spectroscopy (EIS), cyclic voltammetry (CV) and conductivity measurements using a potentiostat (Autolab M101). For EIS and CV, a three-electrode set up was used with an Ag/AgCl reference electrode and a Pt wire counter electrode. The working electrode with a controlled circular exposed area of 0.219 cm^2 was connected to the potentiostat by clamping it with Pt sheets. The electrolyte was Dulbecco's phosphate buffered saline (Sigma). EIS was carried out by recording the impedance in response to 10 mV sinusoids across the frequency range 0.1 Hz-10 kHz. CV was conducted by cycling the voltage between −0.6 to 0.8V at 150 mV.s^{-1} for 11 cycles. Charge storage capacities (CSC) were derived by integrating the current output of the last cycle relative to time. Conductivity was evaluated using a two-probe set up. A strip of CE was clamped on both ends by Pt sheets. CV was applied and the resistance (R) was derived from the CV slope. Conductivity (σ) was computed using the formula:

$$\sigma = L / (R \times A) \tag{1}$$

wherein L = exposed length and A = sample cross-sectional area. All reported values are mean ± one standard deviation (average across three batches, n = 5).

C. Mechanical properties

Mechanical behavior of CE sheets were evaluated by tensile testing (Instron 5543). All samples were stretched to failure at a constant crosshead speed of 30 mm.min^{-1} using a 100 N load cell. The stress-strain characteristics, Young's modulus, elongation to failure and ultimate tensile strength (UTS) were computed from the load-displacement output. All reported values are mean ± one standard deviation (average across two batches, n = 3).

D. Indirect in vitro cytocompatibility

The *in vitro* cytotoxicity of PEDOT nanowire CEs was assessed using an indirect contact study in compliance with ISO 10993-5[17]. Strips of 20 wt% CEs and PU control materials were immersed for 24h in culture media (Dulbecco's modified Eagle's medium/F12, 33 mM D-glucose, 1% L-glutamine, 1% penicillin-streptomycin, 1% fetal calf serum,

supplemented with 2% B27) at 37 °C under agitation at an extraction ratio of 6 cm^2.mL^{-1}. A blank control (only media) was included. Primary astrocytes isolated from hippocampal cultures obtained from P4 Sprague Dawley rat pups[18] were plated into poly-lysine (Sigma P4707) coated 24 well plates and cultured in media at 37°C, 5% CO$_2$ at 25,000 cells.cm^{-2}. After media removal and washing, the cells were exposed to extract solutions of the experimental and control materials and incubated at 37°C, 5% CO$_2$ for 48h. Tissue culture plastic (TCP) and ethanol titrations were used as negative and positive controls, respectively. Samples were run in triplicate and the experiment was repeated twice. Live dead assay was carried out to determine the viability of the cells cultured in extract solutions after 48h. Cells were imaged using a SP8 confocal microscope and analyzed using ImageJ.

III. RESULTS

A. Fabrication of PEDOT nanowire CE

SEM images of the dispersed PEDOT nanowires showed nanostructures of diameters from 50 to 100 nm and lengths ranging from 2.3 to 3 µm (see Fig. 1A). Sheets of pure PEDOT
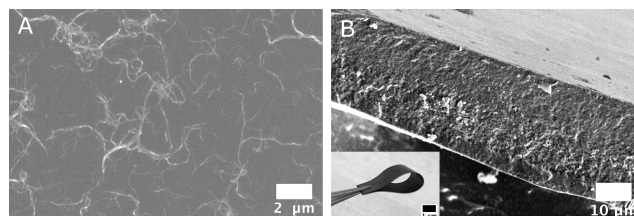

Figure 1. SEM images of A) PEDOT nanowires; B) a cross section of PEDOT nanowire CE. Inset bottom left is a photograph of a CE sheet.

nanowires had conductivities ranging from 84.93 ± 6.66 to 118.20 ± 23.63 S.cm^{-1}. CEs fabricated with PEDOT nanowire loadings ranging from 10 to 40 wt% exhibited thicknesses from 40.66 ± 7.02 to 64.00 ± 10.39 µm (see Fig. 1B).

