HIGHLY SENSITIVE DETECTION OF DNA WITH HNA DEFINED SILICON NANOWIRE FET

Li Dong and Xiaomei Yu*
National Key Laboratory of Science and Technology on Micro/Nano Fabrication, Institute of Microelectronics, Peking University
Beijing 100871, CHINA

ABSTRACT

We herein developed a simple method to process a silicon nanowire field-effect transistor (SiNW-FET) sensor by using HNA to define the nanowire and top-down fabrication method. Problems caused by the dry and TMAH etchings were effectively avoided, and the surface to volume ratio of the nanowire was increased by the HNA etching at the same time. After SiNWs were covalently modified with DNA probes, the detections on target Norovirus DNA were successfully realized with the concentration as low as 1fM and the respond time of a few seconds. The mismatch discrimination ability for single nucleotide polymorphism (SNP) detection was also experimentally certified. This work provides an efficient way for the DNA detection with mass manufacturing ability and potential compatibility with the conventional silicon industry, which definitely facilitate the practical applications.

KEYWORDS: Silicon nanowire, Field-effect transistor, HNA, Norovirous DNA, Surface to volume ratio

INTRODUCTION

Compared to the current cutting-edge techniques such as DNA microarrays, radio-tags and surface plasmon resonance, electronic detection allows integration of sensor arrays with data processing components (amplifiers, registers, analog-to-digital converters...), microfluidic integration and on-chip multiplexing, therefore has more practical applications. Silicon nanowire FET has the potential to function as an ideal biosensor with high selectivity and sensitivity, real-time response, and label-free detection capability. Methods fabricating SiNWs were proposed by combining electron-beam lithography with dry or TMAH wet etching [1-4]. The dry plasma etching will introduce defect, amorphization [1] and polymer layer to the SiNW sidewall, and therefore prevent the functionalization and decrease the sensitivity. On the other hand, it is relatively complicated to obtain SiNWs with the line-width smaller than 100nm by TMAH wet etching [2]. In this work, we developed a simple method to process a silicon nanowire field-effect transistor (SiNW-FET) by using HNA wet etching to define the nanowire. Our approach can avoid above problems and increased the sensitivity of the SiNW sensor.

DEVICE DESIGN AND FABRICARION

Fig 1 is a schematic figure of the FET device that includes source, drain, and gate electrodes. The function of the source and drain electrodes is to bridge the semiconductor channel made of SiNWs and the gate electrode is responsible for modulating the channel conductance. The silicon substrate is used as the back gate electrodes with contact hole opened on the top in this design. When the device works, the biological receptors are anchored to the surface of the SiNW by chemical modification to recognize the target analytes through their high specificity and strong binding affinity in the buffer environment. The target-receptor interaction then varies the surface potential of the semiconductor channel and modulated the channel conductance, and the signal is eventually collected by a detection system [5].

2×8 array of SiNW-FET was designed with the wire lengths varied from 7μm to 18μm and the widths to be 30nm~200nm respectively. P-type nanowires were used in these designs.

The fabrication processes of SiNW-FET are shown in Fig 2. Due to the sensitivity of SiNW-FET biosensor is significantly affected by the channel size, SIMOX SOI wafer with the device layer thickness of 30nm and buried oxide of 30nm~200nm respectively. P-type nanowires were used in these designs.

**Fig 1:** (a) Schematic representation of a SiNW-FET. (b) The separated parts of SiNW-FET device.
2d). E-beam lithography and RIE were used to transfer the nanowire pattern to the oxide layer which was used as a mask for the HNA etching. Different from TMAH, HNA (HF+HNO$_3$+CH$_3$COOH) is an isotropic wet etchant which etches silicon with high selectivity between higher and lower doped silicon, and the etching selectivity between them can up to 160:1. By using HNA with the volume ratio of 1:3:8, an etching rate of approximately 2-3 nm per seconds for the low doped active region (~$10^{15}$ cm$^{-3}$) can be obtained. SiNW with the wire width down to 27 nm were successfully fabricated by finely control the etching condition (Fig 2e). After the metallization for electrical connections (Fig 2f), 1μm thick photoresist was deposited and patterned via contact lithography (Fig 2g). The photoresist layer is used to isolate the metal layer during aqueous sensing experiments and prevent short circuit through the solution. Fig 3a is a microscope picture of the fabricated SiNW-FET and Fig 3b is a SEM photo of an enlarged nanowire with the width of 26.8nm.

