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TECHNICAL PAPER

Detection of specific single-stranded DNA molecules through SiNW surface modulation

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Abstract This paper demonstrate a silicon nanowire biosensor for the detection of specific ssDNA biomarker detection. The biosensor was fabricated using conventional photolithography coupled with an inductively coupled plasma dry etching process. The detection was performed with a semiconductor parameter analyzer which measured the changes in current and conductance of the nanowire electrodes upon target DNA hybridization. The sensor surface was silanized and directly aminated with (3-aminopropyl) triethoxysilane to create a molecular binding chemistry for bio-functionalization. The resulting Si–O–Si-components were functionalized with receptor ssDNA, which interacted with the targeted ssDNA to create a field across the silicon nanowire and increase the current. Hybridization detection discrimination among various concentration, the device response to the targets shows selectivity for the ssDNA in a linear range from ssDNA concentrations of 100 pM to 150 nM. Linearity of the device to molecular concentration, was confirm linear fit curve for the (0.1–0.5) nM concentration and (0–40) nM concentration.

1 Introduction

Swift progress toward advanced nanotechnologies in nanomaterial and nanoelectronics, has been the principal back bone in inventing scientific instrument for applications of various form and degree (Torring and Gothelf 2013; Archana et al. 2014). Medical advancement using Nanotechnology will have wide variety of use over coming years (Petersen et al. 2014; Hu et al. 2014) and could save thousands of lives through early targeted disease detection and will be possible to detect virus, fungi at the first stage when the cell appear and with no risk or side effects (Wamakshi and Alka 2013; Chang et al. 2011). It is also possible to detect in a control manner in which specific disease is detected through detecting specific bio specie (Amit et al. 2013; Juan et al. 2013; Scott et al. 2013; Bhupinder (2014). The nano devices in nanosensor for deoxyribonucleic acid (DNA) identification it is a big development that will allow a platform for cheap, accurate, sensitive and fast detection of specific single-stranded DNA Molecules (Ryan et al. 2014; Aiping et al. 2013). The potential capability to detect specific molecule at an early stage in its clinical form is a viable alternative to the detection and quantification of DNA as it allows to respond to hybridization events by direct measurement of chemical changes that take place in the recognition layer following target binding (Matthew et al. 2014; Hasan et al. 2014). Nano engineered components that are designed into existing clinical diagnostic and detection platform have demonstrated improved sensitivity and specificity compared with traditional testing method have been the focus of many researchers (Mohan and Indira 2014; Eric et al. 2014; Lei et al. 2013; Zhang et al. 2013a, b). Nanowires is one of the nanobiosensors that have been used experimentally proved in the context of detection of specific biomolecule by many research communities among them our study which appears in Biosensors and Bioelectronics Adam and Hashim (2014). The sensor shows selectivity for the target ssDNA in a linear range from target ssDNA concentrations of 100 pM to 25 nM. As has been proved, with its excellent detection capabilities, this sensor platform is promising for detection of specific biomarkers

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Table 1 Shows two different types of ssDNA (Probe and Target)

ssDNA-Probe	(5′-CTG ATA GTA GAT TTG TGA TGA CCG TAG AAA/3ThioMC6-D/-3′)
DNA-Target	5′ CTA CGG TCA TCA CAA ATC TAC TAT CAG-3′

and other targeted proteins. The sensor interacted with the targeted ssDNA to create a field across the silicon nanowire and increase the current. The current work, present a study of detecting specific single-stranded DNA molecules. The direct electrical transduction when a target molecule comes in close contact with the receptor, due to the appearance of non-negligible partial charges in both the receptor and target molecules. This will activate the surface electrical charge of the functional layer, which affects the distribution of the electrostatic potential throughout the nanowire Adam and Hashim (2014). This in turn affects the conductance of the nanowire, and thus fluctuations in current can be detected when a voltage is applied at the appropriate terminals and the amount of current response depends on the concentration of the target molecules.

2 Materials and methods

A 5-inch *p*-type (100) silicon-on-insulator (SOI) wafer and a two-contact chrome mask (wire and pad) were used for device fabrication, we similar speciation used (Siti et al. 2013). The chemicals used were (3-aminopropyl)tri ethoxysilane (APTES), glutaraldehyde, ethanolamine, and phosphate buffered saline (PBS, pH 7.4). Were obtained from Sigma-Aldrich (M) Sdn Bhd and used without further purification. The most important chemical used here was APTES. Its chemical formula is $C_9H_23NO_3Si$, and its molecular weight of 221.37 g/mol. APTES is clear liquid with density of 0.946 g/mL at 25 °C. It was tightly sealed and stored in a dry and well-ventilated place prior to use.

