Flexible Intramuscular Micro Tube Electrode Combining Electrical and Chemical Interface

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Abstract— **With the rapidly developed micromachining technology, various kinds of sophisticated microelectrodes integrated with micro fluidic channels are design and fabricated for not only electrophysiological recording and stimulation, but also chemical drug delivery. As many efforts have been devoted to develop rigid microprobes for neural research of brain, few researchers concentrate on fabrication of flexible microelectrodes for intramuscular electrophysiology and chemical interfacing. Since crude wire electrodes still prevail in functional electrical stimulation (FES) and electromyography (EMG) recording of muscle, here we introduce a flexible micro tube electrode combining electrical and chemical pathway. The proposed micro tube electrode is manufactured based on polymer capillary, which provide circumferential electrode site contacting with electro-active tissue and is easy to manufactured with low cost.**

I. Introduction

Microelectrodes, directly interfacing the tissue (with outside circuits), play a key role in implantable biomedical micro devices for research and application in diagnose and treatment, through means of signal recording and stimulation [1]. With the rapidly developed microelectronics fabrication techniques, various research groups focus on the design and fabrication of sophisticated microelectrodes for neural interface integrated with micro fluidic channels. Such microelectrode structure not only possesses capability of electrophysiological interaction, provides pathway of chemical delivery during the implantation.

Many efforts have been devoted to the development of rigid microelectrodes combining electrical and chemical pathways. Most of the microelectrodes reported in these researches are designed and fabricated based on silicon micro fabrication process [2]. Others manage to develop microelectrodes for electrical interaction compatible with drug delivery micro channels using SU-8 as structural material [3]. Although various microprobes based on silicon and SU-8 have been applied in brain research of neuroscience field, they are not suitable for intramuscular implant because the variation of muscle length and volume may induce the deformation and fracture of microelectrodes.

Flexible microprobes base on polymers could overcome the drawbacks of rigid electrodes for muscle electrophysiological and chemical interfacing. Parylene have been employed to manufacture microelectrodes with integrated fluidic channels [4]. These polymer based microprobes are able to meet the requirements of intramuscular implantation, nevertheless not capable of interfacing muscular tissue circumferentially. More recently, the programmable UV lithography system for micromachining on polymer capillary substrates developed by Yang et al. possesses the ability to manufacture micro tube probes with chemical pathway circumferentially electrode sites [5]. However, it is complex and costly to set up such equipment and fabricate micro tube electrodes.

In this study, we designed and fabricated micro tube electrode for intramuscular electrophysiological interface with drug delivery. Based on polyimide capillary substrate, micro tube electrodes was fabricated by processes including sputtering of noble metal such as gold or platinum and chemical vapor deposition of parylene C. We also electrochemically deposited conducting polymer on electrode sites to improve electrical property. Compared to crude micro tube electrode, the properties were greatly enhanced by tests including electrochemical impedance spectrum (EIS), cyclic voltammogram (CV) and charge injection capacity. Moreover, the calculated flow resistance of micro tube electrode coincides with the volume flow velocity change over pressure when liquid medicine passing through the micro tube. At last, the practicality of micro tube electrode was verified by implantation in skeletal muscle of mammalian and EMG signal recording. The micro tube electrode would definitely open gate for muscular tissue electrophysiology by providing a multi functional electrode-tissue interface with fabrication convenience.

II. Materials and Methods

A. Fabrication Process

The polymer capillary we chose was made of polyimide with outside diameter of 110 μm, wall thickness of 10μm and length of 6 cm. As shown in Figure 1a, the fabrication process began with the rinse procedure of polyimide capillary including ultrasonic cleaning in ethanol and deionized water for 3 minutes, respectively. Then Ti/Pt was sputtered on the capillary surface with the titanium and platinum thickness of 20 nm and 150 nm (Figure 1b). To ensure the whole capillary surface was coated with metal

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layer, the polyimide capillary was overhead during the sputtering process. Polydimethylsiloxane (PDMS) film with thickness of 500 μm was prepared by self-leveling in glass dish and follow-up 3 hours' heat treatment at 85 ℃ for curing. The PDMS film was subsequently sliced and pierced through by capillary sputtered with Ti/Pt (Figure 1c). Then parylene C thin film with thickness of 5 μm was chemical vapor deposited (CVD) on the capillary surface by parylene deposition system (PDS 2010, SCS, USA). The PDMS sacrificial layer was removed to expose the electrode site (Figure 1d). At last, conducting polymer was electrochemically deposited on the electrode site to improve electrochemical property of the micro tube probe.