![Fabrication processes of SiNW FET](image)

**Fig 2**: Fabrication processes of SiNW FET: (a) SOI wafer. (b)Deposition of SiO$_2$/Si$_3$N$_4$ layer. (c) Active region definition. (d) S/D definition. (e) SiNW fabricated by e-beam lithography and HNA etching. (f) Metallization. (g) Passivation layer deposition.

Before the detection on Norovirus DNA, 5’-carboxyl-modified DNA probes (receptors) were anchored to the amine of the (3-aminopropyl) triethoxysilane (APTES)-modified SiNWs, with the help of N-hydroxysuccinimide (NHS) and 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC). SiNW-FET array was firstly cleaned in 3:1 H$_2$SO$_4$/$H_2$O$_2$ to generate hydrophilic surfaces hydroxyl terminating the silicon-oxide surface. Then the SiNW-FET array was functionalized by exposing the surface to 2% ethanol solution of APTES overnight. After that, a self-assembled monolayer with terminal amino group was prepared by blowing the surface with nitrogen and heating at 110ºC for 10 min. Finally, 1 μM 5’-carboxyl-modified ssDNA was added to the surface of the nanowire by exposing nanowire to PBS solution with EDC and NHS solution for 2 hours. When a solution containing fully complementary target DNA was introduced, the hybridization process could be monitored in real time with this SiNW-FET sensor.

**RESULTS AND DISCUSSIONS**

The SiNW-FET was first characterized by measuring the $I_{DS}/V_{DS}$ curve with HP 4156B. As shown in Fig 4, the $I_{DS}/V_{DS}$ curves of the device, which yielded a typical n-type behavior, tend to saturation as the $V_{DS}$ increased. The device shows almost no electronic hysteresis indicating a small density of trapped charges inside the structure.

![Electrical characteristic of SiNW-FET](image)

**Fig 4**: Electrical characteristic of SiNW-FET. The Gate voltage varied from 0V to 20 V in 2 V steps.
The sensitivity of the SiNW-FET sensor was interrogated by challenging it with a series of concentrations of target DNA. Plots of source-drain current change versus time with target DNA at a series of concentrations (1 fM, 10 fM, 100 fM, 1 pM, 10 pM, and 1 nM) for probe DNA modified SiNW device are shown in Fig 5a. It is obvious that the nanosensor could reliably detect the target DNA down to 1 fM concentration with stronger and quicker response ($\Delta I/I_0=0.18$ for 1fM, $\Delta t=10$s) compared with others [2, 4].

We further evaluated the specificity of the SiNW-FET sensor by adding 100 pM noncognate and target DNAs to the sensor, Fig 5b is the contrast result. As shown in Fig 5b, the current change of introduction of a one-base mismatched DNA was significantly lower than that for 100 pM of fully complementary target DNA. This suggests that the SiNW-FET sensor possesses one-base mismatch discrimination ability for single nucleotide polymorphism (SNP) detection.

CONCLUSIONS

In order to improve the sensitivity and reliability of SiNW-FET sensor, we successfully developed a simple, CMOS compatible process for fabricating back-gated nanowire FET. This approach used the critical HNA wet etching step to define silicon nanowire, which can avoid the problems caused by the dry and TMAH etchings. The biosensor showed an ultrasensitive and rapid response for the Norovirus DNA by modifying DNA probe onto the SiNW surfaces. The results have demonstrated that this nanosensor can rapidly and sensitively detect as low as 1 fM Norovirus DNA, with the high specificity for one-base mismatch discrimination.

ACKNOWLEDGEMENTS

This work is funded by National Natural Science Foundation of China (founded No. 61275104, 90923028 and 60911130236).

REFERENCES


CONTACT
* Xiaomei Yu, yuxm@pku.edu.cn