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DNA biosensing using Ga_2O_3 based metal/oxide diode

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Abstract

We propose for the first time, DNA functionalization on a single-crystal β-Ga_2O_3 substrate and the detection of this surface modification through an electrolytically interfaced metal/Ga_2O_3 diode. DNA stabilization on the oxide surface increases resistivity causing a reduction in the diode current. Good selectivity and sensitivity are also reported.

1. Introduction

Ga_2O_3, a transparent conducting oxide, has great potential to be used in future device technologies owing to its technologically important properties such as large band gap, visible light transmittance, chemical stability, and good electrical conductivity [1]. Single-crystal Ga_2O_3 based transistor was reported [2] that exhibited excellent characteristics such as very low leakage current and the fabrication of a Ga_2O_3 based Schottky barrier diode [3] was demonstrated showing the strong potential of Ga_2O_3 for future applications. However, there have been no previous reports of using a single-crystal semiconductor oxide surface for biosensing. There are reports of using other transparent semiconductor oxide (such as doped SnO_2 and InO_2) in similar applications through the deposition of thin oxide films on the glass substrates for preparing sensing electrodes. But the usage of the glass as base material might hinder the development of integrated electrical biosensors. Moreover, the transparency of Ga_2O_3 in deep UV makes it advantageous for use in both electrical sensing and UV adsorption spectroscopy, which can't be realized using other conventional oxide based electrodes.

Here we report the functionalization of a single-crystal Ga_2O_3 surface for DNA sensing and its simple and straightforward electrical detection which indicates the possibility of developing future Ga_2O_3 based electro-biosensing device.

2. Methods

Fabrication

The surface of a Ga_2O_3 substrate was cleaned (Fig.1) with H_2SO_4:H_2O_2. Incubation of the substrate for 2hrs in 4M NaOH was followed by UV treatment to increase the number of –OH groups. The substrate was then left in 0.01M 3-aminopropyl-triethoxysilane (APTES) solution for 1hr at 90ºC. The APTES-modified surface was then incubated in 0.01M 6-maleimidocaproic acid N-hydroxysuccinimide ester (EMCS) which acts as a binder (Fig. 2) between the -NH2 termination of APTES and the thiol connection of the probe DNA. 10µM capture probe DNA was applied to this surface at 40ºC which was then treated with 6-mercepto-1hexanol (MCH) to avoid nonspecificity. 1µM complementary DNA was supplied at a high temperature (70ºC) for hybridization.

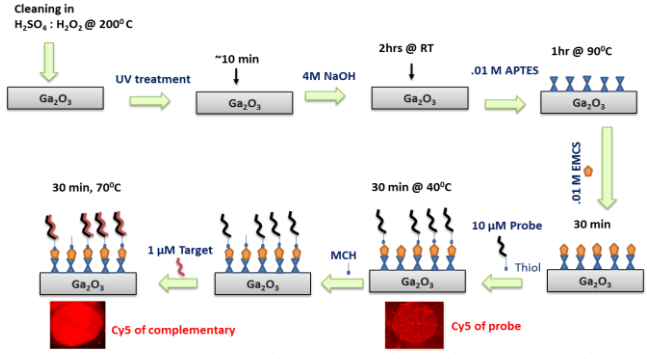

Fig. 1 Functionalization of Ga_2O_3 surface for DNA sensing. The inset shows the confirmation of functionalization through Cy5 tags.

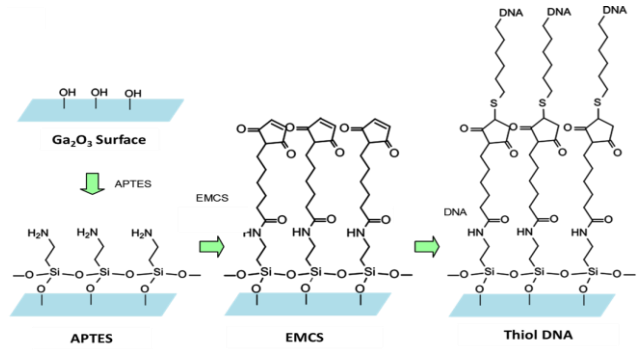

Fig. 2 Detailed chemical structure of DNA binding on Ga_2O_3.

