Article

Fabrication of Iridium Oxide/Platinum Composite Film on Titanium Substrate for High-Performance Neurostimulation Electrodes

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Abstract: Electrode materials for neural stimulation have been widely investigated for implantable devices. Among them, iridium and iridium oxide are attractive materials for bio-interface applications due to their desirable stability, electrochemical performance, and biocompatibility. In this study, iridium oxide/platinum (IrO_x/Pt) composite films were successfully fabricated on titanium substrates by chemical bath deposition and these films are expected to be used as biocompatible stimulation electrodes. We modified the film compositions to optimize the performances. In addition, these IrO_x/Pt composite films were characterized before and after annealing by SEM and XRD. We also identified the hydrophilicity of these iridium oxide/platinum composite films by measuring contact angles. Finally, the charge storage capacities of these iridium oxide/platinum composite films were evaluated by an electrochemical workstation. As a result, the charge storage capacities of the iridium oxide/platinum composite films are largely increased, and this leads to a very efficient neurostimulation electrode. Additionally, we successfully demonstrated the chemical bath deposition of IrO_x film on the surface of the bullet-shaped titanium microelectrode.

Keywords: IrO_x/Pt composite film; stimulation electrodes; biocompatible thin film; bullet-shaped microelectrode

1. Introduction

The importance of biomedical engineering has raised considerable attention recently, especially on implantable neural-interacting prosthesis [1]. Titanium and its alloys have been confirmed as effective groups of traditional biomaterials [2]. Titanium has exceptional corrosion resistance in the physiological environment, therefore, is the chosen material for many structural implantable devices [3]. For instance, Noda et al. reported the development of an implantable neurostimulation system based on structural titanium microelectrodes [4]. A major limiting factor is the lack of stimulation electrodes with both reasonable performance, stability, and safety [5]. The development of stimulation electrodes requires the ability to inject electrical charges to produce a response without any tissue damage at the stimulation site. The electrode materials must be chosen and examined carefully.

Safe neural stimulation requires a reversible charge injection process which can be achieved either by a capacitive process or by a faradaic reversible reaction. The capacitive stimulation electrodes allow signal transmitting to neural tissues by a dielectric film [6]. However, only a limited amount of charge can be stored across the electrode interface. In general, electrostimulation with reversible faradaic reactions brings better charge injection performance than that with capacitive

charge storage. Stimulation electrode materials operating in a faradaic mechanism include platinum, platinum/iridium alloy, iridium oxide, and poly(3,4-ethylenedioxythiophene) (PEDOT) [1,7,8]. Among them, iridium oxide can sufficiently provide necessary charge for stimulation without damaging surrounding tissues by electrochemical reduction and oxidation reactions at the electrode interface [9]. Additionally, advantages such as high charge injection capability, desirable stability, and requisite biocompatibility render iridium oxide to become the most promising material for implantable neurostimulation electrodes.

Iridium oxide has received substantial attention in recent years because of its unique ability to inject electric charge and its resistance to corrosion [10]. Iridium oxide is formed with ionic bonds and the hybridized s orbitals are fully occupied with electrons, which lead to notable thermal and chemical stability [11]. Several deposition techniques have been developed, including thermal decomposition, reactive sputtering, electrochemical activation, and electrodeposition [7,9,12–15]. However, some limitations for the processes listed above have been revealed. For instance, curved titanium substrates are not suitable for physical vapor deposition (PVD). Please define if appropriate. processes such as sputtering which causes cracking due to poor adhesion at the edge. Furthermore, titanium substrates are not suitable working electrodes for electrodeposition in most scenarios [4]. Therefore, an alternative solution for the iridium oxide synthesis is chemical bath deposition (CIROF) [16,17]. In chemical bath deposition, the precursor of Ir-ions undergoes oxidation reactions and forms film on the substrates initiated by selective oxidizers. This approach does not require an externally-imposed current/voltage and thus an insulator can be used as the substrate for film growth. Titanium substrates coated with iridium oxide by the wet synthesis process can overcome the difficulty of electrodeposition.