A Keithley semiconductor parametric analyser (SPA) was used for analysis, and buffered-oxide-etcher was used to remove organic and inorganic contaminants with the standard cleaning procedure using RCA1 and RCA2. After fabrication of the device using conventional photolithography coupled with an inductively coupled plasma dry etching. A solid gold rod of diameter 1 mm and 1 cm length were used for the contact electrode and after the 40 and 100 nm Ti/Au were deposited on the fabricated nanowire based transducer with size of 500 μm × 300 μm using thermal evaporator model CHA-600 for the probing and, the surface modification follows, prior to probe DNA immobilization, the nanogap surfaces were cleaned with DI water and sulphuric acid (H_2SO_4). The silicon electrode surfaces were amine-functionalized using 2 % 3-aminopropyl triethoxysilane (APTES) (Sigma-Aldrich (M) Sdn. Bhd) mixed with 95 % ethanol and 5 % deionized water. APTES modification was done for 3 h, washed with ethanol for five times and dried under nitrogen flow.

Before the probe DNA being immobilized, the nanowire device was placed on a hotplate at 90 °C and 5 μL (APTES) were placed onto the wire active site and were incubated in a dry cabinet for 3 h for drying. The unbound particles were removed by mild washing with DI water and dried under a mild nitrogen flow. The whole procedure was repeated twice to increase the number of particles onto the nanowire surfaces this procedure was proposed by (Dhahi et al. 2013). This followed by dropping of 0.1–150 nM probe DNA onto the modified nanowire surfaces and was incubated for 2 h at 30 °C. The unbound probe washed with of phosphate buffer saline (PBS) for 3 times and the detection was conducted by dropping 0.1–150 nM of target ssDNA serially diluted and incubated for 2 h at 30 °C. The unbound targets were removed by three times washing steps with PBS buffer in interval of 15 min and nitrogen mild blow (Table 1).

3 Results and discussion

The electrical responses of silicon nanowire for the detection of specific DNA was reported by many researchers working in this field (Xie et al. 2012). The study used highly localized changes in the electrical potential during DNA translocation, the electrostatic potential that arises from charges on the analyte molecule during local change decays exponentially toward zero with distance and time and at this point is very easy to determine what happen at the instant of the two ssDNAs coming together to DNA translocation and the approach was also utilized by (Xie et al. 2012). The ~10 nm SiNW was fabricated using novel in-house approach is used for detection and hybridization of DNA. The wire size between two gold electrodes was trimmed to less than ~10-nm via shallow anisotropic etching si-ash-trimming approach which we developed in our lab for first time, the method is simple and required only 4 steps to reduced wire 1 μm to ~10 nm as shown in Fig. 1. The oxide was grown on the surface of the micro (1 μm) sized wire, which consumes 44 % of the micro (1 μm), and is later etched away by the buffered oxide etcher (BOD) Adam and Hashim (2014). The amount of silicon consumed depends on the total penetration of the oxide ions, which is limited by the movement of the oxygen through the oxide-silicon interface Adam and Hashim (2014).

