Highly ordered Ni–Ti–O nanotubes for non-enzymatic glucose detection

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A B S T R A C T

Anodization is used to fabricate Ni–Ti–O nanotube (NT) electrodes for non-enzymatic glucose detection. The morphology, microstructure and composition of the materials are characterized by field emission scanning electron microscopy (FE-SEM), high resolution transmission electron microscopy (HR-TEM) and X-ray photoelectron spectroscopy (XPS). Our results show amorphous and highly ordered NTs with diameter of 50 nm, length of 800 nm, and Ni/Ti ratio (at %) of 0.35 can be fabricated in ethylene glycol electrolyte supplemented with 0.2 wt.% NH4F and 0.5 vol.% H2O at 30 °C and 25 V for 1 h. Electrochemical experiments indicate that at an applied potential of 0.60 V vs. Ag/AgCl, the electrode exhibits a linear response window for glucose concentrations from 0.002 mM to 0.2 mM with a response time of 10 s, detection limit of 0.13 μM (S/N = 3), and sensitivity of 83 μA mM⁻¹ cm⁻². The excellent performance of the electrode is attributed to its large specific area and fast electron transfer between the NT walls. The good electrochemical performance of the Ni–Ti–O NTs as well as their simple and low-cost preparation method make the strategy promising in non-enzymatic glucose detection.

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1. Introduction

Fast, sensitive, and low-cost glucose detection is of great importance to clinical diagnosis of diabetes, bioprocess monitoring, and food analysis [1–4]. Many efforts have been made to develop high-performance glucose sensors, particularly based on amperometric methods, since Clark and Lyons proposed the concept of glucose enzymatic electrodes in 1962 [5]. First-generation glucose sensors use physiological oxygen as an electron mediator between glucose oxidase (GOx) and the electrode but usually suffer from oxygen dependence and interferences [3]. To overcome these drawbacks, the second generation electrode uses an artificial electron acceptor such as ferrocene derivatives, ferricyanide, and so on to mediate the GOx cycling to avoid the dependence on oxygen [1,3]. In addition, a low amperometric potential used in the latter effectively reduces interferences. Because these two generations of biosensors are based on enzymatic reactions, they have high sensitivity and selectivity to glucose. However, despite continuous improvement on the stability of enzymatic biosensors, their short lifetime, narrow windows of temperature (~44 °C) and humidity (ambient) continue to be obstacles [1]. Moreover, ensuring the stability of these electrodes usually requires a sophisticated electro-polymerization process, covalent cross-linking, and sol–gel entrapment on electrode surface thus leading to high cost and low reproducibility.

To overcome these shortcomings of enzyme-based biosensors, third-generation glucose sensors based on direct electrooxidation of glucose are being developed. One key parameter that determines the electrocatalytic activity of the biosensors is the electrode materials. Recent studies have shown some noble metals such as Pt, Au, Ag, Ru, and their alloys have favorable electrocatalytic activity to glucose [6–9]. However, the high cost of these materials undermines their commercial potential. In comparison, many inexpensive transition metal (Ni, Cu, Co, and so on) oxides or hydroxides also exhibit potential in non-enzymatic glucose detection [10–14]. Another important factor that influences the electrocatalytic activity of the biosensors is the active surface area of the electrodes. Because electrooxidation of glucose is a kinetically controlled surface reaction, a large surface area of the electrode is highly desirable. In this respect, the electrodes composed of nanowires [15], nanofibers [16], nanoparticles [17,18], nanoplatelets [19], and nanospheres [20] with improved sensitivity, detection limit, selectivity, and stability have been reported.

Ni-based electrodes have drawn much attention in recent years because of their low cost, high sensitivity and stability, as well as insensitivity to chloride ions [3]. Similar to other electrode materials, their electrocatalytic activity can be improved with a nanostructured surface. Electrochemical anodization is a simple technique to fabricate highly ordered and vertically oriented nano-porous/tubular structures with a large specific surface area. However, unlike valve metals such as Ti that can be easily anodized, it is more difficult to produce well-defined nano-pores and tubes on Ni by anodization. In this work, by using Ti...
as a supporting matrix during anodization, highly ordered Ni–Ti–O nanotubes (NTs) with diameter of 50 nm and length of 800 nm are successfully fabricated. It is shown that the NTs possess desirable glucose sensing ability with good reproducibility and stability thus is very promising for non-enzymatic glucose detection.