A neurostimulation electrode plays a critical role in determining the performance of the bioelectronics [18]. In this study, we developed iridium oxide/platinum composite films on titanium substrates by a multi-step chemical bath deposition and these films are expected to be used as biocompatible stimulation electrodes. We modified the film composition in order to optimize the performance of the iridium oxide/platinum composite films on titanium substrates for neurostimulation devices [19]. Additionally, we employed the chemical bath deposition of IrO_x on the surface of a bullet-shape titanium microelectrode to validate the process we developed in this study on a practical device.

2. Materials and Methods

Based on previous results, a chemical bath deposition has been developed to fabricate high-quality iridium oxide films with thicknesses in the range from 50 to 1000 nm [16,17]. Therefore, a multi-step method can be used to meet the required film thickness. In this study, titanium sheets ($1 \times 3 \text{ cm}^2$) were cleaned and granulated for increasing adhesion of the following coatings by a dilute HF solution (10%) for 1 min at room temperature [20]. Different compositions of IrO_x/Pt composite films were prepared by the chemical bath deposition of iridium oxide on sputtered platinum film on the granulated titanium sheets. The plating bath of iridium oxide contained 0.01 M of sodium hexachloroiridate (III) hydrate ($\text{Na}_3\text{IrCl}_6 \cdot x\text{H}_2\text{O}$, Sigma-Aldrich, St. Louis, MO, USA), 0.15 M of sodium hypochlorite (NaClO , SHOWA, Gyoda, Japan), 0.03 M of sodium hydroxide (NaOH , Mallinckrodt Pharmaceuticals, Dublin, Ireland), and 0.01 M of sodium nitrite (NaNO_2 , SHOWA, Gyoda, Japan). Subsequently, the Ti and Pt-coated Ti sheets underwent a chemical bath deposition of iridium oxide at 25°C for 4 h. The ratios of the IrO_x/Pt composite films are 0 to 100 nm, 100 to 200 nm, 200 to 100 nm, and 300 to 0 nm. After the IrO_x/Pt composite films were formed, a heat treatment was conducted at 450°C for 2 h in air. In addition, we performed the same chemical bath deposition of IrO_x on a bullet-shape titanium electrode which is 0.5 mm in diameter.

The surface morphologies of our samples were analyzed using a scanning electron microscope (FESEM; Hitachi SU-8010, Hitachi, Ltd., Tokyo, Japan) with a 15 keV operating voltage. An X-ray diffractometer (XRD; Bruker D8 Discover, Bruker, Billerica, MA, USA) with a $1.54 \text{ \AA}$ $\text{Cu K}\alpha$ target was employed to identify the characteristic peaks; the scan rate was $0.05^\circ/\text{s}$ from 20° to 80° .

The charge storage capacity (CSC) was determined by integration of the cathodic current in a potential window for IrO_x and Pt between -0.6 to 0.8 V. It has become common practice to characterize the stimulation electrodes by their CSC values. The CSC is calculated from the time integral of the cathodic current in a slow-sweep-rate cyclic voltammetry over a potential range that is just within the water electrolysis window (-0.6 – 0.8 V for IrO_x and Pt). An electrochemical workstation (CHI 614E, CH Instruments, Inc., Austin, TX, USA) was employed to obtain those electrical properties. The geometric surface area was 0.386 cm^2 . Cyclic voltammetry was taken as a sweep rate of 50 mV/s from -0.6 to 0.8 V. All the experiments were taken in phosphate buffer saline (PBS).

The biocompatibility of the IrO_x/Pt composited films was evaluated by a sulforhodamine B (SRB) assay. MDA-MB-231 cells were seeded on different surfaces at a density of 1000 cells/cm^2 . After 7 days, surfaces were washed twice with an excess of phosphate buffered saline (PBS) to remove any dead cells or debris. Cells were then fixed by immersing surfaces in 10% trichloroacetic acid (TCA) overnight at 4°C . The next day, cells were washed 5 times with double distilled water (DDW) and allowed to air dry. Cells were then stained for 1 h with 0.4% SRB (prepared in 1% acetic acid). Samples were washed 4 times with 1% acetic acid and air dried. Samples were then immersed in a 10 mM Tris base for 30 min. Optical density (OD) was recorded at 540 nm using an ELISA reader.

