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Multiplex electrical detection of avian influenza and human immunodeficiency virus with an underlap-embedded silicon nanowire field-effect transistor

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ABSTRACT

The label-free electrical detection of the binding of antibodies and antigens of avian influenza (AI) and human immunodeficiency (HIV) viruses is demonstrated through an underlap-embedded silicon (Si) nanowire field-effect transistor. The proposed sensor was fabricated on a silicon bulk wafer by a top-down process. Specifically, a Si nanowire was fabricated by a combined isotropic and anisotropic patterning technique, which is one route plasma etching process. The sensor was fabricated by a self-aligned process to the gate with tilted implantation, and it allows precise control of the underlap region. This was problematic in earlier underlap field-effect transistors fabricated by a conventional gate-last process. As a sensing metric to detect the binding of a targeted antibody, the transfer characteristic change was traced. Before and after differences between the antibody binding results were caused by changes in the channel potential on the underlap region due to the charge effect arising from the biomolecules; this is also supported by a simulation. Furthermore, the multiplex detection of AI and HIV is demonstrated, showing distinctive selectivity in each case. Thus, the proposed device has inherent benefits for the label-free, electrical, and multiplex detection of biomolecules. Moreover, its processes are compatible with commercialized technology presently used to fabricate semiconductor devices. This advantage is attractive for those involved in the construction of a point-of-care testing (POCT) system on a chip involving simple, low-cost and low-risk fabrication processes of novel structures and materials.

1. Introduction

The most important aspects of modern healthcare are the prevention of disease and appropriate treatments through early diagnosis. For effective treatment, swift and accurate diagnoses of particular diseases are essential; these requirements arouse interest in a simple and rapid on-site diagnosis system. Over the past half century, since the ion-sensitive field-effect transistor (ISFET) was introduced by Bergveld (1970), a basic structural key element based on the field-effect transistor (FET) has dominated the field of chemical and biological sensors based on the possibility of label-free detection and the potential for adaptability to signal-processing systems (Schasfoort et al., 1990a, 1990b, Bergveld, 1991; Bausells et al., 1999; Uslu et al., 2004; Yuan et al., 2011). With these approaches, however, integrating sensors and readout circuits monolithically on a chip remains a challenge.

The integrability issue can be readily overcome by adding a gate electrode, the material of which is highly compatible with the standard complementary metal-oxide semiconductor (CMOS) process (Bousse et al., 1988; Jakobson et al., 2002; Gu et al., 2009; Kim et al., 2013). Referring to the concept, a revamped FET structure termed an underlap-FET was demonstrated as a sensor for detecting antigen–antibody reactions (Lee et al., 2010). It has a gate electrode which partially covers the channel, whereas the gate entirely straddles the channel in the conventional CMOS structure. The region not covered by the gate dominantly controls the channel potential. Thus, the current flow is mostly influenced by the potential of the opened channel, leading to the use of the term underlap. An individual gate electrode for an independent sensor device is advantageous in that the sensor can be controlled separately, which is essential for sensor array processing (Baek et al., 2012) compared to a back-gate structure in that the entire

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wafer was used as a gate. Moreover, the underlap-FET is highly compatible with the CMOS process, implying that monolithic integration with a readout circuit and batch-fabrication at a low cost can be achieved.

The sensor performance of planar device can be improved by applying a 1-dimensional nanowire based structure due to the enhancement of gate-to-channel controllability (Singh et al., 2006; Cui et al., 2001). The miniaturization of the sensor therefore promises enhanced device performances as well as dense arrays of sensors and peripheral circuits. In other words, a Si nanowire (SiNW) wrapped by the gate will help accommodating further miniaturization of the sensor size by suppressing the short-channel effects. Nevertheless, as the previously demonstrated underlap-FET relied on the gate-last process, the fabrication method should face limitations when the underlap dimensions must be controlled precisely. Because the source and drain are formed before the patterning of the gate, the length of the underlap region critically depends on the gate alignment step (Supplementary Fig. 1a). In particular, an unreliable underlap length due to misalignment will be more critical for nano-scale devices.

Herein, we demonstrate an underlap-embedded SiNW-FET (referred to as an underlap-NWFET hereafter) fabricated by a top-down process for the label-free detection of biomolecules. To overcome the aforementioned issues, a tilted implantation process is introduced to ensure self-aligned source and drain after gate patterning (Supplementary Fig. 1b). This allows for a uniform underlap length of the NWFET. In addition, the demonstrated underlap-NWFET is fabricated on a bulk silicon substrate using a simple reactive-ion etching (RIE) technique (Moon et al., 2011) involving anisotropic and isotropic etching. This is a low-cost fabrication method compared to SiNW biosensors using silicon-on-insulator (SOI) wafers (Ahn et al., 2012). As the proposed device is based on an underlap-FET, it shares the merits of underlap-FETs and has the additional advantage of being compatible with dense arrays of sensors.

