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Dissolving Behavior and Stability of ZnO Wires in Biofluids: A Study on Biodegradability and Biocompatibility of ZnO Nanostructures**

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Fabrication of nanoscale biosensors based on nanowires (NWs),[1–5] nanotubes (NTs),[6–9] and other nanomaterials[10] has recently attracted enormous attention. In comparison to nanoparticles, 1D NWs and NTs have higher sensitivity because of depletion or accumulation of charge carriers at the surface that is caused by binding of charged biological macromolecules at the surface, and affects the entire cross-sectional conduction pathway.[4] Among all 1D nanomaterials, Si NWs and carbon NTs are the most studied materials as biosensors. Functionalized Si NWs and carbon NTs have been demonstrated for detecting proteins,[2] DNA and DNA sequence variations,[4] and cancer markers.[3] However, the biocompatibility and biodegradability of these nanostructures remain to be studied. For example, carbon NTs injected into human blood vessels might accumulate and occlude capillaries in the human brain, which could cause serious damage or be fatal.

Being a key functional material with versatile properties, such as dual semiconducting and piezoelectric properties, ZnO has important applications in optoelectronic devices, sensors, lasers, transducers, and photovoltaic devices.[11–13] In addition, the morphology[12,14–18] and the dopant concentration[19] of ZnO nanostructures can be well controlled by tuning the growth conditions, which further broadens their applications. ZnO nanoparticles are believed to be nontoxic, biosafe, and possibly biocompatible, and have been used in many applications in our daily life, such as drug carriers and cosmetics. However, no literature is available on the biodegradability and biocompatibility of ZnO nanowires or nanobelts, which is crucial for the application of ZnO nanostructure for biosensing.

In this paper, we present the first study on biodegradability and biocompatibility of ZnO wires. We have conducted a systematic study on the etching and dissolving behavior of ZnO NWs in various solutions with moderate pH values, including deionized water, ammonia, NaOH solution, and horse blood serum. The result shows that ZnO can be dissolved by deionized water (pH ≈ 4.5–5.0), ammonia (pH ≈ 7.0–7.1, 8.7–9.0) and NaOH solution (pH ≈ 7.0–7.1, 8.7–9.0). The study of the interaction of ZnO wires with horse blood serum shows that the ZnO wires can survive in the fluid for a few hours before they eventually degrade into mineral ions. The results of this study are of great significance. First, biosensors made of ZnO nonmaterial have a certain time to perform a device function. Secondly, once completing the corresponding service, the ZnO wires can eventually dissolve into ions that can be completely absorbed by the body and become part of the nutrition. The biodegradability and biocompatibility of ZnO NWs would allow their use for in vivo biosensing and biodetection.

Synthesized by a vapor–solid growth process,[12] the ZnO wires used in our study grew along the [0001] direction with a hexagonal cross section and were of high crystalline quality. We studied the dissolving behavior of ZnO wires in deionized water (pH ≈ 4.5–5.0), ammonia (pH ≈ 7.0–7.1, 8.7–9.0), NaOH solution (pH ≈ 7.0–7.1, 8.7–9.0), horse blood serum solution (pH ≈ 7.9–8.2), and pure horse blood serum (pH ≈ 8.5). The two kinds of ammonia used in our study were prepared by diluting concentrated ammonia with deionized water. The two kinds of NaOH solution were prepared by dissolving solid NaOH in deionized water, and the horse blood serum solution was prepared by diluting pure horse blood serum with NaOH solution (pH ≈ 7.0–7.1) with a volume ratio of 1:10.

