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Enhancement of electro-chemical properties of TiO_2 nanotubes for biological interfacing

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ABSTRACT

Micro/nano electrodes employing nanotubes has attracted paramount attention in recent years due to their inherent superior mechanical and structural properties. Electrical interfaces with different geometries and sizes have been developed as electrodes for measuring action potentials and investigating neural information processing in neural networks. In this work, we investigated the possibility of using TiO_2 nanotube arrays that were grown using electrochemical anodization technique, as a micro/nano electrode for neural interfacing. The morphology of fabricated nanotube arrays were found to be significantly affected by the applied voltage. Annealing and doping of TiO_2 nanotube arrays has been performed to improve the structural and electrical properties of the nanotube arrays. It was found that the annealing and doping with nitrogen improve the electrical conductivity of the nanotube arrays. Moreover, the tube diameter and length can be controlled by changing the applied voltage and that can significantly affect the biocompatibility of the nanotube arrays. It was observed that nitrogen doped nanotubes with morphology consisting of 61 nm diameter, 25 nm wall thickness and tube length of 2.25 μm could be good candidate to be used as electrodes for biological interfacing. This is due to the fact that the nitrogen doped nanotubes with aforementioned morphology possess great properties necessary for effective biological interfacing such as low impedance, high capacitance and good biocompatibility.

1. Introduction

“The key philosophical theme of modern neural science is that all behaviour is a reflection of brain functions” [1]. Extracellular and intracellular recordings are two major methods that have been developed to measure the neural electrical activity resulting from unequal distribution of ions across cellular membrane [2]. It has been established that the vertical geometry of the nanoelectrodes has a major impact on improving the signal detection by reducing the membrane-electrode gap and increasing the contact area as a result of the wrap of the plasma membrane around the electrode [3–6]. Electrical interfaces with different geometries and sizes have been developed as electrodes for measuring action potential and investigation neural information processing in neural networks. Planar type microelectrode made of non-toxic and high corrosion resistant metals such as gold, platinum and iridium is a common electrode with a diameter of a few tens of a micrometers used for measuring action potentials [7]. Hai et al. [8] have successfully enhanced the neuron-microelectrode electrical coupling coefficient from 0.1% to 50% compared to the extracellular recording recorded by planar micro electrodes using micrometer-size gold electrodes with a mushroom-shape to gain an intracellular recording. The authors have attributed this to three main causes. The first is the suitable shape of the electrode that can be easily engulfed by cultured cells. The second is the high seal resistance between the cells membrane and the mushroom-shaped electrode and the third is the high junctional membrane behaviour. Gold nanopillar electrodes are another type of electrodes used for extracellular and intracellular recordings. For more precise and better quality signal recording, three studies discussed that the size of the electrode can be scaled down to match the neuron size [9–11]. Three different strategies were

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employed to fabricate nanowire electrodes. In the first strategy, Duan et al. [9] coated germanium nanowires with SiO_2 using an atomic layer deposition technique. The nanowire cores were then etched using Hydrogen Peroxide. The second was achieved by Xie et al. [10] who used an ion beam to deposit platinum nanowires with a diameter of 100 nm on a planar electrode made of platinum. Another strategy includes the thermal growing of silicon oxide on silicon nanowires, the oxide layer subsequently removed from the tips of the nanowires. These tips were coated with an evaporated platinum or gold film [11]. Recently Lin et al. [12] used an electro deposition technique to produce iridium oxide nanotubes. The electrochemical studies confirm that iridium oxide nanotubes have lower impedance and a higher charge storage capacity than the gold nanopillars that have the same surface area. Scanning electron microscopy (SEM) images reveal that the cells engulf and wrap around the nanotubes and also extend into these nanotubes. The authors have shown that a larger signal can be recorded using iridium oxide nanotube electrodes compared to gold nanopillar electrodes. The low sensitivity of some of the aforementioned electrodes as well as the high cost associated with the use of noble metals in these electrodes and their fabrication complexity pose severe constraints towards the development of functional electrodes for the proposed application. Different methods were employed to fabricate TiO_2 nanotube arrays and to improve their electrical properties as well as their biocompatibility [13–16]. Anodization is a common method was used to fabricate TiO_2 nanotube arrays. Anodization parameters have been widely studied as crucial factors influencing nanotube morphology. Alsammarraei et al.[17] fabricated TiO_2 nanotube arrays with different morphologies by controlling the applied voltage. While Macak et al. [18] adjust the electrolyte acidity locally at the pore bottom to produce nanotubes with high aspect ratio. A nanotube membrane with thickness of 720 μm was formed by subjecting both sides of titanium foil 250 μm to electrochemical oxidation in electrolyte consist of ethylene glycol, water and ammonium fluoride [19]. It was reported that nanotubes with length up to 134 μm could be achieved by anodizing a titanium foil in fluoride ion bath containing variety of nonaqueous organic polar electrolytes [20]. Prakasam et al.[21] have successfully fabricated titania membrane with aspect ratio of approximately 1500 and safely separated the TiO_2 membrane from titanium substrate. However, there is a significant lack in the investigation of the combined effect of TiO_2 nanotube morphology on their electrochemical properties and biocompatibility. In this work we demonstrate how the nanotube morphology impact their electrochemical impedance, capacitance and biocompatibility. We introduce TiO_2 nanotube arrays (NTAs) as a candidate material to fabricate micro/nano electrodes for neural interfacing. Electrochemical anodization has been used as a simple technique for the fabrication of TiO_2 nanotube arrays. Annealing and doping with nitrogen were employed to improve the electrical conductivity of the nanotube arrays. Electrical properties of the developed nanotube arrays have been studied in relation to their morphological and microstructural characteristics.