3. Results and Discussion

The adhesion of the first coated layer plays a key factor in the stability of the film synthesized by multi-step chemical bath deposition. Platinum, especially, has been reported that its adhesion issue causes peeling of the deposited film [21]. The granulated titanium can sufficiently increase the adhesion of sputtered platinum film on the titanium surface. Figure 1 shows the optical microscope images of titanium surface before and after surface granulating process. The treated titanium shown in Figure 1b, presents more and finer grains compared to the raw titanium sheet shown in Figure 1a. Therefore, the adhesion of the IrO_x/Pt composite films on titanium substrate can be increased.

Figure 1. Optical microscope images of (a) untreated Ti foil; and (b) granulated Ti foil.

Figure 2 shows SEM images of the IrO_x/Pt composite films. Figure 2a is the sputtered platinum on titanium substrate; some particles can be observed on its surface. Figure 2b–d show top-view SEM images of 100/200 nm, 200/100 nm, and 300/0 nm of IrO_x/Pt composite films, respectively. As shown in Figure 2b–d, the Ti substrates were fully covered by a dense layer of IrO_x and IrO_x particles on the surfaces. More particles appeared on the 200/100 nm of IrO_x/Pt composite film, as shown in Figure 2c, than that on the 300/0 nm composite film, as shown in Figure 2d. Although thicker IrO_x films generally have more particles by chemical bath deposition, the sputtered platinum provides more nucleation sites compared to the pure titanium substrate. The contact angles also altered with the composition of the coated films as listed in Table 1. A negative correlation can be found between the thickness of IrO_x films and measured contact angles. It implies that composite films become more hydrophilic along with the increasing thickness of IrO_x film. The result matches the relationship between thickness and hydrophilicity reported by Miyashita et al. [22]. The thicker IrO_x film by chemical bath deposition presented more hydrophilicity, which is a desirable property for an implantable material.

Figure 2. Top-view SEM images of annealed IrO_x-Pt composite films on Ti substrate; (a) sputtered Pt, (b) 100 nm/200 nm of IrO_x/Pt, (c) 200 nm/100 nm of IrO_x/Pt, and (d) 300 nm/0 nm of IrO_x.

Table 1. A summary of relations between IrO_x/Pt ratio and contact angle.

IrO _x /Pt Ratio	Contact Angle
0/100	59.44
100/200	24.48
200/100	12.22
300/0	5.58

The crystallinity of the CIROF was improved by annealing the as-deposited film at 450 °C for 2 h in air. Figure 3 provides the XRD patterns of the annealed IrO_x/Pt composite films. The as-deposited film was amorphous but after annealing, the crystalline rutile phase of IrO₂ was confirmed by comparing with the standard IrO₂ pattern (ICDD 00-043-1019), Pt pattern (ICDD 00-001-1194), and Ti Pattern (ICDD 01-089-5009). The crystalline film is expected to reduce defects and improve the film stability. We can determine the charge storage capacity (CSC) of the films by performing the cyclic voltammetry tests in PBS solution. It has become common practice to characterize the stimulation electrodes by their CSC, which is essentially a measurement of the total amount of charge available for a stimulation pulse.

Figure 3. XRD patterns of different compositions of IrO_x-Pt composite films on Ti substrates with IrO_x/Pt ratio of (a) 300/0, (b) 200/100, (c) 100/200, and (d) ICDD standards of IrO₂, Ti, and Pt.

The cyclic voltammograms (CV) shown in Figure 4 are the as-deposited and annealed IrO_x/Pt composite films, respectively. The high CSC value shows that the IrO_x/Pt composite films may have high charge-injection capacity and have a potential to stimulate cells at a lower voltage. Figure 4a presents the CV curves for various composition of IrO_x/Pt composite films. The CSC values decreased after the annealing process due to the effect of crystallinity [12,23]. The heat treatment process efficiently crystallized the composite films, and the CSC values changed accordingly. Furthermore, the 200/100 nm of IrO_x/Pt composite film presented the largest CSC value of 46.28 mC/cm² because the sputtered platinum increases the surface roughness of the composite film. Figure 4b shows the comparison of the CV curves of as-deposited and annealed IrO_x film (300/0 nm) as well as annealed Pt (0/100 nm), and the CSC values were 35.22, 24.19, and 1.07 mC/cm², respectively. IrO_x can largely increase the CSC value compared to the traditional commercial electrode material of Pt. Therefore, we can expect IrO_x to become the next generation biocompatible electrode for implantable neurostimulation devices [24,25].