We adopted two processes to investigate the dissolving behavior of a single ZnO wire in different liquids. To study the dissolving process of ZnO wires in deionized water, ammonia, and NaOH solution, we used Process 1 illustrated in Figure 1a. Individual ZnO NWs were firstly manipulated with a pin and placed on a silicon substrate. After that, a droplet of

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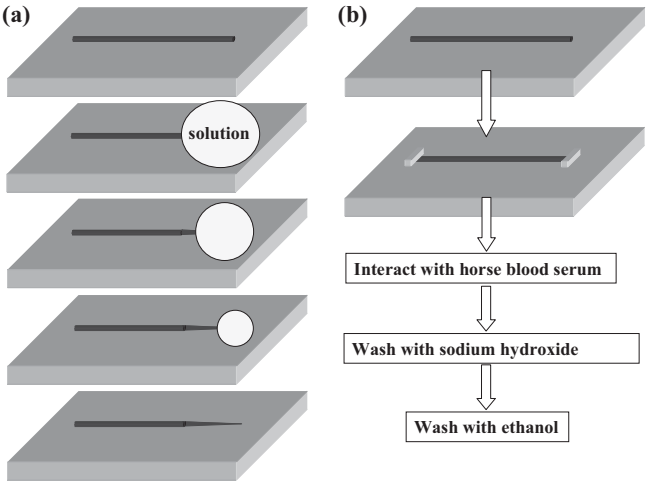

Figure 1. a) Procedure for studying the interaction of ZnO wires with deionized water, ammonia, and NaOH solution. b) Procedure for studying the interaction of ZnO wires with horse blood serum.

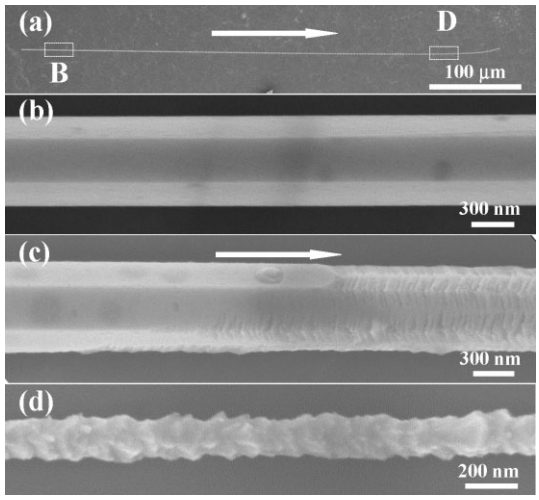

Figure 2. SEM images of an individual ZnO wire that has interacted with deionized water of pH ≈ 4.5–5.0. a) Low-magnification SEM image of the ZnO wire. b,c) High-magnification SEM images taken from the rectangular area B in (a) before and after interacting with deionized water, respectively. d) High-magnification image of the rectangular area D in (a) after about 30 min interaction.

the designated liquid was carefully dropped at one end of the ZnO wire. The size of the droplet gradually decreased as the solution evaporated slowly in air at room temperature. The center of the liquid droplet moved towards the end of the wire. Thus, the dissolving time increased towards the end of the wire, resulting in a time dependent dissolving process along its length. Normally, the liquid droplet completely evaporated in 30 min.

However, Process 1 could not be applied for studying the stability of the ZnO wires in horse blood serum because a layer of biological species is deposited on the surface of the wires as the horse blood serum dries. Therefore, an alternative approach (Process 2) was taken, as shown in Figure 1b. A ZnO wire was fixed onto a Si substrate with Pt metal on two ends deposited by focus ion beam (FIB) microscopy. The Si substrate and the ZnO wire were immersed in the designated liquid (ca. 5 mL) for a controlled time. Subsequently, the Si substrate was taken out and washed with NaOH solution (pH ≈ 7.0–7.1) and ethanol for ca. 1 min, respectively.

After each step, the morphology of the ZnO wires was examined by field emission scanning electron microscopy (FE-SEM: LEO 1530 FEG) and the results are presented in the following discussion.

