Abstract

PLA Electrospun Fibres Coated with PEDOT by Vapor-Phase Polymerization for Neural Regeneration †

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† Presented at the Materiais 2022, Marinha Grande, Portugal, 10–13 April 2022.

Keywords: neural regeneration; electrospinning; PEDOT; Fe(III)tosylate; vapor phase polymerization

Whether because of sudden trauma or neurodegenerative diseases, nerve injuries impact millions of people worldwide, as in many cases there is no nerve recovery after damage, leaving patients with life-long repercussions. The central nervous system cannot spontaneously regenerate due to the local immune response that amplifies damage and, ultimately, prevents axonal regrowth. Currently, there is no available solution to surpass this condition. The peripheral nervous system has some capability of spontaneous regeneration, but this regeneration is often compromised, since axonal growth can engage in random pathways. When nerve suturing is impossible, the medical community uses grafting techniques (autografts, allografts and xenografts) to bridge nerve gaps. There are some commercially available artificial nerve conduits (NCs) for grafting, thereby surpassing limited availability, donor site morbidity, pain and immune reactions associated with nerve tissue grafts. Despite the continuous effort with the current grafting solutions, delayed axonal regeneration through large gaps still leads to partial or total loss of function, chronic pain, and numbness.

Better NCs require scaffolds that are able to provide cells with regenerative stimuli. Guidance cues for axonal regrowth can be included in the scaffold by aligned electrospun fibers and electrical stimulation (ES) applied through the scaffold may also promote nerve regeneration. However, to this day, there are still no biomaterials with adequate conductivity for the application of ES.

This work focuses on the development of a biocompatible conductive scaffold, based on aligned electrospun fibres of polylactic acid (PLA) to be used in the ES of cells, envisioning the promotion of neuronal regeneration. The conductivity is imparted to the scaffold by the conductive polymer Poly[(3,4-ethylenedioxythiophene) (PEDOT). PEDOT was synthetized via vapor-phase polymerization (VPP) using Fe(III)tosylate (FeTos) as an oxidant.

Scaffolds composed of PLA fibres incorporating FeTos were produced by electrospinning a solution prepared by mixing PLA and FeTos solutions. Different solvent systems were considered, and a rotatory cylinder was used to induce alignment on the collected fibres. To synthesize PEDOT by vapor-phase polymerization (VPP), the scaffolds were submitted to EDOT vapours in a closed chamber placed at 70 °C for 2 h. The post-polymerization scaffolds were washed in ethanol and chemically characterized by Fourier-transform infrared (FTIR) spectroscopy, which confirmed the presence of PEDOT. Scanning electron microscopy (SEM) imaging reveals that PEDOT coats the fibres without compromising the scaffold’s porous structure, as shown in Figure 1a. Using a probe method,
the conductance of the scaffolds was measured, leading to an estimated conductivity of the order of $1.5 \times 10^{-1}$ S/cm, which is in agreement with values reported for scaffolds that were used for the ES of both in vitro and in vivo assays. Furthermore, the scaffolds cytotoxicity was tested following the ISO 10993-5, and cultures of SH-SY5Y cells were established on the scaffolds, with cells under differentiation conditions using retinoic acid. No cytotoxic effects are observed, and the SH-SY5Y cells are able to grow and differentiate on the scaffolds with neuritic extensions, following the preferential alignment of the scaffold’s fibres, as shown in Figure 1b.

![Figure 1.](image1)

**Figure 1.** (a) PLA scaffold incorporating PEDOT synthesized through VPP. The PEDOT coated the fibres, providing the scaffold with electrical conductivity, without compromising the porous structure. (b) Fluorescence images of SH-SY5Y cells that were cultured on the conductive scaffold and differentiated using RA. Nucleus are marked in blue, stained with DAPI, and the cytoskeletons are marked in red, stained with Acti-stain 555 Phalloidin.

**Author Contributions:** These authors contributed equally to this work. All authors have read and agreed to the published version of the manuscript.

**Funding:** This work was co-financed by FEDER, European funds, through the COMPETE 2020 POCI and PORL and National Funds through FCT, Portuguese Foundation for Science and Technology and POR Lisboa2020, under the projects PIDDAC (POCI-01-0145-FEDER-007688, reference UIDB/50025/2020–2023) and PTDC/CTMCOM/32606/2017 (NEURiTES).

**Institutional Review Board Statement:** Not applicable.

**Informed Consent Statement:** Not applicable.

**Data Availability Statement:** Not applicable.

**Conflicts of Interest:** The authors declare no conflict of interest.