2. Materials and methods

Mirror-polished nearly equiatomic NiTi alloy (50.8 at.% Ni) sheets with dimensions of 10 mm × 10 mm × 2 mm were used as substrates and anodization was carried out at a constant voltage (25 V) and temperature (30 °C) for 1 h in an ethylene glycol electrolyte of 100 ml containing 0.2 wt.% NH₄F and different H₂O contents (0.0 vol.%, 0.5 vol.% and 1.5 vol.%). The current–time curve during anodization was recorded on an electrochemical workstation (CS350, CorrTest). The morphology, microstructure and composition of the anodized samples were characterized by field emission scanning electron microscopy (FE-SEM, JSM-7001F, JEOL) and high resolution transmission electron microscopy (HR-TEM, JEM-2100F, JEOL). The chemical composition of the NiTi alloy and Ni–Ti–O NTs as well as chemical states of Ni were determined by X-ray photoelectron spectroscopy (XPS, K-Alpha, Thermo) with monochromatic Al Kα radiation (6 mA, 12 kV and 1486.68 eV). The survey spectra were obtained at a constant pass energy of 200 eV over a binding energy range of 200 to 950 eV at 1.0 V/step and high-resolution spectra of Ni were acquired at a constant pass energy of 50 eV at 0.1 eV/step. The elemental composition and chemical states were analyzed by Thermo Avantage 4.51 software and the binding energies were calibrated according to C 1 s peak at 284.8 eV.

Cyclic voltammetric (CV) and chronoamperometric measurements were conducted on the electrochemical workstation in a 0.1 M NaOH solution at room temperature using a three-electrode system. The system was constructed of a magnetic stirrer with a three-hole bracket to fix the three electrodes and a glass breaker of 100 ml placed on the stirrer. Pt foil was used as the counterpart and Ag/AgCl as the reference electrode. Before the electrochemical measurements, the working electrode (anodized sample) was activated in 0.1 M NaOH solution at a scanning rate of 50 mV/s for 100 cycles.

<table>
<thead>
<tr>
<th>Position</th>
<th>Elemental composition (at.%)</th>
<th>Ni/Ti ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ni</td>
<td>Ti</td>
</tr>
<tr>
<td>Top</td>
<td>0.74</td>
<td>3.25</td>
</tr>
<tr>
<td>Bottom</td>
<td>6.50</td>
<td>17.21</td>
</tr>
</tbody>
</table>

Fig. 1. SEM images of Ni–Ti–O NTs prepared in the electrolyte containing different H₂O contents: (A) 0.0 vol.%, (B) 0.5 vol.%, and (C) 1.5 vol.%. Higher magnification (D) and cross-sectional (E) SEM images of the Ni–Ti–O NTs prepared in the electrolyte containing 0.5 vol.% H₂O. (F) Current–time curve of NiTi alloy during anodization in the electrolyte containing 0.5 vol.% H₂O.

Fig. 2. (A) TEM image of the Ni–Ti–O NTs fabricated in the electrolyte containing 0.5 vol.% H₂O. (B) HR-TEM image of the Ni–Ti–O NTs and its corresponding SAED (inset image). (C) Elemental composition of the Ni–Ti–O NTs at rectangular regions in Fig. 2A.
3. Results and discussion