Detection

An ohmic contact was formed on the unused Ga_2O_3 surface through the sputtering of Ti (~30 nm) and Au (~200 nm) followed by oxygen plasma treatment to increase conductivity. A Ag/AgCl electrode acts as a floating type metal contact and there are electrolytic solutions between the electrode and the sensing oxide surface, forming a Schottky type diode (Fig. 3a) interfaced with an electrolytic barrier. The total barrier impedance, which mainly comprises the contributions from the solution resistance and double-layer capacitance, can be controlled through surface modification by DNA. The measured diode current or the shift in the potential drop can thus be used for DNA detection making it a very simple DNA sensor.

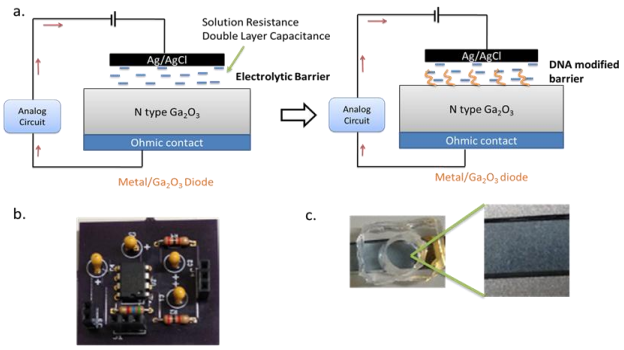

Fig. 3 a. DNA detection through electrolytically interfaced metal/Ga_2O_3 diode. b. small sensing circuit c. sensing area surrounded by PDMS wall. The inset shows the transparent Ga_2O_3 sensing surface.

3. Experiment

Different concentrations of capture probe DNA (10μM - 0.01μM) were used throughout the experiments. The target and nontarget DNA used both had concentrations of 1μM. The capture probe, target and nontarget DNA all consisted of 30 base pairs. All measurements were carried out in 1×PBS buffer solution, which also acted as an electrolytic barrier in the diode-type measurement.

4. Results and Discussion

Figure 4 shows details of the observation of the functionalization through the measurement of current in each step. After the blank surface was modified by APTES, the sensed current decreased slightly owing to the covering of the active sensing sites by the APTES. It is notable that this reduction in current flow was not as significant as that when capture probe DNA (ssDNA) was immobilized. The negative electrical charges present in ssDNA further increased the resistivity of the surface, decreasing the current. A further shift in the current was observed after the surface was incubated in MCH which was mainly used for blocking the sites unused by the ssDNA. The shift observed after MCH incubation confirms the availability of unused sites.

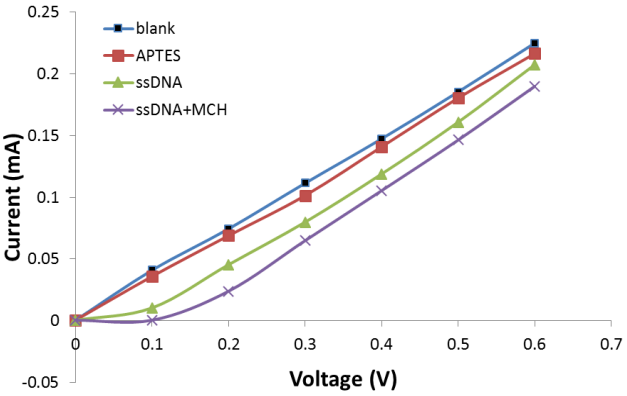

Fig. 4 Surface functionalization with APTES, ssDNA, and MCH observed through shift in current measured after each modification.

