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Lethal Disease Discrimination Using Silicon Nanowire-Based Field-Effect Transistors

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Abstract:
We present a sensor chip with an array of silicon nanowire-based field-effect transistors, biofunctionalized with different antibodies for multiplexed biosensing. The fabrication is done following a reproducible top-down process, defining honeycomb-shaped nanowires for an enhanced sensing area and an improved mechanical stability. A covalent immobilization of the antibodies provides a strong stability of the bioreceptors. The demonstration is done by discriminating Ebola virus VP40 matrix protein from Cholera toxin B subunit and Staphylococcal enterotoxin B. The array shows a high sensitivity by responding to femtomolar concentrations, and allowing to distinguish a lethal disease from others showing similar initial symptoms. Such device would allow performing early diagnosis to prevent a fast spreading of the diseases.

Key words: silicon nanowires, honeycomb nanowires, field effect transistors, multiplexed biosensor, disease diagnostics.

Introduction

Multiplexed detection of several diseases or toxins within a single chip would be helpful to distinguish the presence of a suspicious lethal infection from others. Silicon nanowire-based field-effect transistors (FETs) are ideal candidates with mass production compatibility, easy biofunctionalization and sensitivity high enough for an early diagnosis [1]. More specifically, honeycomb-shaped nanowires have shown an excellent biosensing performance [2] due to their large sensing area. They have already been demonstrated for the discrimination of Ebola biomarker from others causing similar initial symptoms. Yet, the differential functionalization in a nanosensor array for the simultaneous detection of various diseases was not achieved.

Here, we propose an ultrasensitive array with honeycomb-nanowire FETs with specific bioreceptors for three disease indicators, namely Staphylococcal enterotoxin B (SEB), subunit B of Cholera toxin, and VP40 matrix protein from Ebola virus, all of them showing similar initial symptoms such as diarrhea, vomits, and fever. The FETs exhibit detection capabilities in femtomolar concentrations, and can be operated simultaneously when analyzing the sample for disease discrimination.

Design, fabrication and biofunctionalization

The 50 nm wide nanowires were defined in a honeycomb shape by electron-beam lithography, providing a high device-to-device reproducibility. Stacked Al_2O_3 (10 nm) and SiO_2 (2 nm) were deposited as high-k dielectric layer with a hydroxyl rich surface for biofunctionalization. Silver electrodes served as source and drain contacts, passivated with 500 nm SiO_2. A third silver terminal electrochemically modified with an AgCl layer was left exposed as reference electrode. The overall chip (Figure 1a) contained 16 n-type FETs in a 4 cm^2 space, with an ON/OFF ratio of 10^4 and a subthreshold swing of 370 mV/dec (Figure 1b) where current increases upon gate activation (Figure 1c). They were conveniently aligned for the integration of a microfluidic channel.

Antibodies against the three analytes were covalently immobilized on the nanowires through silane and carbodiimide chemistry, followed by a surface blocking using bovine serum albumin. The ready-to-use chips were kept in phosphate buffered saline (pH 7.4) at 4 °C until their use.

Results

The biosensing response was measured during analyte injection in 5 mM sodium phosphate buffer (pH 7.0) by continuously sweeping the gate voltage along the subthreshold regime and monitoring the threshold voltage (V_t) shift in real time. The results for each of the analytes is shown in Figure 2. All of them were detected in fM range with saturation at lower pM levels. Concentrations as low as 70 fM, 28 fM, and 42 fM could be sensed for SEB, VP40 and Cholera toxin respectively.

Conclusions

A highly sensitive multiplexing biosensor has been developed allowing to discriminate between lethal disease caused by Ebola virus and others with similar initial symptoms caused by Cholera toxin and SEB. The hereby presented device relies on silicon technology allowing its mass production for early and label free diagnosis, helping in the prevention of disease spreading.