The use of anodization to produce highly ordered Ni–Ti–O NTs on the NiTi alloy as a pseudocapacitive electrode was first reported by Kim et al. [21] and pertinent applications of the NTs such as biomedical coatings [22] and hydrogen sensors [23] have subsequently been explored. The objective of the present work is to investigate the non-enzymatic glucose sensing capability of the electrode constructed of the Ni–Ti–O NTs. SEM images of the anodized samples are depicted in Fig. 1. The surface of sample fabricated without H2O shows an obvious irregular layer and underneath the layer regular NTs can be observed (Inset photo of Fig. 1A). Increase of the H2O content in the electrolyte (0.5 vol.%) leads to the formation of highly ordered Ni–Ti–O NTs (Fig. 1B), but excessive H2O content (1.5 vol.%) results in disordered structure (Fig. 1C) because of rapid dissolution of the NTs during anodization. Higher magnification (Fig. 1D) and cross-sectional (Fig. 1E) SEM images of the Ni–Ti–O NTs prepared in the electrolyte containing 0.5 vol.% H2O show the diameter and length of the NTs is 50 nm and 800 nm respectively. The variation of current versus anodization time shown in Fig. 1F is similar to that observed from pure titanium (Ti), but the steady-state current is relatively high. Four distinct stages, namely initial rapid decrease, slight increase, gradually decrease, and

![Image](image_url)

Fig. 3. (A) XPS survey spectra of the NiTi alloy and Ni–Ti–O NTs fabricated in the electrolyte containing 0.5 vol.% H2O. (B) High-resolution XPS spectra of Ni 2p3/2.

![Image](image_url)

Fig. 4. (A) CVs of the NiTi alloy and Ni–Ti–O NTs in 0.1 M NaOH at a scanning rate of 20 mV/s. (B) CVs of the Ni–Ti–O NTs at various scanning rates in 0.1 M NaOH. (C) Plot of peak current vs. v^{1/2}. (D) CVs of the Ni–Ti–O NTs for 50 cycles at a scanning rate of 50 mV/s.
finally stabilization, can be observed and they correspond to the formation of Ni and Ti oxide thin film, nanopits, nanopores, and nanotubes, respectively [24].

Fig. 2 shows the TEM results of the Ni–Ti–O NTs fabricated in the electrolyte containing 0.5 vol.% H2O. The diameter and length of the NTs obtained from TEM image (Fig. 2A) are consistent with that from SEM images (Fig. 1). HR-TEM image (Fig. 2B) reveals the amorphous characteristics of the NTs and this result is also confirmed by selected area electron diffraction (SAED) (inset image of Fig. 2B). The elemental composition of the NTs detected by energy dispersive spectroscopy (EDS) is shown in Fig. 2C. The contents of Ni and Ti in NTs are far less compared to that in the NiTi substrate. The Ni/Ti ratio at top and bottom of the NTs is 0.23 and 0.38 respectively, which implies that Ni oxide is more easily dissolved compared to Ti oxide. O and C are dominant elements both at the top and bottom of NTs. The presence of F element can be attributed to the use of F-containing electrolyte and Cu is coming from Cu mesh that supports the samples during observation.

The elemental composition of the NTs fabricated in the electrolyte containing 0.5 vol.% H2O detected by XPS survey spectra (Fig. 3A) is consistent with that of EDS results (Fig. 2C). The high-resolution XPS spectra of Ni in Fig. 3B reveal that both the oxidized (Ni(OH))2, 856 eV) and elemental (Ni, 852.5 eV) states are on the surface of the NiTi alloy, but only the oxidized state of Ni can be observed from the surface of Ni–Ti–O NTs. The large specific surface area and Ni2+ content of the Ni–Ti–O NTs are expected to enhance the electrooxidation ability of the electrode towards glucose. In the following electrochemical experiments, the NTs fabricated in the electrolyte containing 0.5 vol.% H2O were used.

Electrochemical behavior of the Ni–Ti–O NTs was investigated by CV in a 0.1 M NaOH electrolyte. As shown in Fig. 4A, the untreated NiTi alloy does not show any redox peaks. In contrast, after anodization, a pair of anodic peak at about 0.47 V and cathodic peak at about 0.39 V corresponding to the Ni3+/Ni2+ couple can clearly be observed, yielding a ΔEp value of 0.08 V. The CV curves of the electrode acquired at different scanning rates are shown in Fig. 4B. The anodic peak potential moves positively and the cathodic one exhibits a small negative shift with increasing scanning rates, indicating that the electrochemical reaction is a quasi-reversible electron transfer one. A continuous increase in the anodic and cathodic peak currents is also observed as the scanning rate is increased. The good proportional relationship between the anodic and cathodic currents and square root of the scanning rates is demonstrated in Fig. 4C. The correlation coefficients (R) of 0.997 and 0.992 are derived after linear regression fitting of the square root of the scanning rates versus the anodic and cathodic peak currents, respectively. These results imply that the electrochemical reaction on the surface of the electrode is a typical diffusion-controlled process, which is ideal for electrochemical glucose sensing. The electrochemical stability of the electrode is investigated by recording consecutive CV curves in the 0.1 M NaOH electrolyte at a potential sweep rate of 50 mV/s for 50 cycles. As shown in Fig. 4D, no obvious variation in the anodic and cathodic peak currents can be observed, suggesting that the Ni–Ti–O NTs possess good electrochemical stability and are suitable for glucose sensing electrodes.