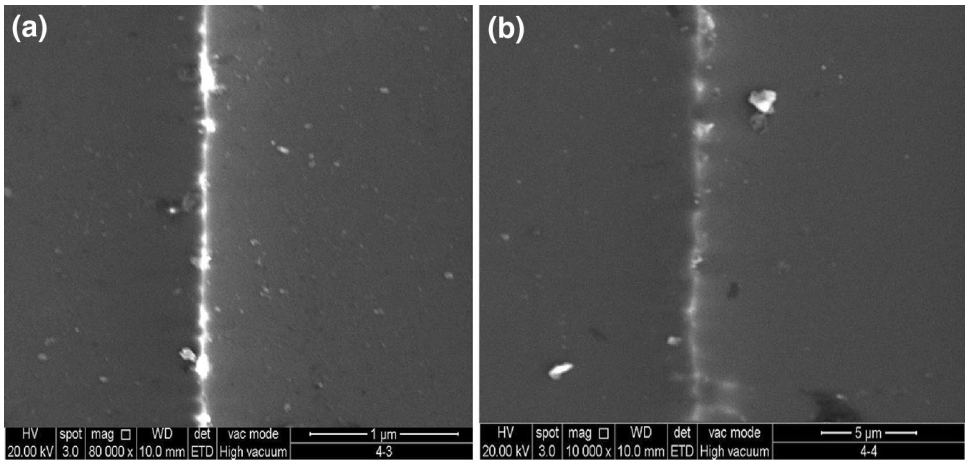

Fig. 1 Show nanowire **a** before trimming, **b** after trimming

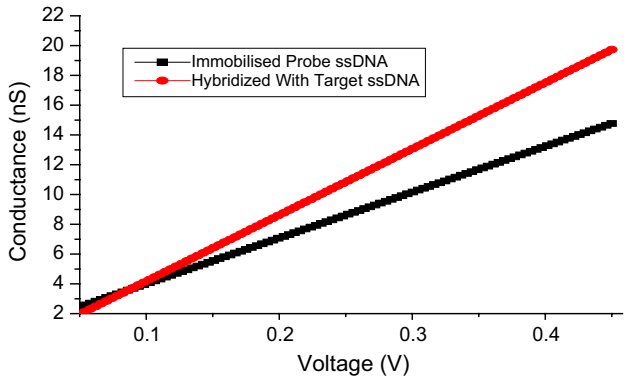

Fig. 2 The immobilization and hybridization graph showing different response for probe and target ssDNA

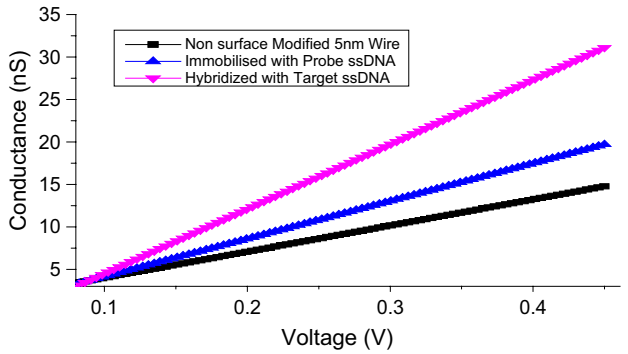

Fig. 3 The immobilization and hybridization graph showing different response for probe and target ssDNA

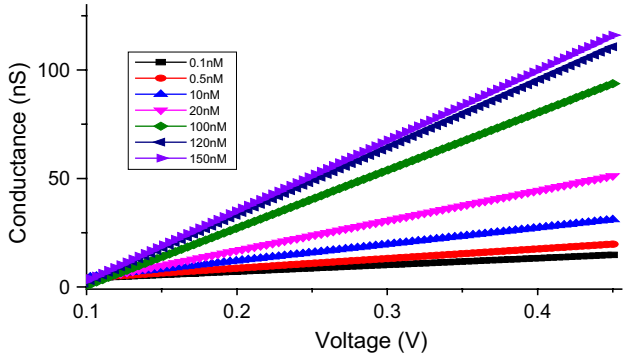

Fig. 4 The concentration response of SiNW showing different conductance level with concentration

The ion concentration at the Si/SiO_2 is related to the concentration of the oxide in the thermal evaporator and this has direct link with the degree of ion penetration, which in can used to control the rate of the ion penetration. The oxidation process is affected by number of factors relating to the number of oxidant species arriving at the interface per unit area to the thickness of SiO_2 grown on that same area if all oxidant species react with the substrate, the problem of these factors can be controlled by the suggestions offered in (Jung et al. 2014; Linsheng 2014). Amine-group with chemical formular $C_9H_23NO_3$ were used. The sensor surface was silanized and directly aminated with (3-amino propyl)triethoxysilane to create a molecular binding chemistry for biofunctionalization according Adam and Hashim (2014). The resulting Si–O–Si-components were functionalized with receptor ssDNA, which interacted with the targeted ssDNA to create a field across the silicon nanowire and this resulted increase the current being measured. This platform allow the manipulation electrons to passage through the electrical circuits.

The difference in conductance seen in Fig. 2 when the probe and target ssDNA was applied on the nanowire active site was for a reason associated with a change in counterion concentration upon hybridization, leads to a change in the conductance of the nanowire. This is due to the localized charge electrons to probe ssDNA cannot propagate through the ssDNA itself because its lack the ability of cationic charge interacting with the anionic backbone charge