B. Electrochemical Deposition

The electrolyte for conducting polymer deposition on electrode site contained 0.01 M 3,4-ethylenedioxythiophene (EDOT, Sigma-Aldrich, USA) and 5 mg/ml poly(sodium-p-styrenesulfonate) (PSS, Sigma-Aldrich, USA) in deionized water. The aqueous solution was stirred for 2 hours to dissolve solute completely. Then pure nitrogen gas was purged into the solution for 10 minutes to eliminate dissolved oxygen. The micro tube electrode was connected with the working electrode of electrochemistry workstation (CHI660c, CH Instrument), and a platinum foil was used as counter electrode. The electrochemical deposition of PEDOT/PSS was performed in galvanostatic mode with deposition current density of 0.2 mA/cm2 for 1800 seconds.

C. Electrochemical Characterization

The electrochemical characterization of bare platinum micro tube electrode and electrode coated with PEDOT/PSS includs 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). CV was scanned over the potential range between -0.6 V and 0.8 V at scan rate of 50 mV/s. EIS was measured at frequency ranging from 0.1 Hz to 100,000 Hz.

D. Stimulation

In order to investigate the electrical stimulation performance, bare platinum micro tube electrode and PEDOT/PSS coated electrode were connected with the anode of electrical stimulator (Master 8, A. M. P. I., Israel) in phosphate buffered saline (PBS, pH 7.2-7.4), respectively. The counter electrode was a platinum foil connected with cathode of electrical stimulator, and the reference electrode was a saturated calomel electrode (SCE, CH Instrument). A series of charge balanced, cathodic first, biphasic current pulses with amplitude of 1 mA at frequency of 50 Hz was applied by the electrical stimulator. An oscilloscope (TDS-2000, Tektronix, USA) was used for voltage responses recording.

E. EMG Recording

The in vivo electromyography (EMG) recording was performed to evaluate the practical performance of the micro tube electrode. The experimental subject was a New Zealand rabbit of specific pathogen-free grade, aged 6 months and weighing 2.8 kg, which was provided by the Laboratory Animal Center of Shanghai First People's Hospital, Shanghai Jiao Tong University (permission No. SYXK (Hu) 2009–0086). The micro tube electrodes were implanted in the muscle belly of gastrocnemius by syringe needle. A copper foil with dimension of 1 cm × 2 cm was used as ground and negative electrode, which placed on the surface of epimysium. The EMG signal was recorded by a multi-channel BioAmp Processor (RZ5D, Tucker-Davis Technologies, USA).

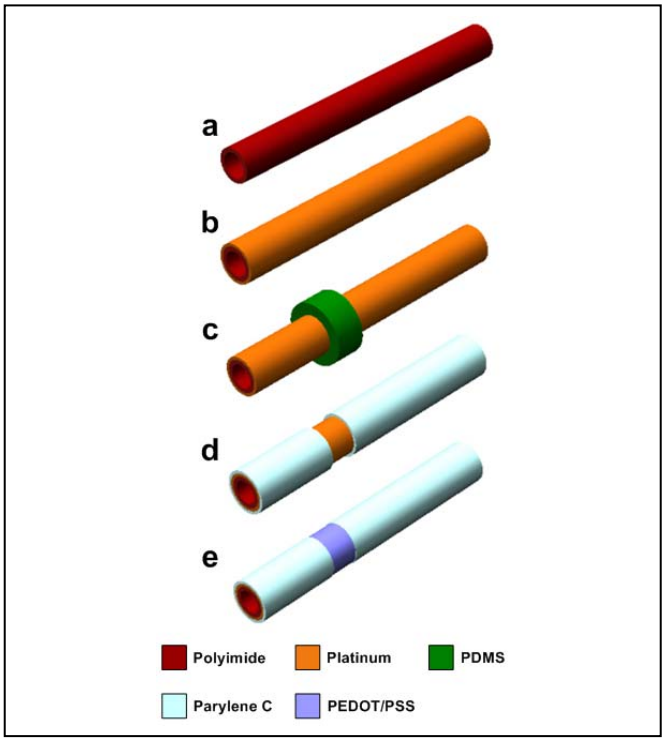

Figure 1. Schematic diagram of the fabrication process of micro tube electrode.