B. Electrochemical properties

Increasing PEDOT nanowire content of the CE sheets from 10 wt% to 40 wt% resulted in a reduction in impedance magnitude (see Fig. 2). Comparison with Pt revealed a lower impedance for all CE sheets at frequencies below 100 Hz. The impedance at the biologically relevant frequency of 1kHz was decreased with higher PEDOT nanowire loadings, ranging from 19.50 ± 1.72 Ω cm^2 at 10 wt% to 10.88 ± 1.56 Ω cm^2 at 40 wt%, which is similar in magnitude to Pt at 12.97 ± 2.79 Ω cm^2. The low and flat phase response observed across all CEs showed evidence of resistive charge transfer at the
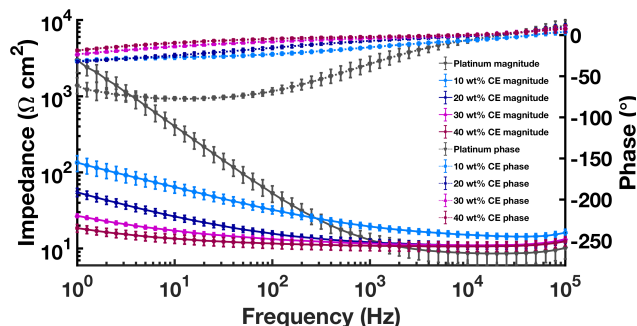

Figure 2. Impedance magnitude and phase angle of PEDOT nanowire CE at varying PEDOT nanowire loadings compared to Pt.

interface (see Fig.2). This improvement in electrochemical properties was also supported by CV. The CSC was found to increase with further addition of PEDOT in CEs, from 19.36 ± 1.46 mC.cm^{-2} at 10 wt% to 153.05 ± 17.01 mC.cm^{-2} at 40 wt%. (see Fig. 3). It should be noted that these CSC were at least one to two orders of magnitude larger than that of Pt (1.55 ± 0.20 mC.cm^{-2}). Fig. 4 displays the DC conductivity of the bulk CEs. Improved levels of conductivity were observed with higher loadings of nanowires, from 8.85 ± 1.27 S.cm^{-1} at 10 wt% to 109.84 ± 9.28 S.cm^{-1} at 40 wt%.
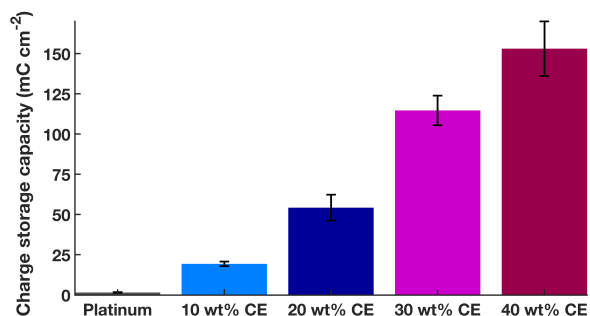

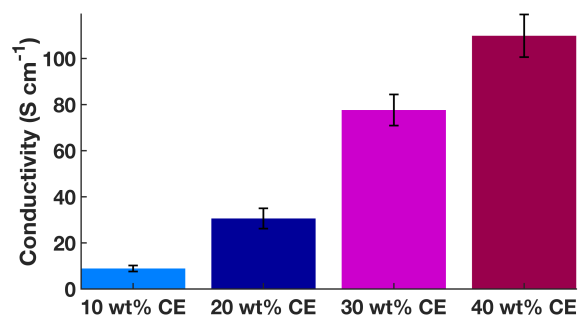Figure 3. CSCs of PEDOT nanowire CE composites with varying PEDOT nanowire loadings compared to Pt.

Figure 4. Conductivity of PEDOT nanowire CE composites with varying PEDOT nanowire loadings.