The electrocatalytic ability of the Ni–Ti–O NTs towards glucose was first studied by CV at a scanning rate of 50 mV/s (Fig. 5). Increase in the glucose concentration leads to correspondingly larger anodic peak current thus indicating good catalytic activity of the electrode to glucose oxidation. Furthermore, a small positive shift in the anodic peak potential is observed after addition of glucose. As reported in the literature [3, 17], a possible mechanism of electrooxidation of glucose on the Ni-based electrode is the Ni3+/Ni2+ redox couple in an alkaline medium according to the following reactions:

\[
\text{Ni(OH)}_2 + \text{OH}^- \rightarrow \text{NiOOH} + \text{H}_2\text{O} + e^- \quad (1)
\]

\[
\text{NiOOH} + \text{glucose} \rightarrow \text{Ni(OH)}_2 + \text{glucoolactone.} \quad (2)
\]

Initially, a transient dynamic balance is established between Ni3+, Ni2+, and OH− at the anodic peak potential (Eq. (1)) and subsequently, glucose in the solution consumes a part of the Ni2+ (Eq. (2)). To reach a new balance between Ni3+, Ni2+, and OH−, Ni2+ reacts with OH− resulting in a higher anodic current and concentration polarization of OH− at the electrode/electrolyte interface. A large glucose concentration accelerates the reaction described by Eqs. (1) and (2) thus leading to more pronounced concentration polarization of OH− and a larger driving force (more positive potential) to form Ni3+.

The amperometric response of the electrode to successive step-wise addition of glucose was carried out in 50 ml of the 0.1 M NaOH solution under magnetic stirring (20 rpm) in the applied potential range between 4.5 V and 7.0 V at an interval of 0.5 V (data not shown), and the maximum response is observed at 0.6 V. As shown in Fig. 6A, the electrode shows a sensitive response even at a 2 μM glucose concentration (inset in Fig. 6A) and it may be attributed to the highly ordered architecture that facilitates direct electron transfer in the NT walls. The response time of the electrode after addition of 0.01 mM glucose is 10 s. The calibration curve (Fig. 6B) displays a linear range from 0.002 mM to 0.2 mM with a correlation coefficient of 0.997, sensitivity of 83 μA mM−1 cm−2, and detection limit of 0.13 μM with a signal-to-noise ratio of 3. A large glucose concentration reduces the current response and leveling off is observed from the calibration curve. The observation is consistent with the Michaelis–Menten kinetics indicating that all active sites on the electrode are covered by glucose [25,26]. The linear range, detection limit and sensitivity of the proposed electrode