III. Results and Discussion

As illustrated in Figure 1 and described in Experimental section, the micro tube electrodes integrated electrical and chemical interface were not only flexible for intramuscular implantation, but also provide circumferential interface for electrical stimulation and recording. Also, the electrodes were conveniently fabricated and flexibly designed with different tube size, electrode number and sites distribution. The micro tube electrodes were easy to implant in the muscle tissue with the guidance of syringe needles, and integrated with peripheral circuits. Moreover, the cost of production is relatively low as the fabrication process including sputtering metal and chemical vapor deposition only.

The surface morphology of sputtered platinum and electrochemically deposited PEDOT/PSS on the polyimide capillary was observed by scanning electron microscope (SEM, ULTRA 55, Zeiss, Germany). As shown in Figure 2a, the sputtered Ti/Pt layer uniformly and densely covered on the whole surface of capillary. This mainly attributed to the capillaries were horizontally suspended in the chamber during sputtering process. The cracks observed on the platinum

surface were probably induced by bending during fabrication process and surface stress, nevertheless did not lead to exfoliation of platinum layer or electrical breakage. The electrochemically deposited PEDOT/PSS coated on electrode site uniformly and densely similarly as sputtered platinum (Figure 2b). The rough surface morphology of PEDOT/PSS coating enlarged the effective surface area of electrode site, which would contribute to the improvement of electrochemical performance of micro tube electrode.

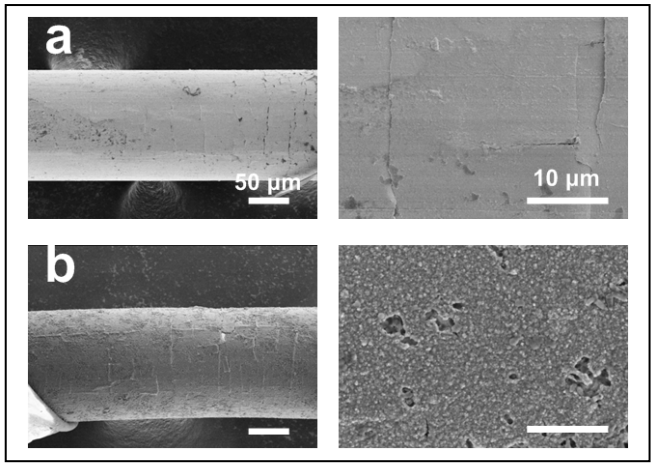

Figure 2. Scanning electronic microscopy (SEM) of sputtered platinum on polyimide capillary (a) and PEDOT/PSS deposited on platinum electrode sites (b), respectively.

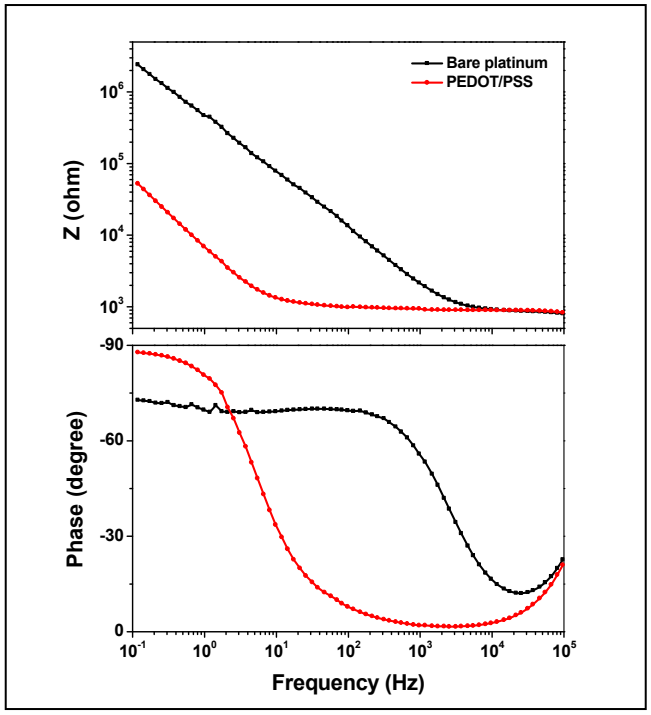

Figure 3. Typical EIS of bare platinum (black) and PEDOT/PSS coated (red) micro tube electrode.

