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Flexible multi-channel microelectrode with fluidic paths for intramuscular stimulation and recording

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ABSTRACT

Biomedical microelectrodes play a significant role in motor paralysis recovery caused by spinal cord injury (SCI). As most researchers focused on implantable microelectrodes with multiple functions for neural studies and application, we developed flexible intramuscular microelectrodes integrated wire electrodes for functional electrical stimulation (FES) and electromyogram (EMG) recording with micro tube channels for fluidic drug delivery. The electrodes were electrochemically deposited with conducting polymer (PEDOT/pTS) coating to improve the electrode performance including electrochemical impedance and charge storage capacity (CSC). Moreover, the excellent mechanical and electrochemical stability of PEDOT/pTS coated electrodes was verified by withstanding ultrasonic bath and experiencing repeated cyclic voltammetry (CV) scan. Furthermore, the fluidic property of the micro channels of electrodes was investigated to be suitable for intramuscular drug delivery. In addition, electrophysiological experiments in vivo comprising FES and EMG recording were performed to evaluate the practical application of flexible intramuscular microelectrodes. As a consequence, the developed multi-functional intramuscular microelectrodes are suitable for intramuscular implantation and electrophysiological application, and open a new gate for future researchers on intramuscular motor prostheses for paralysis recovery.

1. Introduction

More than 130,000 people suffer from extensive paralysis resulted by spinal cord injury (SCI) each year worldwide [1]. Injury above the sixth cervical vertebra occurs among approximately half of these patients who would sustain tetraplegia. Since motor paralysis brings extreme inconvenience and great of pain to not only patients themselves but also their relatives, lots of efforts have been devoted in researching treatment for motor paralysis recovery. Some of these studies focus on replacing damaged motor nerve by artificial nerve system, which is used to direct subsequently neuromuscular functional electrical stimulation (FES) [2,3] and independently controlled robotic prosthesis [4,5].

One of the most significant components of the artificial protheses is the microelectrodes which act as tissue–machine interface [6–8]. To functionalize well in live muscle and nerve tissue, the biomedical microelectrodes should meet the requirements including: (1) miniature dimension that minimizes the tissue damage and power consumption, (2) excellent performance that ensures effective operation of the prostheses device and, (3) good biocompatibility that guarantees relatively long term implantation without inducing severe immune response. Complying with these disciplines for biomedical electrodes mentioned above, various kinds of microelectrodes were developed to execute electrical stimulation and electrophysiological signal recording for paralysis recovery after spinal cord injury. Among these manifold electrodes, Michigan neural probes and Utah electrodes array are widely used in central nerve prostheses applications [9,10], while LIFE electrode are usually applied in peripheral nerve and intramuscular researches [7,11].

It is a significant symptom should be confronted that only electrical interaction between electrodes and muscle or nerve tissue without nutrition factor delivery would eventually lead to denervation-induced skeletal muscle atrophy [12–14]. Considering these facts, the microelectrodes integrated with micro channels for fluidic drug delivery were developed in recent year [15–17]. As

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majority of these studies focused on stiff electrodes which made of silicon or SU-8 for applications on central nerve system, only a few concentrated on flexible electrodes which made of parylene, polyimide (PI) and polydimethylsiloxane (PDMS) [18–20]. The problem that limits the precise stimulation by the polymer based flexible electrodes described above is that the electrode sites distributed on one side of the electrode. Moreover, most of the microelectrodes mentioned above were developed for neural applications, but rare electrode was designed for intramuscular research. The microelectrodes for intramuscular electrical stimulation and electromyogram (EMG) recording in recent years mainly were restricted to crude wire electrodes and simply constructed electrodes with single function [21,22]. For the current situations, it is necessary to design and fabricate multi-functional microelectrodes with circumferential electrode sites distribution for intramuscular prostheses.

The implantable microelectrodes for tissue–machine interface benefit from the minimized volume which provides high spatial selectivity determining precision, little harm to tissue and low power consumption [23,24]. While on the other hand, the electrical performance gets deteriorated including increased impedance and decreased charge storage capacity (CSC) [25]. This might lead to poor performance of electrical stimulation and recording and tissue injury [26]. Therefore, it is necessary to modify the electrode sites with functional coating to improve the electrical performance of electrodes.

Besides the commonly used noble metals and iridium oxide, newly emerged conducting polymer possesses distinct properties to be biomedical electrode coating material for its excellent electrochemical performance, good biocompatibility and easy modification by different doping [27–30]. As two kinds of the most widely investigated conducting polymers for electrode–tissue interface materials, poly (3,4-ethylenedioxythiophene) (PEDOT) doped with various counter ions exhibits better properties in electrical stimulation and recording performance (better electrochemical performance) and biocompatibility (longer neurites growth) than those of polypyrrole (PPy) in biomedical electronics applications [31,32]. Different negatively charged molecules, such as poly(4-styrenesulfonate) (PSS) and carboxylated carbon nanotubes (CNTs), were incorporated into PEDOT for biomedical microelectrodes coating [33,34]. It was reported that PEDOT doped with para-toluene sulphonic acid (pTS) showed potential to be electrode sites coating with excellent electrochemical property, biocompatibility and especially electrical stability [35,36].