We first show the result of an individual ZnO wire that had interacted with deionized water with pH ≈ 4.5–5.0. Figure 2a shows a low-magnification SEM image of a ZnO wire ca. 500 μm in length. The arrowhead indicates the direction that the droplet moved as it evaporated. This means that the right-hand side of the ZnO wire interacted longer with the deionized water than the left-hand side. The high-magnification SEM images in Figure 2b and c were taken from the area indicated by the rectangular area B in Figure 2a before and after interacting with deionized water, respectively. Figure 2b shows that the ZnO wire in this area has a diameter of 300 nm. The boundary at which the wire makes contact with the deionized water is presented in Figure 2c. This is clear evidence that ZnO wires can be slowly dissolved by water. The etching rate is higher at the edge, possibly due to higher local surface energy with the presence of dangling bonds.[20] Contact with deionized water for about 30 min resulted in an intensively etched ZnO wire with very rough and irregular surfaces, as shown in Figure 2d, which is a magnification of the rectangular area D in Figure 2a. In addition, the wire shape is not hexagonal anymore, indicating anisotropic etching around the wire.

To our knowledge, ZnO is poorly soluble in water. The deionized water used in our experiment had a pH ca. 4.5–5.0. Accordingly, the etching of the ZnO wire can be attributed to the chemical dissociation

$$ZnO(s) + 2H^+ \rightarrow Zn^{2+} + H_2O \quad (1)$$

where the Zn^{2+} ions are dissoluble.

The second liquid used in our study was ammonia. Figure 3 shows the SEM images of an individual ZnO wire partly interacting with ammonia of pH ≈ 8.7–9.0. Figure 3a is a low-magnification SEM image of a ZnO wire after contacting ammonia. The arrowhead illustrates that the left-hand side of the ZnO wire had a longer interaction time than the right-hand side. Figure 3b was taken from the rectangular area B in Figure 3a after interaction of the wire with ammonia, where the arrowhead indicates the direction along which the interaction time increased. Figure 3b reveals that the etching started from the edge of the ZnO wire and that the side flat surfaces were preserved at the initial stage of etching. The etching effect is enhanced with increased time. Figure 3c and d are high-magnification SEM images from the rectangular area C in Figur-

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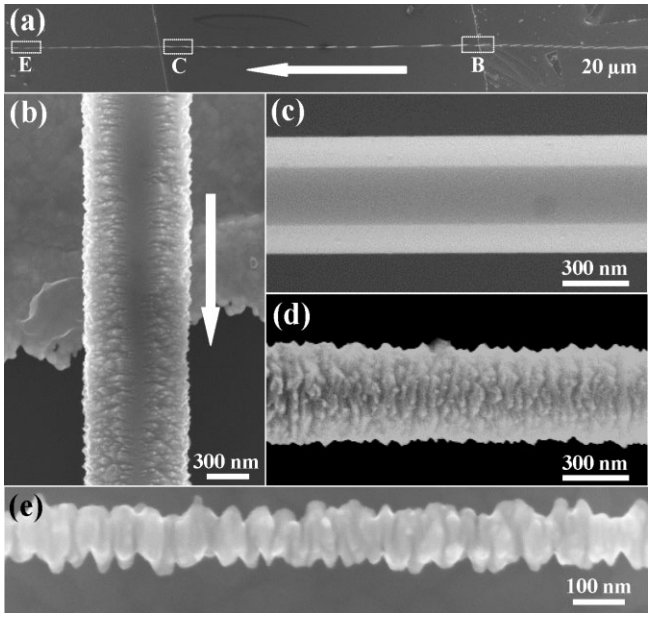

Figure 3. SEM images of a ZnO wire that has interacted with ammonia of pH ≈ 8.7–9.0. a) Low-magnification SEM image of the ZnO wire. b) High-magnification SEM image of the rectangular area B in (a) after interacting with ammonia. c,d) High-magnification SEM images taken from the rectangular area C in (a) before (c) and after (d) interacting with ammonia. e) High-magnification image of the rectangular area E in (a) after interacting with ammonia.

e 3a before and after interacting with ammonia, respectively. In comparison to area B shown in Figure 3b, area C was more intensively etched because of a longer interaction time. Figure 3e, taken from the rectangular area E in Figure 3a, shows that the surface morphology of the ZnO wire was totally changed and its width was quite small compared to the original size after 30 min of etching.