The electrochemical impedance spectroscopy (EIS) of both bare sputtered platinum tube electrodes and tube electrodes coated with PEDOT/PSS were measured at the frequency range from 0.1 to 100,000 Hz. As shown in Figure 3, the impedance amplitude of PEDOT/PSS modified electrodes was much smaller than that of bare Pt electrodes in the whole frequency range below 10,000 Hz. Especially, the impedance of electrodes with PEDOT/PSS coating at frequency of 10 Hz and 1,000 Hz, which related to the frequency electromyography and neuronal recording respectively [6], was 985±87 Ω and 941±56 Ω, while that of bare Pt electrodes was 13620±672 Ω and 2174±173 Ω, respectively. Therefore, the impedance of micro tube electrodes was sharply reduced with conducting polymer coating.

The cyclic voltammogram (CV) (shown in Figure 4) was obtained to evaluate the charge storage capacity (CSC) of the tube electrodes. Both bare Pt tube electrodes and PEDOT/PSS coated tube electrodes were experienced CV scanning from -0.6V to 0.8V (vs. SCE) at a scan rate of 50 mV/s. The CSC of PEDOT/PSS coated electrodes was 44.78±8.56 mC/cm^2, which was approximately 13 times larger than that of bare Pt tube electrodes (3.44±0.73 mC/cm^2). The enhancement of CSC after PEDOT/PSS modification mainly attributed to the enlargement of effective surface area of electrode site and excellent electrochemical property of conducting polymer.

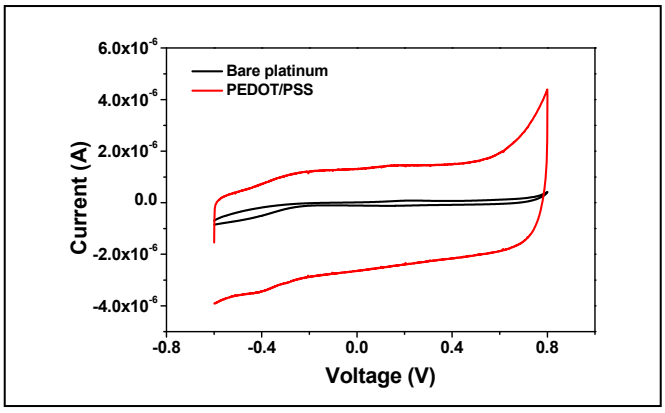

Figure 4. Typical CV of bare platinum (black) and PEDOT/PSS coated (red) micro tube electrode.

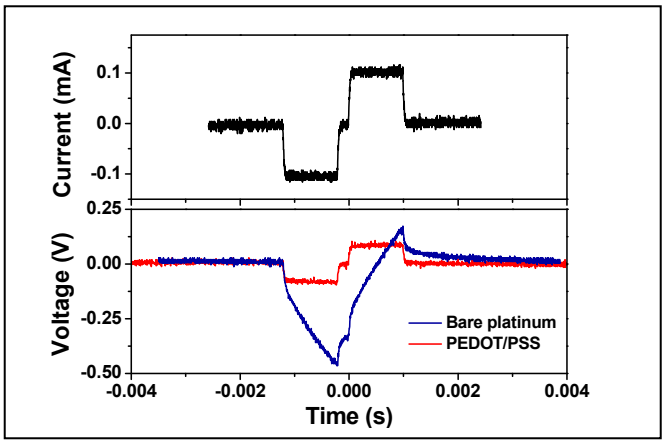

Figure 5. Typical current stimulation pulse (upper black) and voltage respones of bare platinum (blue) and PEDOT/PSS coated (red) micro tube electrode.