In this paper, we report the results of label-free detection tests of antibodies to verify the concept of underlap-NWFET as a biosensor. These finding are also supported by simulation data to determine the pertinent underlying mechanisms. First, the electrical characteristics of the proposed sensor are analyzed by the commercialized simulator SILVACO. Second, antigens and antibodies for the avian influenza (AI) and human immunodeficiency (HIV) viruses are used to investigate the sensitivity and selectivity of the sensor. Finally, this work is extended to the multiplex detection of different antibodies for sensor arrays. Successful multiplexed sensing of antibodies for the AI and HIV viruses is observed with proposed sensor.

2. Operating principle and simulation results

Scanning electron microscopy (SEM) images and the cross-sectional schematic of the underlap-NWFET are illustrated in Fig. 1. The sensor is composed of a source and a drain connected by a SiNW channel, which is wrapped by two separated gate and biomolecules. The source and drain were heavily doped with arsenic ion, while the underlap region ($L_{Underlap}$ in Fig. 2b) was lightly doped with boron. Biomolecules are immobilized onto the surface of the SiNW in the underlap region, which serves as a sensing site. The same bias is applied to two separate gates (G1 and G2), which are used to modulate the channel potential. Hence, the current flow is also controlled by these gates.

Here, a dominant factor influencing the current flow is the channel potential at the underlap region because the underlap region has the highest resistance throughout the SiNW due to the light doping concentration. It should be noted that the channel potential at the underlap region is sensitively modulated by the external charge arising from the immobilized biomolecules. This concept is analogous to a virtual gate which modulates the channel potential. As the first approximation, the sensor can be modeled as a simple circuit which consists of three MOSFETs (MOS1, MOS2, and MOS3) in a series, as shown in Fig. 2(a). MOS1 and MOS3 are related to the channel region with G1 and G2, and MOS2 is related to the underlap region (sensing site) with a biomolecular gate. To obtain the total drain current, it is necessary to solve each individual MOSFET equation with the condition of $I_D=I_{MOS1}=I_{MOS2}=I_{MOS3}$ according to the current conservation law and $V_{DS}=V_{DS,MOS1}+V_{DS,MOS2}+V_{DS,MOS3}$. However, when two components are connected in a series, the element with lower conductance will dominantly determine the total current. Moreover, the underlap effects influence I_{MOS1}; thus, MOS2 is also the valve of the current flow of MOS1. Therefore, the total drain current can be approximately expressed in the simple form shown below.

$$I_D(V_G,V_D,V_S)=\left(\frac{1}{I_{MOS1}(V_G,V_D,V_S)\times\beta}+\frac{1}{I_{MOS3}(V_G,V_D,V_S)}\right)^{-1} \quad (1)$$

Here, V_G, V_D, and V_S are the gate, drain and source voltages, respectively. The term β as employed here is primarily affected by the amount of charge arising from the biomolecules on the underlap region; it roughly represents the exponential relationship with the

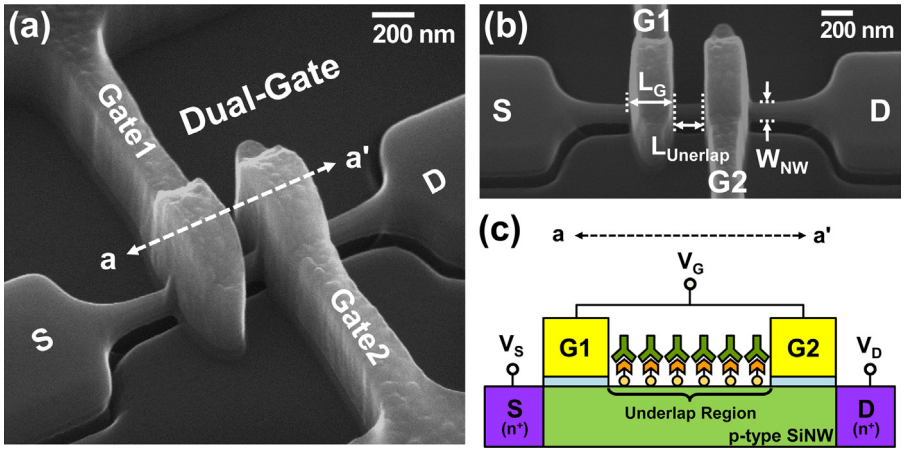

Fig. 1. SEM images and a schematic of the underlap-NWFET. (a) A tilted SEM image and (b) a top-view SEM image of the underlap-NWFET are illustrated. The device has a width (W_{NW}) of 50 nm, a gate length (L_G) of 300 nm, and underlap region ($L_{Underlap}$) of 200 nm. (c) A schematic showing an underlap-NWFET along the channel length ((a)–(a′)) direction is presented. The same gate bias, V_G, is applied to G1 and G2, and it modulates the total drain current level. The exposed channel region between G1and G2 serves as an underlap region, and biomolecules immobilized on the underlap surface affect the channel potential, resulting in a change in the drain current at a given gate bias.