3RD ARTICLE

Silicon Nanowires/ Nanoribbons for label-Free Electrical Detection Of Biomolecules

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ABSTRACT

Silicon nanowires/nanoribbons (SiNW/SiNR) offer a highly sensitive and label free detection principle for biochemical applications, such as DNA and protein detection. The technique has potential both for low concentration detection as well as in scaling down the size of complete analysis systems required for rapid on-site applications. The sensor function is similar to that of a MOSFET transistor where the current passing from source to drain is dependent on the gate voltage. For SiNW/SiNR this current is dependent on the surface charges of the thin wire. When charged molecules are present at the surface, the conductance of the SiNW/SiNR is affected which is detected as a change in the drain current. Us-

ing localized functionalizion of individual SiNW/SiNR with antibodies and DNA probes and a multiplexed readout system, we can simultaneously detect different target molecules. We have demonstrated both DNA and protein detection using SiNW/SiNR. Combining the sensor system with a microfluidic delivery system, the sample volume can be minimized in order to take full advantage of the potentially very high detection sensitivity. The SiNW/SiNR are fabricated using standard CMOS technology which together with the label free electrical detection method enables mass production of fast, reproducible and low cost devices for disposable uses.

GENERAL INTRODUCTION

There is an increasing demand for portable sensor systems in health care at local medicare centers, in ambulances or even at home for diagnosis of various biomarkers. On-site analysis is also important for environmental control, in food production, security checkpoints and industrial bio-processing. Another area with growing interest is the development of high sensitivity measurement for low copy analysis, even on single cell level. Diagnosis of circulating tumor cells (CTCs) in the blood is one example where analyses on individual cells are highly desired.

Detection of specific biomolecules is usually based on the capture of target molecule to a complementary receptor molecule. Measurement can then be done by binding a fluorescent, radioactive or electrochemical label molecule. These methods are well established, but have the drawback that they require several preparation steps, and special laboratories. Label-less detection can be achieved optically by monitoring change in refractive index with Surface Plasmon Resonance (SPR) or mechanically by measuring change in resonance frequency due to mass change with Quartz Micro Balance (QCM). The sensitivity is however limited and advanced equipment is required and difficult to scale down.

Silicon nanowire/nanoribbon field-effect transistors (SiNW/NR)

Silicon nanowire/nanoribbon field-effect transistors (SiNW/NR) functionalized with receptor molecules offer a highly sensitive and label-free detection scheme for biochemical applications. Electronic systems can not only easily be downscaled but also simplify the complete analysis systems. Thus, SiNW/NRs show great potential as an electrical sensor in effectively providing rapid on-site detection to avoid costly laboratory analyses.

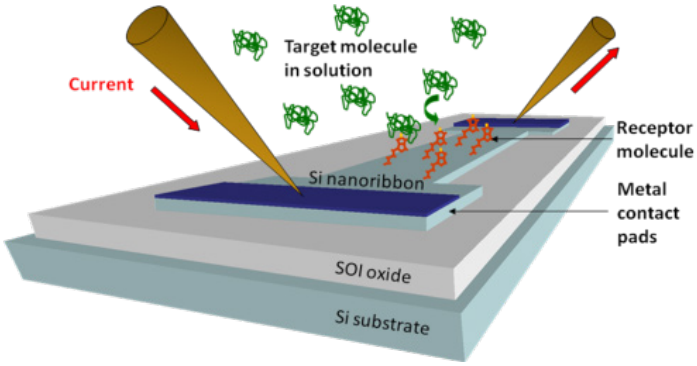

Figure 1. Three-dimensional sketch and the detection principle. Binding of target molecules induce charge changes on the surface affecting the conductance of the SiNW/NR.

The sensing function is similar to that of an ordinary MOSFET where the drain current is dependent on the gate voltage. For a SiNW/NR sensor, the drain current is sensitive to the surface charge variations. Charged molecules present at the surface will affect the conductance of the SiNW/NR which can be detected as a change in channel current. Functionalization of the SiNW/NR with i.e. antibodies activates the sensor for detection of specific target molecules (Fig. 1). Acting like a gate in a MOS transistor, this provides an internal gain mechanism and a very high sensitivity approaching the femto-molar (10^{-15}M) range has been demonstrated [1]. Indeed, for a model system (biotin/streptavidin) with high affinity, we have demon¬strated a sensitivity approaching $6x10^{-13}$M, corresponding to ~20 target molecules (referring to the ~1 μm^2 surface area of the nanowire) [2]. Thus the SINW/NRs are also a very interesting for high sensitivity measurements. Lately, it has also been demonstrated that SiNWs can be used for kinetic data evaluation of for instance a protein-DNA binding pair [3].