The main objective of this paper is to demonstrate multi-functional intramuscular microelectrode with conducting polymer coating for intramuscular implantation. We designed and fabricated the intramuscular microelectrode which consists of noble metal based micro wire electrodes for electrical stimulation and EMG recording, fluidic channels made of polyimide (PI) capillaries for drug delivery and Teflon casing for package. Briefly, the micro wire electrode was prepared by chemical vapor deposited Parylene insulation on the surface of gold micro wire. Then the prepared micro wire electrodes and PI capillaries were pierced though the Teflon casing to compose the intramuscular microelectrode. The overall flexible structure was preferred for intramuscular implant. Moreover, the microelectrode was electrochemically deposited with pTS doped PEDOT to improve the electrochemical performance. The morphology of electrode sites deposited with and without PEDOT/pTS was examined by scanning electron microscope (SEM). The electrochemical property comprising electrochemical impedance spectra (EIS) and cyclic voltammograms (CV) of bare metal electrode and PEDOT/pTS coated electrode were characterized. The electrochemical and mechanical stability of PEDOT/pTS coated electrodes was investigated by repeated CV scanning and ultrasound bathing, respectively. At last, the practical application including flow resistance test, functional electrical stimulation for paralysis recovery and intramuscular EMG recording was carried out with the multifunctional intramuscular microelectrode.

2. Materials and methods

2.1. Microelectrode fabrication process

The intramuscular microelectrode integrated electrical stimulation and recording sites with fluidic drug delivery channels consists of three parts: micro wire electrodes, polymer capillary fluidic channel and polymer package casing. Firstly, the micro wire electrode was made of gold in this study and could be replaced by other metals such as platinum, iridium, wolfram and stainless steel. The golden micro wire with diameter of 100 μm and appropriate length was prepared and cleaned successively by ultrasonic bath in acetone, ethanol and deionized (DI) water. The prepared polydimethylsiloxane (PDMS) bulk with certain thickness was sliced into small pieces (approximately 2 mm × 2 mm) and pierced through by golden wire as sacrifice layer. Parylene C with thickness of 5 μm was then chemical vapor deposited (CVD) on the golden wire surface as insulated layer by parylene deposition system (PDS 2010, SCS, USA). The electrode site was exposed by carefully removal of PDMS sacrifice layer (with circumferential electrode site) or cutting the tip of golden wire (with circular electrode site). Secondly, the polyimide (PI) capillary (outer diameter of 110 μm and wall thickness of 10 μm) and Teflon capillary (outer diameter of 650 μm and wall thickness of 140 μm) was cleaned by ultrasonic bath as that of golden wire. At last, four micro wire electrodes and two PI capillaries were pieced through the Teflon capillary and the Teflon capillary ends were sealed by biocompatible glue (3M Vetbond Tissue Adhesive, USA). In this study, the displayed intramuscular microelectrode was composed of four-channel electrical interface and two fluidic channels for drug delivery.

2.2. Electrochemical deposition

The conducting polymer electrolyte for electrode site coating was composed of 0.01 M 3,4-ethylenedioxythiophene (EDOT, Sigma–Aldrich, USA) and 0.05 M sodium para-toluenesulfonate (pTS, Sigma–Aldrich, USA) in deionized water. The solution was stirred for over 2 h to dissolve solute completely. Then the pure nitrogen was purged into the solution for 10 min to eliminate dissolved oxygen preserving EDOT from pre-oxidized. The four micro wire electrodes were connected to the working electrode of electrochemistry workstation (CHI660c, CH Instrument) separately, and a platinum foil was connected with the counter electrode and reference electrode together. The electrochemical deposition of PEDOT/PSS was performed in galvanostatic mode with deposition current density of 0.2 mA/cm^2 for 1800 s.

2.3. Electrochemical characterization

The electrochemical characterization of bare gold micro wire electrodes and electrodes coated with PEDOT/pTS comprising electrochemical impedance spectrum (EIS) and cyclic voltammogram (CV). Both the two kinds of measurement processes were performed with electrochemistry workstation (CHI660c, CH Instrument) in phosphate buffered saline (PBS, pH 7.2–7.4) versus saturated calomel electrode (SCE, CH Instrument) as reference electrode and a platinum foil as counter electrode. EIS was measured at frequency ranging from 0.1 Hz to 100,000 Hz with input voltage amplitude of 0.01 V. CV was scanned over the potential range between −0.6 V and 0.8 V at scan rate of 50 mV/s. The EIS results