The etching of the ZnO wire by ammonia can be attributed to the following chemical reaction:

$$ZnO(s) + 4\,NH_3{\cdot}H_2O \rightarrow Zn(NH_3)_4^{2+} + 2\,OH^- + 3\,H_2O \qquad (2)$$

where $Zn(NH_3)_4^{2+}$ is soluble. In addition, we also studied the interaction of a ZnO wire with ammonia that has a lower pH of ca. 7.0–7.1. A similar etching effect was observed (Supporting Information) with less etching depth and a slower rate compared to that shown in Figure 3, which is expected because the ammonia with a lower pH has a lower concentration of $NH_3{\cdot}H_2O$.

NaOH solution of the same pH and the same etching time as that of ammonia has a slightly smaller etching effect on ZnO wires in comparison to ammonia. Figure 4a and b show the SEM images of the ZnO wires after interacting for ≈ 30 min with NaOH solution with pH of ≈ 7.0–7.1 and ≈ 8.7–9.0, respectively. Only the edges of the two ZnO wires were etched, and the etching

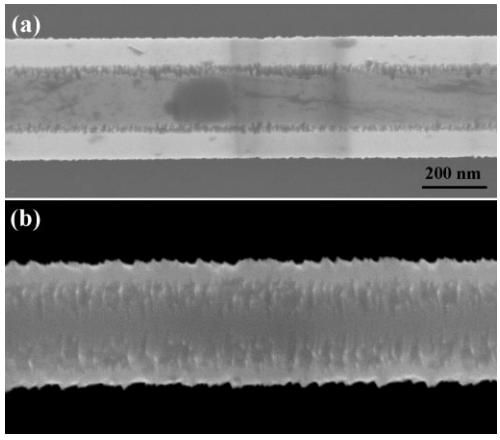

Figure 4. SEM images of a ZnO wire that has interacted with NaOH solution of a) pH ≈ 7.0–7.1 and b) pH ≈ 8.7–9.0.

depth was lower with the NaOH solution with a lower pH value. Because of the full solubility of ZnO_2^{2-}, the etching of the ZnO by NaOH solution can be attributed to the chemical process

$$ZnO(s) + 2\,OH^- \rightarrow ZnO_2^{2-} + H_2O. \qquad (3)$$

ZnO nanowires, nanobelts, and other nanostructures are important materials that have potential application as biosensors that are likely to interact directly with biological systems. In order to address the concern about the biodegradability and biocompatibility of ZnO in the human body, we first studied the solubility of ZnO wires in horse blood serum.

Figure 5a–f shows SEM images of a ZnO wire that has been dipped into horse blood serum diluted with 10 % aqueous NaOH (pH ≈ 7.9–8.2) for 0, 1, 3, 6, 8, and 11 h, respectively. After 1 h in the solution, the ZnO wire shows no visible etching on the surface except some adsorbed species (Fig. 5b). The etching became severe after 3 h of interaction as indicated by the reduced wire diameter. After etching for 11 h (Fig. 5f), ca. 94 % by volume of the ZnO wire was dissolved.

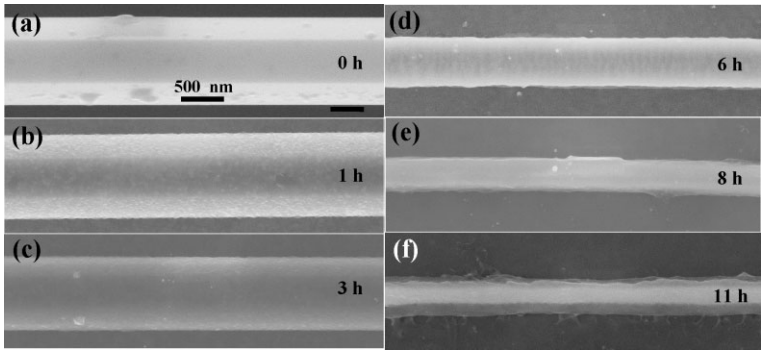

Figure 5. SEM images of a ZnO wire that has interacted with horse blood serum diluted in 10 % aqueous NaOH solution (pH ≈ 7.9–8.2) for different lengths of time. a–f) SEM images of the ZnO wire after 0, 1, 3, 6, 8, and 11 h in the blood solution, respectively. The scale bar in (a) is the same for (b–f).