2. Methods

2.1. Fabrication of TiO_2 nanotube arrays

Rectangular samples of titanium (1 cm × 1.5 cm × 50 μm purity of 99.7%, Sigma-Aldrich) were cleaned in an ultrasonic bath in a beaker containing 30% acetone, 30% ethanol and 40% distilled water for 10 min. Titanium samples were used as the anode and a standard platinum electrode (99.9% Sigma-Aldrich) was used as the counter electrode in the anodizing cell separated at a distance of 2 cm. The anodizing process was carried out in ethylene glycol (anhydrous, 99.8% Sigma Aldrich) containing 0.5 wt% NH_4F (98% Sigma-Aldrich) and 4 vol% of deionized water. Previous studies pointed out that highly ordered nanotubes with a wide range of nanotube morphology could be obtained using this electrolyte. Chemical dissolution and fluoride ion transmission rate is relatively low in organic solutions and the formed tubes in the organic electrolyte will be more homogeneous [22,23]. It was reported that with the presence of (0.3 wt %)NH_4F and (2 vol %) H_2O in ethylene glycol, the resulting tube diameters and wall thicknesses decrease with decreasing NH_4F percentage in the electrolyte [24]. It has been also reported that increase the concentration of NH_4F more than 0.5 wt %, irregular nanotubes formed due to the extremely high dissolution rate. A previous study demonstrated that increase of the water content in the electrolyte leads to the decrease in tube length [25]. Considering the focus of our work to improve the electrochemical conductivity of the nanotubes requiring nanotubes with thick walls and short tubes; employed electrolyte is considered to be the most suitable option. The samples were anodized at applied voltages of 10 V, 20 V, 30 V, 40 V, 50 V and 60 V. All experiments were performed at 20 °C for 1 h. The anodized samples were directly rinsed by water and dried by nitrogen gun.

2.2. Annealing and doping of TiO_2 nanotube arrays

To improve the electrical conductivity of TiO_2 nanotube arrays, all samples were annealed at a temperature of 500 °C in a SCE Horizontal tube Furnace (Jetlow furnaces,with a FP93 Controller/ Programmer) with a heating rate of 4 °C/min and dwell time of 3 h. Doping with nitrogen was conducted under the same conditions as the annealing process with a flow of dry nitrogen.

2.3. Characterization of phase structure and morphology of TiO_2 nanotube arrays

To determine the phase and crystal structure of TiO_2 nanotubes, X-ray diffraction (XRD, Panalytical X-Pert Pro MRD XL, CuKα radiation, $\lambda = 1.5418$ Å) was used. The measurements were performed within the range of 2 θ from 20° to 60°. Scanning electron microscopy (Zeiss Supra 55VP) and Image J software were used for morphological characterization of nanotube arrays.

2.4. Electrochemical measurements

To evaluate the effect of heat treatment and doping processes on the conductivity of the TiO_2 nanotubes layer, electrochemical impedance spectroscopy (EIS) was performed on samples before and after the heat treatments. EIS measurements were performed using a potentiostat (VSP Biologic science instruments). The platinum standard electrode and the saturated Ag/AgCl electrode (Sigma-Aldrich) were used as a counter electrode and reference electrode, respectively. Potassium buffered saline solution (PBS, pH 7.4, Sigma-Aldrich) was used as the electrochemical cell electrolyte. Biologic EC-lab software was used for data acquisition and analysis. Bode plots of log impedance /Z/ vs log frequency were used to compare the electrochemical properties. EIS values for all samples were measured at a frequency of 1 kHz. Cyclic voltammetries of the doped samples were conducted at a scanning rate of 100 mV/s in Potassium buffered saline solution. The potential range of −0.1 V to 0.6 V versus saturated Ag/AgCl electrode was employed in the cyclic voltammetry test. In all electrochemical measurements, the exposed area to the electrolyte was constant (4.9 mm^2). The electrochemical measurements were performed on nanotube layers on Ti substrates. The exposed area was with a circular shape with a diameter of 2.5 mm. Both of electrochemical impedance and cyclic voltammatery measurements were repeated five times for each sample.