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Silicon-based Multi-nanowire Biosensor with High-k Dielectric and Stacked Oxide Sensing Membrane for Cardiac Troponin I Detection

Shih-Hsiang Shen\textsuperscript{b}, Hua Cheng\textsuperscript{a}, Tung-Yi Kao\textsuperscript{c}, Miin-Jang Chen\textsuperscript{c}, Chih-Ting Lin\textsuperscript{a, b}

\textsuperscript{a}Graduate Institute of Biomedical Electronics and Bioinformatics, National Taiwan University, Taipei, Taiwan
\textsuperscript{b}Graduate Institute of Electronics Engineering, National Taiwan University, Taipei, Taiwan
\textsuperscript{c}Department of Materials Science and Engineering, National Taiwan University, Taipei, Taiwan

Abstract

In order to diagnose acute myocardial infarction (AMI) quickly by detection of cTnI, silicon nanowire (Si-NW) transistor is chosen to be the bio-sensor. We demonstrate Si-NW biosensors coated with different dielectric materials to detect cTnI. Based on the experimental results of 14nm SiO\textsubscript{2} and 28nm SiO\textsubscript{2}, it is found that high capacitance dielectrics contribute better sensitivity than that of low capacitance dielectrics. In addition, high-k material dielectrics stacked with ultrathin SiO\textsubscript{2} sensing membrane structures are used for Al\textsubscript{2}O\textsubscript{3} and HfO\textsubscript{2} because SiO\textsubscript{2} has better compatibility with 3-Aminopropyltriethoxysilane (APTES). The results show that high-k stacked structure improve the sensitivity. Based on this work, the proposed Si-NW biosensor structure is experimentally demonstrates a good potential for future applications in cTnI detections.

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1. Introduction

Over years, cardiovascular diseases (CVDs) always be stated as one of major death causes in the world. AMI, also known as a heart attack, is the most severe one within different CVDs. As AMI happened, patient’s heart muscle fails to obtain enough oxygenated blood. This results in a death of patient. Nowadays, nanotechnology is being widely used in a numbers of biosensor investigations. Among them, Si-NW biosensors have potential to be detector of cTnI, which is a promising biomarker of AMI, with advantages of label-free, high accuracy and fast time responding. For more accuracy of diagnosis, it is required to increase sensitivity of Si-NW. Researchers have demonstrated improvements of pH-value sensitivity with high-k materials [1]. Because the capacitance of dielectrics is enhanced, the biomolecules on the surface can induce more potential changes in Si-NW. In this work, high-k materials (Al\textsubscript{2}O\textsubscript{3} and HfO\textsubscript{2}) are used to improve the sensitivity of Si-NW. However, while using Si-NW, surface
functionalization is important for biomolecules detection. To functionalize the Si-NW, APTES is used as cross-linker to the Si-NW surface. Based on fluorescent testing results, we found that compatibility to APTES of high-k materials is not as well as SiO₂ although the high-k materials contribute higher capacitance. Therefore, we proposed a stacked structure of high-k materials and an ultrathin SiO₂ to enhance cTnI sensibility in Si-NW biosensors.

2. Experimental

2.1. Device fabrication

The multi-channel Si-NW devices is manufactured on silicon-on-insulator (SOI) wafer with buried oxide (BOX) thickness 150nm and 100nm top single crystalline silicon. Devices is designed as Figure 1 by using conventional CMOS top-down method. Si-NW and source/drain (S/D) pad region are defined by e-beam lithography. Figure 1 shows the structure of device. After e-beam lithography process, reactive ion etching (RIE) was used to transfer the Si-NW pattern to silicon layer by CF₄. A UV lithography technique was employed to pattern S/D contact wires region. S/D contact wires with 20nm thickness Titanium and 60nm thickness gold were deposited by e-beam evaporator. Next, dielectric layer was deposited by atomic layer deposition (ALD). After deposition, a rapid thermal anneal (RTA) was used to anneal devices at 380°C in N₂ ambient for 5 minutes for better ohmic contact. To reduce leakage current of S/D contact wires, a passivation layer, e.g. photoresist layer, was utilized to cover devices. Finally, 7 um width of passivation layer was removed by lithography to generate a window for testing solution.

Fig. 1. (a) Schematic of device structure; (b) SEM photos of Si-NW; (c)TEM photo of dielectrics.