We estimated that the ZnO wire would be totally etched by the horse blood serum in no more than 12 h.

We have also studied the interaction of ZnO wires with pure horse blood serum (pH ≈ 8.5), shown in Figure 6. Figure 6a–d shows the SEM images of a ZnO wire dipped in pure horse blood serum for 0, 1, 3 and 6 h, respectively, with the arrowhead indicating the same reference area after each stage of interaction. The ZnO wire immersed in horse blood serum was visibly etched in about one hour, and thereafter, the surface got even rougher.

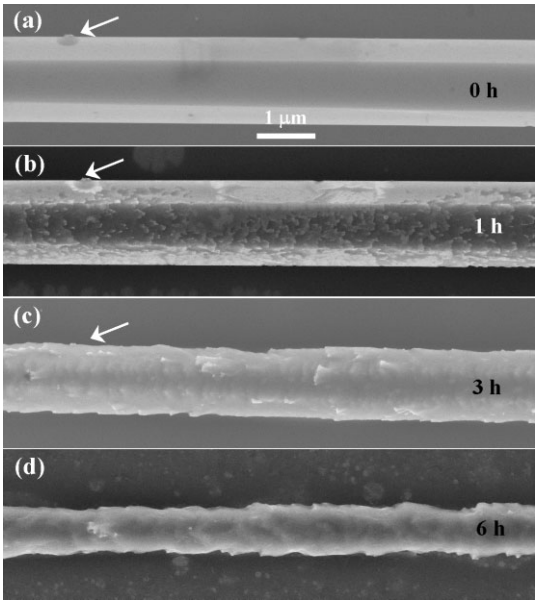

Figure 6. SEM images of a ZnO wire that has interacted with pure horse blood serum (pH ≈ 8.5) for different lengths of times. a–d) SEM images of the ZnO wire after 0, 1, 3, and 6 h in the blood solution, respectively, with the arrowhead indicating the same reference area. The scale bar in (a) is the same for (b–d).

In summary, we have systematically investigated the interaction of hexagonal ZnO wires with different solutions, including deionized water, ammonia, NaOH solution, and horse blood serum. The result shows that ZnO can be dissolved by deionized water (pH ≈ 4.5–5.0), ammonia (pH ≈ 7.0–7.1, 8.7–9.0) and NaOH solution (pH ≈ 7.0–7.1, 8.7–9.0). The etching process starts from the edge of the ZnO wires. The study of the interaction of ZnO wires with horse blood serum shows that the ZnO wires can survive in the fluid for a few hours, after which they degrade into mineral ions. The biodegradability and biocompatibility of ZnO wires could potentially allow their applications in in situ biosensing and biodetection. This will inspire a lot of research in the near future.

Studying the solubility of ZnO wires in biofluids has important implications for its applications in biomedical science. Firstly, ZnO has the potential to be used for biosensors, where it requires a reasonable time to function in biological systems and perform a device function. A "survival lifetime" of a few hours would be good. Secondly, if the ZnO wire is lost in the body or in a blood vessel, it can be dissolved by the biofluid into ions that can be absorbed by the body and become part of the nutrition without forming a blockage. Zn ions are needed by each one of us every day. Finally, the slow solubility and high compatibility of ZnO in biofluid is required for its applications in biology. The study presented in this paper sets the foundation for expanding the application of ZnO nanostructures in bioscience.

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