Figure 5 shows the contributions of each of the surface modifications to the average relative resistivity of the surface. The relative resistivity was calculated using the eq. (1) and (2),

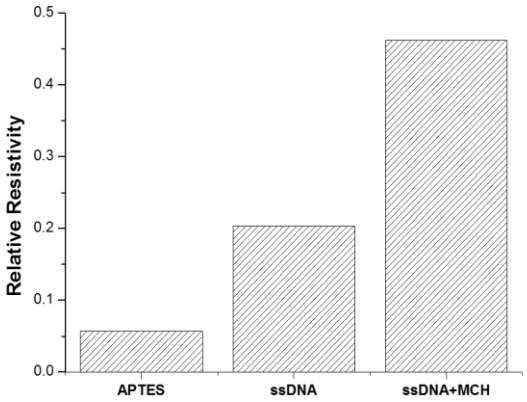

Fig. 5 contribution of each of the surface modifications to the relative resistivity. Each modification increased the resistivity on the functionalized surface.

$$R_a = \frac{V}{I_a} \quad (1)$$

$$R_r = \frac{R_a - R_0}{R_0} \quad (2)$$

where V is the applied voltage, I_a and R_a are the measured current and the calculated resistance respectively of APTES, ssDNA or ssDNA+MCH, R_r is relative resistivity, R_0 is the calculated resistance of the blank surface.

Figure 6 shows the sensitivity achieved for the detection of 1μM target DNA using a low capture probe DNA of 0.01μM. Figure 7 plots the selectivity for the detection of target and nontarget DNA of 1μM concentration. The potential shift was monitored with the sensor biased at 0.5 - 1.5V.

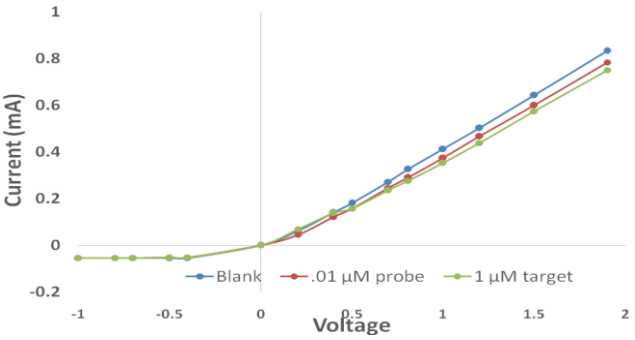

Fig. 6 Current measured on blank Ga_2O_3 surface, after modification with 0.01μM capture probe DNA and after capture probe DNA was hybridized with 1μM complementary DNA.

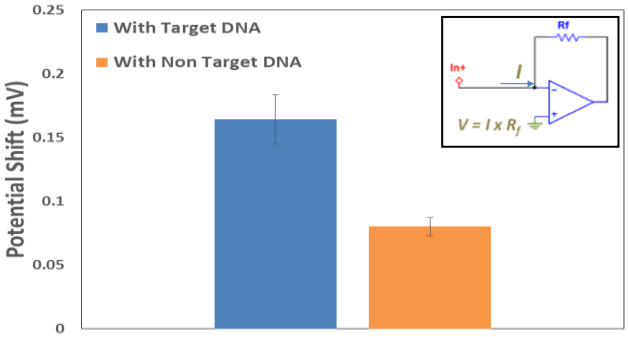

Fig. 7 Average potential shift from immobilization to hybridization for target/non-target DNA. The potential was measured by applying the sensed current to a resistance (inset)

5. Conclusions

We have successfully functionalized a single-crystal Ga_2O_3 surface with capture probe and target DNA. The electrical detection of this surface modification was carried out by an inexpensive method using a metal/oxide-type diode interfaced with an electrolytic barrier. A target sensitivity of 1μM was achieved using only 10 nM capture probe DNA and an approximately 2-fold potential shift was observed upon hybridization with target DNA compared with that for nontarget DNA. The sensing mechanism and ability demonstrated in this study indicate the potential use of Ga_2O_3 surfaces as biosensors and the possible development of Ga_2O_3 based integrated bioelectronics in future.

References

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[2] Masataka Higashiwaki *et al*, Applied Physics Letters **100**, (2012) 013504

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