The first demonstrations of biomolecule sensing used nanowires fabricated by gas phase epitaxy [4, 5] or nanowires defined in the top layer of SOI (silicon on insulator) wafers using a nano-lithographic step [6, 7]. In our approach, however, electron beam lithography can be replaced by ordinary photolithography, provided that the top silicon layer is thinned to about 30 – 50 nm [2, 8]. The resulting nanoribbon technology (Fig. 2) is fully CMOS compatible and provides for inexpen¬sive manufacturing of chips enabling disposable use.

By integrating the SiNW/NR sensors with a microfluidic delivery system (Fig. 2), the sample volume and the molecule diffusion length can be minimized so that fast response can be achieved. Using multiple nanowires functionalized with different antibodies, several different target molecules can be detected simultaneously. The fabrication process also takes advantage of the high alignment accuracy provided by MEMS technology enabling well defined fluidic channels that can be connected to the macro world by using standard interfaces.

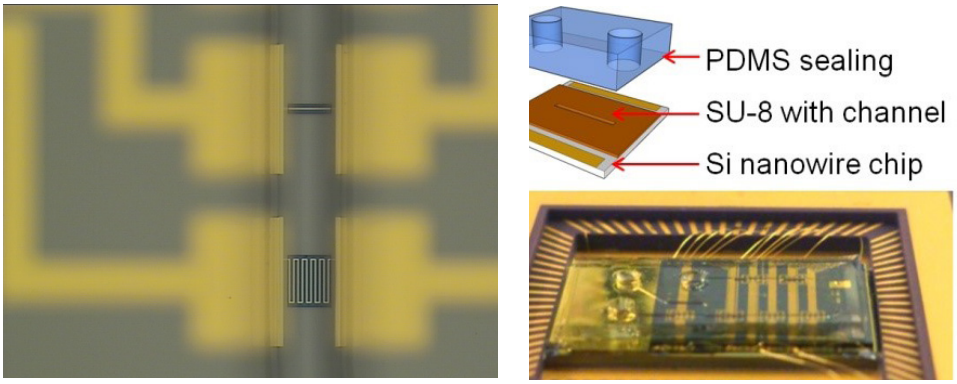

Figure 2. (Left) Optical micrograph of two SiNR geometries having sizes of 33nm×1μm×50μm respectively 33nm×500μm×1μm. (Right) Experimental arrangement for real-time electrical measurements with a microfluidic system integrated on the wirebonded chip.

RESULT AND DISCUSSION

For proof-of-concept, the sensor device and microfluidic system are first tested using pH measurement to detect the interaction between hydrogen ions and the SiO2 surface or APTES functionalized surfaces, see Fig. 3. The sensor surface is functionalized by silane reagents (e.g. the APTES) in order to introduce amino groups that can be further derivatized with chemical reagents to produce an activated surface. The capture reagents required for sensing of specific biomolecules are then covalently coupled to the functionalized silicon surface. Successful detection of biomolecules has been carried out. We have i.e. demonstrated biotin/streptavidin detection using our sensor chips [2], and are currently studying parallel detection of different biomolecules such as DNA and proteins. As the detection principle is generic, the nanowire sensors can be adapted to detecting contaminants, bacteria, drugs or other specimens.

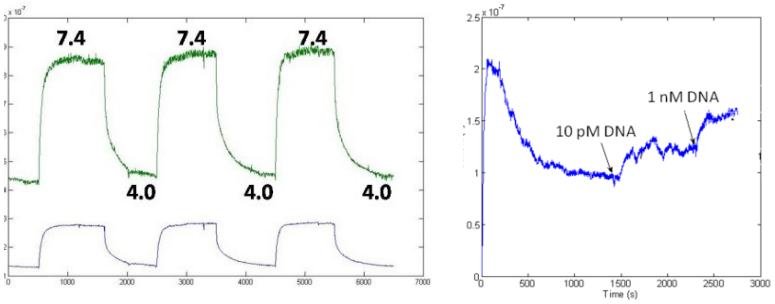

Figure 3. (Left) real-time pH measurements using two SiNR devices with different widths to follow the source-drain current (IDS) when the pH value was changed between 7,4 and 4,0. (Right) Example of current (IDS) measurement of a functionalized SiNR reacting to DNA injections.

CONCLUSIONS

Silicon nanowire/nanoribbon field-effect transistors (SiNW/NR) offer a highly sensitive and label-free detection scheme for biochemical applications. The sensor fabrication uses standard CMOS processes, which provides for inexpen¬sive manufacturing of chips for disposable use. For the majority of applications, potentially in handheld devices, the electronic systems can not only easily be downscaled but the handling is also simplified due to the label-free detection principle. No regent mixing is in example needed. We have demonstrated the sensing functionality for biosensing using container as well as microfluidic delivery system. The SiNW/NR has potential in low concentration detection and we have demonstrated detection $6x10^{-13}$M streptavidin binding to SiNR surface functionalized with biotin [2]. Currently we are working on parallel detection system, where spotting is used to achieve localized functionalization of an SiNW/NRs array for expressions analyses of RNA/DNA and protein of individual circulating tumor cell (CTC) from blood samples.

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