2.2. Experimental setup and measurement

For specific detection of cTnI, Si-NW surface has to be functionalized by conventional immobilization process [2]. To form amino group (-NH₂) on Si-NW surface, 2% APTES as cross-linker was added. Next, 2.5% Glutaraldehyde was utilized to generate aldehyde group (R-CHO). After that, Si-NW device was heated at 100°C for 5 minutes to remove residual water. After annealing, antibody of cTnI was added and preserved at 4°C for at least 12 hours. Next, antibody of cTnI was washed off by Phosphate Buffered Saline (PBS) solution. In order to eliminate noise from non-specific binding, BSA solution was added to cover unconnected functional group on Si-NW surface.

Si-NW devices’ characteristic, i.e. drain current versus back gate voltage (I_d-V_bg) curve, is measured by Agilent B1500A semiconductor analyzer. Figure 2 shows the experimental setup. Voltage from drain to source (V_ds) is biased at 1 V. Three concentrations of cTnI (320fM, 32pM and 3.2nM) is used in this experiments. First, the base I_d-V_bg curve is measured with 0.01x PBS solution (pH=7.4). Next, 320fM of cTnI is added and we waited 10 minutes for cTnI to link with antibody. After the 10 minutes waiting, unbinding cTnI were removed by PBS washing. Finally, we measured I_d-V_bg curve of 320 fM with PBS as an environmental solution. The I_d-V_bg curve of 32pM and 3.2nM are measured following the same steps above.
To examine immobilized efficiency of dielectrics’ surface, we performed a fluorescent measurement. Glass slides are respectively deposited with different material (HfO₂, Al₂O₃ and SiO₂). Antibody of cTnI is labelled with rhodamine. Labeled antibody is applied to glass slides by previous immobilization process. Fluorescent microscope is set as Figure 2. 16 bits fluorescent pictures are captured by camera with 6 seconds exposure time.

Fig. 2. Experimental setup: (a) electrical characteristic measurement and (b) fluorescence measurement.

3. Results and discussion

In this work, we chose Gm-max methods [3] to get our threshold voltage (V_{th}) from I_d-V_{bg} curve. In order to explain the V_{th} shifting effect, we write the V_{th} as:

\[ V_{th} = V_{FB} + 2\phi_B \cdot \{Q_d(2\phi_B/C_{OX}) + V_a \} \]  

(2)

Where first three term on right side is original V_{th} of a FET [3]. The V_a is the effective coupling electrical potential-induced threshold modification, which is a function of surface potential and capacitance of dielectrics. When applied cTnI protein to Si-NW surface, the surface potential changed. Surface potential depends on cTnI concentration, isoelectric (pI value) and environmental solution, which affects the Debye length. Carriers in silicon are attracted by surface potential and relate to capacitance of dielectrics. The V_a can be expressed as:

\[ V_a = [Q_d(\phi_s)/C_{OX}] \]  

(3)

\[ Q_d(\phi_s) \propto C_{Dielectric} \phi_s \]  

(4)

The I_d-V_{bg} curve apparently right shifts, which means V_{th} increases, with higher concentrations of cTnI are applied. We defined V_{th} shifting (\Delta V_{th}) as follow:

\[ \Delta V_{th}[Concentration] = V_{th}[Concentration] - V_{th}[PBS] \]  

(5)

Figure 4 shows the \Delta V_{th} of different dielectrics: 14nm Al₂O₃, 14nm/28nm SiO₂, and 10nm HfO₂. Device with 14nm SiO₂ dielectric has better sensitivity, which means larger V_{th} shifting. However, both HfO₂ dielectric device and Al₂O₃ dielectric device with higher capacitance show poor sensitivity than SiO₂ dielectric device. Based on Eq.3, we guess that high-k dielectrics have lower surface potential because less cTnI is connected. To verify our deduction, we conducted a fluorescent method to check amount of antibody on HfO₂, Al₂O₃ and SiO₂ film. Fluorescent photos are shown in Figure 3. According to fluorescent density difference, it is obviously that SiO₂ film can immobilize with most cTnI antibody. Therefore, the reason of sensitivity degradation is resulted from the fact that high-k materials are not compatible with APTES, which is the cross-linker in first steps of immobilization.
To overcome this problem, we stacked ultrathin SiO₂ layer as a sensing membrane by ALD on the top of high-k dielectric covered Si-NW devices. Figure 4 shows the testing results of high-k stacked with 1nm SiO₂ sensing membrane. Sensitivity of cTnI of stacked structure Si-NW device has apparent improvement compared to the Si-NW device without stacked structure.

4. Conclusion

In this paper, we demonstrate that sensitivity not only relates to capacitance but also surface potential. The result of Al₂O₃ and HfO₂ dielectric devices show lower sensitivity because of poor APTES immobilized efficiency is verified. Finally, we successfully improve the sensitivity of device with high-k dielectric by stacking ultrathin SiO₂ layer.

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