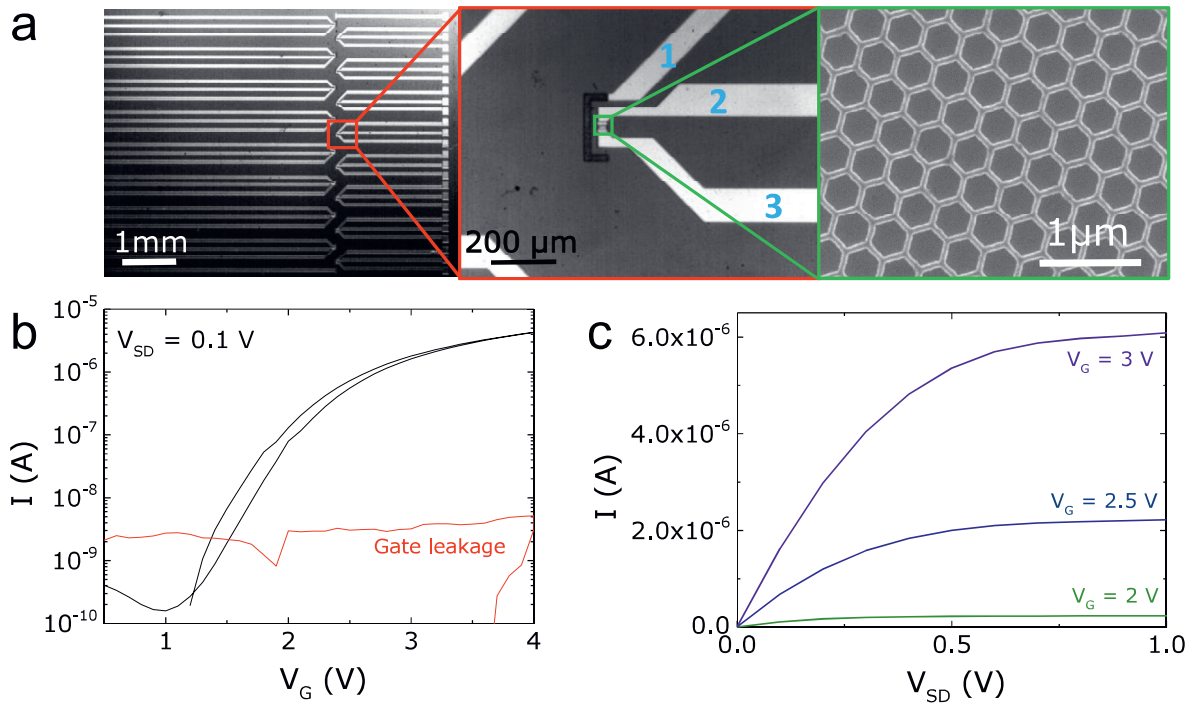

Fig.1.Array of FETs containing reference (1), source (2) and drain (3) electrodes. Next magnification shows scanning electron microscopy of honeycomb nanowires. (b) Transfer and (c) output characteristics of the FETs.

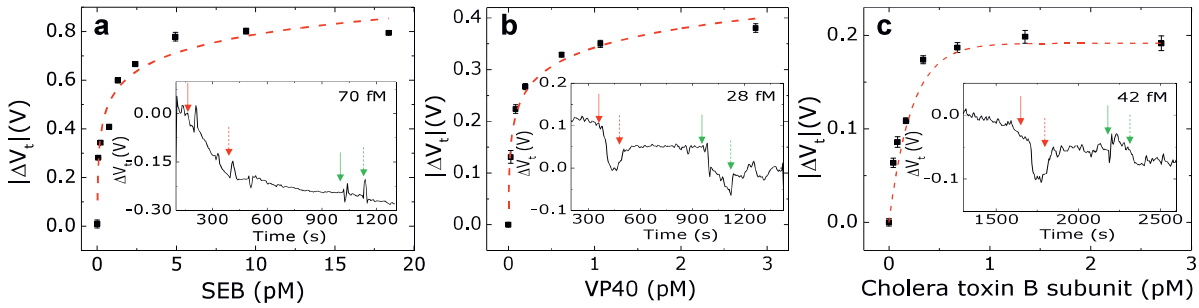

Fig.2.Biosensing response for (a) SEB, (b) VP40, and (c) Cholera toxin B subunit. Insets show real-time V_t shift for the smallest tested concentrations. Red and green arrows indicate sample and buffer manipulation respectively (straight arrow for injection and dashed arrow for stop of flow).

References

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