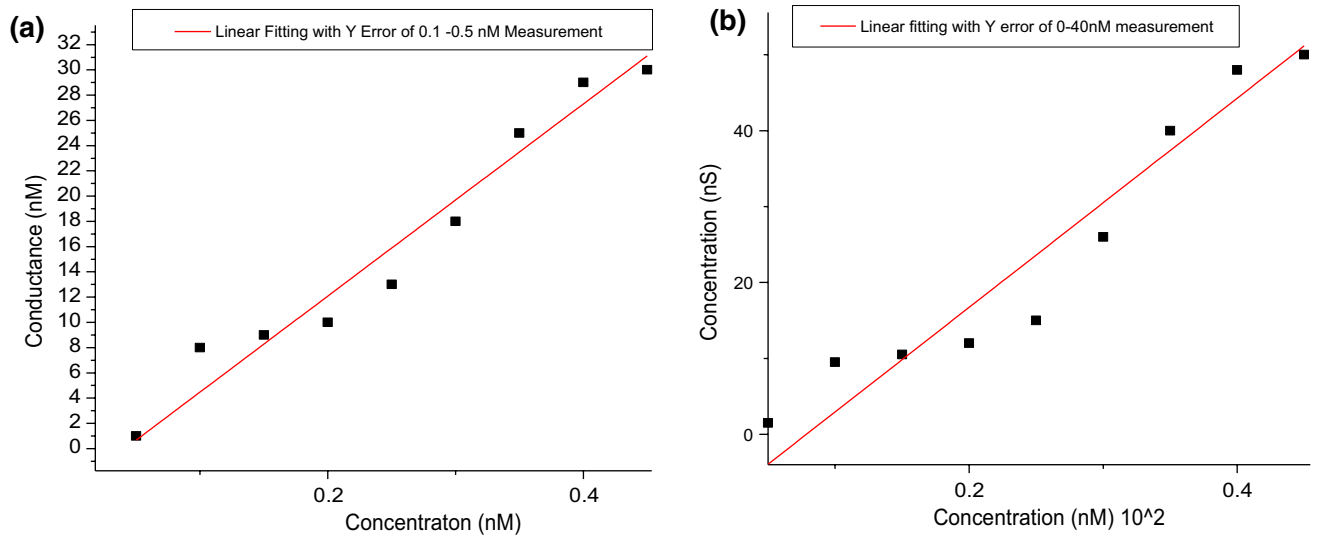

Fig. 5 The linear fitting curve for the **a** (0.1–0.5) concentration, **b** (0–40) concentration

of DNA Carmona-Ribeiro and de Melo Carrasco (2013). However, the conductance was significantly increased with the hybridization of ssDNA targets that constituted the double-stranded DNA which can allow the formation of local electric field charges that will modulate the nanowire surface upon application of electric voltage at the two terminal of the sensor, this can be seen in Fig. 3 with pink line curve.

Figure 4 showing the device response to concentration from 150 nM to 0.1 nm and this due to the large surface area of the silicon nanowires and it response are linear and this means that it achieves a far higher mass per area sensitivity than other types of sensor, the nanowire surface phenomena is formed by attraction of carriers to the it surface, and the current drawn through the nanowire is nearly a constant independent of voltage applied. However, near the two electrodes, the nanowire and two electrodes, and molecular interaction determine the electric field pattern. Thus, carriers flow in a subsurface pattern made possible because the electrode and the molecule interaction both control the current. In Fig. 4, the conductance measured increasing and initially it weaker with 0.1 nM and this indicate the device sensing limit and when the higher concentration introduced, the magnitude of the current extends further, this might be due to uninverted region, shortening the length of the surface layer by layer region mobile carriers inside the nanowire and the effect can be classified as wire-surface modulation. Because resistance is proportional to wire surface, shortening the surface contact in layer by layer decreases its resistance, causing an increase in current with increase in molecular interaction.

To confirm the linearity of the device to molecular concentration, linear fitting curve for the (0.1–0.5) concentration and (0–40) concentration were taken as can be seen in Fig. 5a, b The changes of wire conductance properties during hybridization were observed nanowire surface area is the sensitive medium able to respond to the changes in the ion concentration in the present of the dipoles in response to the changing of the electric field applied. At low concentration, the scope for interaction of the dipole is very low because of the interval time need to react between ions. At the higher concentration, the mean interval time is minute which allow rapid ions interaction of the dipoles, producing stronger signals. The line fit in Fig. 5a showing the sensor response to the 0.1 nM concentration to 0.5 nM concentration and the fitting is very good indicating the sensor ability to response to concentration difference with ~90 % accuracy and similar trend can be seen in Fig. 5b for higher concentration measurement conducted. With the above proves, we are confident that this proposed device could use for detecting a specific biomarker and has the potential to use in medical diagnostic for specific disease. However, for the clinical application, the device further validation and optimization are required before using in a real clinical environment.

4 Conclusions

The study described detection of specific single-stranded DNA Molecules. The sensor based on silicon-nanowire devices, its detection capabilities was examine by the hybridization event which lead identification through measuring the changes in conductivity and current. The method explored only change in sensor electrical properties, thus, does not need any labeling steps. The proposed device may enable new routes to low concentration detection of

biomatter. Electrochemical modulated signal are attractive for biosensing as their response depend very sensitively on changes to their mass, allowing them to detect the tiny masses associated with DNA and small molecules. This enables specific and single molecule detection, while the large surface area of the silicon nanowires means that it achieves a far higher mass per area sensitivity than other types of sensor. This makes it a promising system for biosensors involving solutions with low concentrations of material, such as DNA or proteins.

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