C. Mechanical properties

Fig. 5 depicts representative stress-strain curves of PU and CE sheets. While PU displayed a viscoelastic behavior typical of elastomers, incorporation of an increasing amount of nanowires in the PU matrix resulted in degradation of the elastomeric properties. As PEDOT nanowire content increased, the curves showed an initially stiffer response, followed by a shorter compliant behavior and earlier failure of the CEs. Table 1 summarizes the mechanical parameters derived from the stress-strain curves. The Young's modulus of
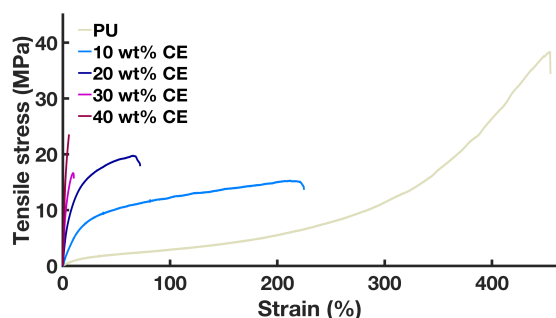

Figure 5. Representative tensile stress-strain curves of PEDOT nanowire CEs with varying PEDOT nanowire loadings compared to PU.

CEs increased with the nanowire loadings from 31.35 ± 4.86 MPa at 10 wt% to 728.08 ± 38.74 MPa at 40 wt%, which is one to two orders of magnitude higher than that of PU. An elongation to failure of $194.25 \pm 57.55\%$ was achieved for CEs at 10 wt%, which was significantly reduced with additional nanowires, reaching a $4.79 \pm 0.66\%$ extension to failure for the 40 wt% CEs. It was found that the UTS were within the range of $9 - 21$ MPa, resulting in values slightly lower than PU.

TABLE I. MECHANICAL PARAMETERS

Elastomers	Young's modulus (MPa)	Elongation at failure (%)	UTS (MPa)
PU	5.58 ± 1.91	621.88 ± 67.37	27.05 ± 9.67
10 wt% CE	31.35 ± 4.86	194.26 ± 57.55	9.30 ± 2.28
20 wt% CE	179.35 ± 20.50	63.97 ± 6.64	18.36 ± 1.42
30 wt% CE	528.39 ± 73.95	13.61 ± 1.52	21.07 ± 1.17
40 wt% CE	728.08 ± 38.74	4.79 ± 0.66	17.77 ± 1.12

D. Indirect in vitro cytocompatibility

Fig. 6 shows cell viability of primary astrocytes following exposure for 48h to 20 wt% CEs and control extracts. Overall, cell viability in all experimental samples were similar to the TCP control. However, PU samples showed the lowest cell viability after 48h when compared to CEs samples with a $57.87 \pm 22.89\%$ viable cells. which may be due to presence of solvent leftovers. Overall this indicate that no CE leachables had a significant impact on cell viability. The ethanol control (not shown) produced an expected cytotoxic response.
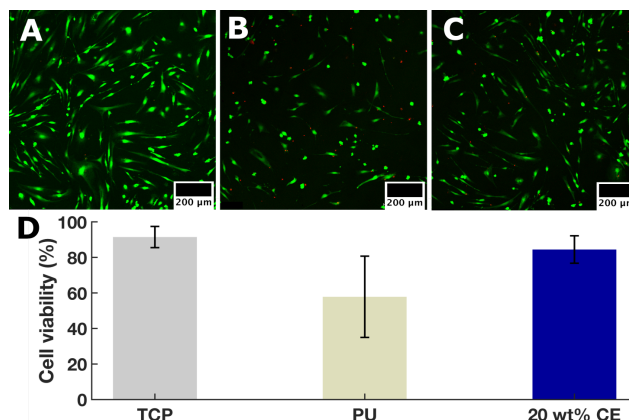

Figure 6. Cell viability images of primary rodent astrocytes cultured for 48h in extract solutions from A. TCP; B. PU and C. 20 wt % PEDOT nanowire CEs. Calcein AM (green) stains live cells and ethidium homodimer-1 (red) stains dead cells. D. Cell viability (%) for each of the experimental and control group. Data represent the mean ± one standard deviation (average across two experiments, n = 3).