As shown in Figure 5, a series of current pulses was applied on bare Pt tube electrodes and PEDOT/PSS coated electrodes in PBS for electrical stimulation performance investigation. The voltage responses of both kinds of micro tube electrodes were observed by an oscilloscope. As shown

in the under chart of Figure 5, the voltage excursion amplitude of PEDOT/PSS coated electrode was much smaller than that of bare Pt electrode. The lower voltage amplitude generated by current stimulation was preferred because smaller harm to tissue would be induced. The charge injection limit was defined as the maximum charge density per unit area of the electrode site when the maximum residual potential got to the water reduction potential [7]. According to the definition, the charge injection limit was tens times increased from 0.13±0.06 mC/cm^2 of bare Pt tube electrodes to 5.02±0.89 mC/cm^2 of PEDOT/PSS coated tube electrodes. This improvement of charge injection limit would ensure that large quantity of charge could be delivered into tissue without generating high voltage amplitude.

In order to evaluate the fluid injection performance of micro tube electrodes, deionized water was injected by a syringe passing through the polyimide capillary. As presented in Figure 6, the volume flow rate was approximately linearly increased with the addition of the pushing pressure. Moreover, the measured results approached to the calculated flow resistance results, which was calculated by the equation mentioned in reference [8].

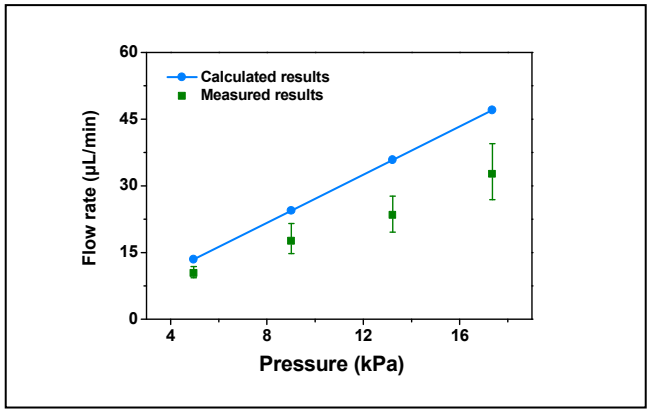

Figure 6. Calculated and measured pressure–flow rate property of micro tube electrode with length of 5.4 cm.

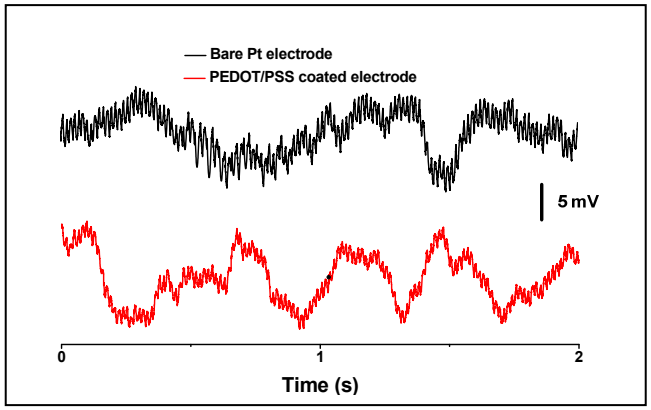

Figure 7. Typical EMG recorded by bare platinum (black) and PEDOT/PSS coated (red) micro tube electrode.

In addition, in order to assess practical performance of micro tube electrodes, we implant both kinds of micro tube electrodes into gastrocnemius of rabbit for intramuscular EMG recording with sampling rate of 4 kHz. The recorded EMG signal was band-pass filtered at frequency from 0.3 Hz to 100 Hz and trapped at 50 Hz. As shown in Figure 7, there was little difference between the amplitude of EMG recorded by bare Pt electrode and that of PEDOT/PSS coated electrode. The amplitude of noise was reduced from 1.91±0.21 mV recorded by bare Pt electrode to 1.21±0.15 mV of PEDOT/PSS coated electrode. The signal quality of EMG recording was obviously improved after electrode site modification with conducting polymer.

IV. Conclusion

In summary, we designed and fabricated a flexible micro tube electrode based on polyimide capillary. The tube microprobe combined electrical circuit with fluidic channel was facilely fabricated with low cost. The electrodes were electrochemically deposited with PEDOT/PSS to improve their electrical performance, which was evaluated by EIS, CV and charge injection limit measurements. Moreover, the fluid injection performance was assessed by injecting water through tube electrodes to air. Furthermore, the micro tube electrodes were implanted in skeletal muscle for practical EMG recording. The micro tube electrode presented in this study provide a novel approach to precisely intramuscular monitoring, while chronic implant test and integration of biosensors on micro tube electrodes would be considered in the future work.

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