<table>
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<th>Electrode</th>
<th>Linear range/μM</th>
<th>Detection limit/μM</th>
<th>Sensitivity</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>NiO nanoparticle-loaded carbon nanofiber</td>
<td>2–2500</td>
<td>1</td>
<td>3. μA mM−1</td>
<td>[27]</td>
</tr>
<tr>
<td>NiO/MWCNT/GCE</td>
<td>200–12,000</td>
<td>160</td>
<td>–</td>
<td>[28]</td>
</tr>
<tr>
<td>NiO hollow spheres</td>
<td>2–10</td>
<td>0.3</td>
<td>–</td>
<td>[29]</td>
</tr>
<tr>
<td>NiO spherical nanoparticles</td>
<td>1–110</td>
<td>0.16</td>
<td>55.9–66.0 μA mM−1 cm−2</td>
<td>[12]</td>
</tr>
<tr>
<td>Ni–Ti–O NTs</td>
<td>2–200</td>
<td>0.13</td>
<td>83 μA mM−1 cm−2</td>
<td>Present work</td>
</tr>
</tbody>
</table>
are compared with that of other Ni-based ones and the results are summarized in Table 1. Clearly, the electrode constructed of the Ni–Ti–O NTs exhibits wide linear range, low detection limit, and satisfactory sensitivity compared to those reported previously. The good performance of the proposed electrode may be attributed to its nanotubular structure with large specific area and fast electron transfer between the NT walls. Although the linear range cannot cover the glucose concentration in real blood, the Langmuir fitting equation based on the Langmuir isothermal theory can be adopted to fit the curve (Fig. 6B) to provide a wider range [25]. It is also expected by further optimizing the dimension, composition, and crystallinity of the Ni–Ti–O NTs, the electrocatalytic properties can be further improved.

Selectivity is very important for high-performance non-enzymatic glucose sensors because other electroactive biomolecules such as uric acid (UA) and ascorbic acid (AA) usually co-exist and interfere with the glucose detection. To analyze the roles of the electroactive species on glucose sensing, 0.1 mM UA and AA were added to the 0.1 M NaOH solution successively after injection of 1 mM glucose. As shown in Fig. 7A, the variation in the current is 47.5 μA upon addition of 1 mM glucose but for UA and AA, the values are 5.1 (11% added error) and 9.9 μA (21% added error), respectively. Since the glucose concentration we used is one fifth of that in normal blood (~5 mM), for real samples the added error for UA and AA should only be 2.2% and 4.2% respectively. The influence of chloride ions on the amperometric response of the electrode is shown in Fig. 7B and only a small current change is observed.

The reproducibility and stability of the Ni–Ti–O NTs are evaluated. The current response of the electrode to 1 mM glucose obtained from five independent measurements is 48.3, 54.8, 48.7, 45.5, and 50.6 μA, respectively with a standard deviation of 3.44 μA, thus indicating good reproducibility. After exposing the electrode to air for 30 days, the current still retains 98.2% of the original value therefore its stability is also confirmed.

Finally, to verify its workability for routine analysis, the sensor was applied to the determination of glucose in blood serum samples. 100 μl of the serum sample was added to 50 ml of the 0.1 M NaOH solution and the current value was recorded at 0.6 V. The results presented in Table 2 indicate that the data obtained from the proposed sensor are in good agreement with that obtained from the dry chemical method performed in a local hospital.

Compared to other techniques to fabricate Ni-based glucose sensors, the method reported here is very simple, low-cost, environmentally friendly, and reproducible thus boding for large-scale industrial production. Moreover, other functional elements such as Au, Pt, Pd, Cu, Co, and

Table 2

<table>
<thead>
<tr>
<th>Sample</th>
<th>Dry chemical method reported in a local hospital/mM</th>
<th>Proposed non-enzymatic method/mM</th>
<th>RSD/%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5.1</td>
<td>5.02 ± 0.13</td>
<td>2.6</td>
</tr>
<tr>
<td>2</td>
<td>5.4</td>
<td>5.30 ± 0.09</td>
<td>1.7</td>
</tr>
<tr>
<td>3</td>
<td>5.1</td>
<td>5.08 ± 0.22</td>
<td>4.3</td>
</tr>
</tbody>
</table>

* Triplicate analysis was performed for each sample.
so on usually used in non-enzymatic glucose detection can be alloyed with Ti to further increase the versatility of the technique.

4. Conclusion

Highly ordered Ni–Ti–O NTs are prepared by anodization of nearly equiatomic NiTi alloy. The materials show a low detection limit, satisfactory linear range, as well as good sensitivity and stability pertaining to non-enzymatic glucose detection. Optimizing the dimension, composition, and crystallinity of the Ni–Ti–O NTs may further enhance the electrocatalytic properties. The method reported here is simple, low-cost, environmentally-friendly, and reproducible thus boding well for commercial adoption and can easily be transferred to fabricate glucose sensors utilizing different catalysts.

Acknowledgments

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