Figure 4. Cyclic voltammograms of (a) as-deposited IrO_x/Pt composite films with IrO_x/Pt ratio of (i) 300/0, (ii) 200/100, (iii) 100/200; and annealed IrO_x/Pt composite films with IrO_x/Pt ratio of (iv) 300/0, (v) 200/100, (vi) 100/200; (b) charge storage capacity (CSC) comparison of (i) as-deposited IrO_x film, (ii) annealed IrO_x film, and (iii) Pt film.

We further employed the chemical bath deposition of iridium oxide on a bullet-shaped titanium microelectrode (0.5 mm in diameter). Noda et al. reported that they developed a retinal prosthesis using the curved titanium microelectrodes [4]. Figure 5a displays the optical microscopy (OM) image of the bullet-shaped titanium microelectrode. IrO_x film was deposited on the surface of the bullet-shaped titanium microelectrode by chemical bath deposition developed in this study. As shown in Figure 5a, the surface of the bullet-shaped titanium microelectrode was uniformly covered by a thin layer of IrO_x film. Figure 5b displays the CV curve of the fifth cycle of the IrO_x-coated bullet-shaped titanium microelectrode at 50 mV·s⁻¹. The oxidation/reduction peaks that appeared in the CSC profile of the IrO_x-coated bullet-shaped titanium microelectrode were identical to the CSC profiles of the IrO_x-coated titanium and IrO_x/Pt-coated titanium shown in Figure 4. Consequently, we successfully implemented chemical bath deposition to replace deposition techniques such as sputtering. In addition, the CSC value of the IrO_x-coated bullet-shaped titanium microelectrode was 30.12 mC/cm² correlated to the electrode performance of the IrO_x thin film using chemical bath deposition. We would like to further explain the reason we only deposited IrO_x on the bullet-shaped titanium microelectrode. The IrO_x and Pt in the composite films were prepared using chemical bath deposition and DC sputtering, respectively. We only demonstrated the feasibility of the chemical bath deposition of IrO_x on the bullet-shaped titanium microelectrode to prevent cracks on the sputtered Pt film formed on the curved titanium substrate. However, IrO_x/Pt composite film can be deposited on the bullet-shaped titanium microelectrode as long as both IrO_x and Pt films can be prepared using chemical bath deposition [26].

Figure 5. (a) Optical microscope image of IrO_x-coated bullet-shaped titanium microelectrode; (b) cyclic voltammogram of IrO_x-coated bullet-shaped titanium microelectrode.

In order to evaluate the biocompatibility of the IrO_x/Pt composite films, an MDA-MB-231 cell line was cultured on top of the IrO_x/Pt composite films and on a culture dish as the control group. The cell viability was assessed by measuring the optical density (OD) of the resulting solution at 595 nm. The cell viability percentages were calculated as: $OD_{\text{sample}}/OD_{\text{control}}$. Figure 6 shows the cell viability results. Each sample of IrO_x/Pt composite film had a viability of ~90%, which indicates that the IrO_x/Pt composite film provides a biocompatible environment for cell survival. The IrO_x/Pt composite films fabricated in this study have good crystallinity and hydrophilicity; these properties can provide a desirable matrix for cell attachment according to studies on the relationship between crystallinity and biocompatibility [10,27].

Figure 6. Cell viability percentage of IrO_x/Pt composite films.

4. Conclusions

In this study, we successfully developed a hybrid deposition process to prepare IrO_x/Pt composite films on titanium substrates by combining chemical bath deposition and sputtering. A relationship is found as well; when the deposited thickness of IrO_x increases, the surface roughness also increases, but the contact angle decreases. These IrO_x/Pt composite films with different compositions can be used for many applications. Furthermore, the chemical bath deposition is a simple and inexpensive alternative for fabrication. In addition, the IrO_x/Pt composite films were characterized by their morphology, composition, crystallinity, surface roughness by SEM, XRD, and contact angle, respectively. As a result, the IrO_x/Pt composite films present higher charge storage capacities than Pt film does, so they can be utilized in implantable neurostimulation devices and largely enhance the efficiency. Additionally, we successfully demonstrated the chemical bath deposition of IrO_x film on the surface of the bullet-shaped titanium microelectrode and the redox behavior of the IrO_x-coated bullet-shaped titanium microelectrode was identical to that of the IrO_x-coated titanium sheet.

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