IV. DISCUSSION

The ability of nanowires to entangle and form a continuous conductive network within the insulative PU matrix enabled charge transduction, conferring electroactivity to CEs. Increasing the nanowire content from 10 wt% to 40 wt% was associated with improved electrochemical performance including reduced impedance and higher CSC. The CSCs were of similar magnitude to others PEDOT composite materials[2], [19], [20]. This enhancement in charge transfer

abilities suggests a better nanowire network connectivity with further addition of nanowires, leading to the formation of additional conductive paths. Further evidence of network connectivity in CEs is the increase in conductivity as a function of nanowire loading, resulting in values in the semi-conducting range up to 109.84 ± 9.28 S.cm^{-1}. This conductivity dependency on CP loadings in elastomer composites has previously been reported [7], [9], [20], [21]. These nanowire CEs conductivities were within the range of conductivities reported by other CP-elastomer composites[8]–[10]. Although large nanowire loadings is critical to impart high conductivity to CEs, deterioration of elastomeric properties of CEs with higher nanowire loadings were assessed. These findings are consistent with the behavior observed in other CP-elastomers composites[7], [8], [20], [21]. This may be explained by several factors, including the effective interfacial interaction between the nanowires and the PU[8] as well as the hydrodynamic effect, generated by introduction of brittle and rigid CP component within softer elastomers[22]. Future work will seek to assess the CEs electromechanical properties.

Comparison to conventional Pt electrode material demonstrated the superior electrochemical performance of nanowire CEs *in vitro*, including reduced impedance at low frequencies and a substantial CSC increase of up to two orders of magnitude. These highly efficient charge transfer abilities of CEs in wet environment is of particular interest for materials aiming to directly communicate with nervous tissues. Furthermore, while Pt have a Young's modulus in the GPa scale[2], nanowire CEs displayed flexibility with a Young's modulus in the MPa range, hence suggesting that the mechanical mismatch at the tissue-electrode interface will be reduced.

Key requirements for electrodes include electronic functionality and mechanical compliance. Of all the CEs explored, the 20 wt% PEDOT nanowire CEs were identified as an ideal candidate. Its significantly improved electrochemical performance compared to Pt, coupled to a Young's modulus of 179.34 ± 20.50 MPa and a strain at failure of 63.96 ± 6.64 % render this CE appropriate for interfacing with nervous systems, where the strain is around 20%[1]. The high level of conductivity of this material (30.55 ± 4.37 S.cm^{-1}) makes it suitable for applications involving fast charge transfer such as implanted polymeric bioelectronic devices. For materials intended to operate within biological systems, one major concern is the potential release of toxic material leachables including unreacted monomers, polymer chains, dopant ions or leftover reactants. An indirect contact study showed that CEs leachables has no cytotoxic effect on primary astrocytes. Further cytocompatibility studies will be required to expand on these preliminary results.

V. Conclusion

Fully polymeric CEs fabricated using dispersions of PEDOT nanowires into PU produced a soft, flexible and electrically active material. Increasing PEDOT nanowire content resulted in the formation of an interconnected nanowire network within PU, leading to improved CSC, reduced impedance and higher conductivity while altering the elastomeric properties of CEs. CEs with a 20 wt% nanowire loading were chosen as an optimal trade-off based on mechanical and electrochemical properties. Furthermore, *in vitro* cytotoxic tests showed that leachables from the 20 wt% CE had no detrimental impact on cell viability. Overall, CEs demonstrated many benefits over conventional Pt electrodes, providing superior electrochemical performance and softer mechanics. These findings support the use of highly conductive nanowire CEs in flexible and fully organic bioelectronic implants, which will promote improved chronic device functionality.

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