Sensing and Bio-Sensing Research 4 (2015) 103–108

Contents lists available at ScienceDirect

Sensing and Bio-Sensing Research

journal homepage: www.elsevier.com/locate/sbsr

Real-time electrical detection of the formation and destruction of lipid bilayers on silicon nanowire devices

Elissa H. Williams [a,b,c,*], Jong-Yoon Ha [c,d], Melanie Juba [a], Barney Bishop [a], Sergiy Krylyuk [c,d], Abhishek Motayed [c,d], Mulpuri V. Rao [b], John A. Schreifels [a], Albert V. Davydov [c]

[a] Department of Chemistry and Biochemistry, George Mason University, 4400 University Drive, Fairfax, VA 22030, USA
[b] Department of Electrical and Computer Engineering, George Mason University, 4400 University Drive, Fairfax, VA 22030, USA
[c] Material Measurement Laboratory, National Institute of Standards and Technology, 100 Bureau Drive, Gaithersburg, MD 20899, USA
[d] Institute for Research in Electronics and Applied Physics, University of Maryland, College Park, MD 20742, USA

ARTICLE INFO

Keywords:
Nanowire biosensor
Two-terminal device
Lipid bilayer
Cell membrane
Escherichia coli

ABSTRACT

Silicon nanowire (Si NW) two-terminal devices were fabricated to electrically probe the real-time formation and destruction of lipid bilayers. A liposome solution, containing the same ratio of zwitterionic/anionic lipids that are present in an *Escherichia coli* cell membrane, was applied to the NW devices. Lipid bilayer formation on the Si NWs was detected in-situ by observing electrical resistance changes complemented by confocal fluorescence microscopy imaging. The formation of lipid bilayers resulted in a 1% to 2% decrease in device current, consistent with the negative gating effect of the lipids on the NW surface. The devices demonstrated a ≈ 1 min electrical response time to lipid encapsulation. Removal of the lipid layer was achieved by exposing the devices to a detergent, which resulted in NW conductance returning to its original value with a ≈ 2 min recovery time. The lipid bilayer coated Si NWs demonstrate a novel platform to enable in-situ electrical probing of bacterial cell membrane mechanisms, interactions, and reactions.

1. Introduction

Over the past decade, silicon (Si) nanowires (NWs) have been studied extensively as biosensing platforms. Due to the fact that biomolecules can act as an electrical gate upon adsorption onto NW surfaces and change NW device conductivity, the label-free, real-time electrical detection of a wide variety of biomolecules has been realized [1–7]. The high surface-to-volume ratio of the electrically active NW enables its extremely high sensitivity to analytes, while selectivity is realized through biomolecule specific NW surface functionalization.

The success of Si NW devices in the detection of biological compounds has opened up the possibility of using NWs to study the mechanisms of cellular reactions [8,9]. Since cell membranes play a critical role in cellular interactions, studies have recently been carried out to encapsulate NWs in a lipid bilayer as to mimic a cell membrane [9–12]. The electrical detection of ion transport through pore channels in a lipid bilayer coated Si NW was recently demonstrated in [13], revealing the potential of using Si NW devices as artificial cell constructs.

While the in-situ formation of lipid bilayers on Si NWs was studied using fluorescence microscopy in [12], real-time electrical measurements performed to analyze the temporal effect of the membrane formation process on NW conductivity were absent. A change in the electrical resistance for a bilayer coated vs. uncoated NW was demonstrated only ex-situ by Misra et al. [13] and Martinez et al. [10]. In this paper, we sought out to study in-situ lipid bilayer formation and destruction on Si NW surfaces using electrical measurements, complimented by ex-situ confocal fluorescence microscopy imaging. Liposomes consisting of 80% zwitterionic lipids (phosphatidylcholine (PC)) and 20% anionic lipids (phosphatidylglycerol (PG)) were utilized to mimic the charged lipids present in an *Escherichia coli* cell membrane [14]. The liposomes were applied to Si NW devices to study lipid bilayer formation and a common detergent, Tween20, was used to remove the lipid layer from the NW surface [15]. This work demonstrates that

---

* Corresponding author at: Department of Chemistry and Biochemistry, George Mason University, 4400 University Drive, Fairfax, VA 22030, USA. Tel.: +1 703 993 1070; fax: +1 703 993 1055.

E-mail addresses: ewilliah@gmu.edu (E.H. Williams), jongyoon.ha@nist.gov (J.-Y. Ha), mjuba@gmu.edu (M. Juba), bbishop1@gmu.edu (B. Bishop), sergiy.krylyuk@nist.gov (S. Krylyuk), abhishek.motayed@nist.gov (A. Motayed), rmulpuri@gmu.edu (M.V. Rao), jschreif@gmu.edu (J.A. Schreifels), albert.davydov@nist.gov (A.V. Davydov).

http://dx.doi.org/10.1016/j.sbsr.2015.04.005
2214-1804/© 2015 The Authors. Published by Elsevier B.V.

changes in NW electrical conductivity directly correlate to the formation and the consecutive removal of lipid bilayers over NW surfaces. The membrane encapsulated two-terminal Si NW devices demonstrated here present a novel platform to enable the electrical probing of bacterial cell membrane reactions.

2. Materials and methods

2.1. Device design

A schematic of the Si NW sensor chip utilized in the experiments is shown in Fig. 1(A). The 25 mm × 25 mm chip included twelve 1 mm × 1 mm electrical contact pads at the top of the sensor chip (see Section 2.5 below for more details). The twelve metal pads extended as 20 μm wide lines to the center of the chip where they paired at a 10 μm gap. As shown in Fig. 1(B), a single Si NW bridged each gap resulting in a total of six NW devices on the chip. A 5 μm wide, 6 mm long photolithographically etched channel encompassed all six NW devices and connected to a fluid reservoir at the bottom of the chip (see Fig. 1(A) and (B)).

2.2. Device fabrication

A 4″ Si (100) wafer, coated with a 300 nm SiO_2 layer (see Fig. 2, A1), was utilized as the substrate for device fabrication. The wafer was diced into 25 mm × 25 mm squares, cleaned using acetone and isopropanol, rinsed in distilled water, and then dried using a stream of nitrogen. Photolithography processing steps defined the openings for the bottom metal contacts (Fig. 2, A2) followed by electron beam deposition of 15 nm of Ti metal (Fig. 2, A3). N-type Si NWs, with a length of about 30 μm and a diameter of 120 nm, grown using catalyst assisted vapor–liquid–solid chemical vapor deposition [16], were dielectrophoretically aligned onto the Ti contact pads (Fig. 2, A4) as described in our previous paper [17]. Dielectrophoretic alignment was carried out at 20 V to 30 V of alternating current at 1 kHz. Photolithography steps were utilized to define openings for the top metal contacts (Fig. 2, A5). Electron beam deposition was used to deposit a stack of metals (70 nm of Ti, 70 nm of Al, 50 nm of Ti, and 50 nm of Au) onto the patterned chips (Fig. 2, A6). The completed devices were annealed in argon at 550 °C for 30 s to facilitate ohmic contact formation (Fig. 2, A7).

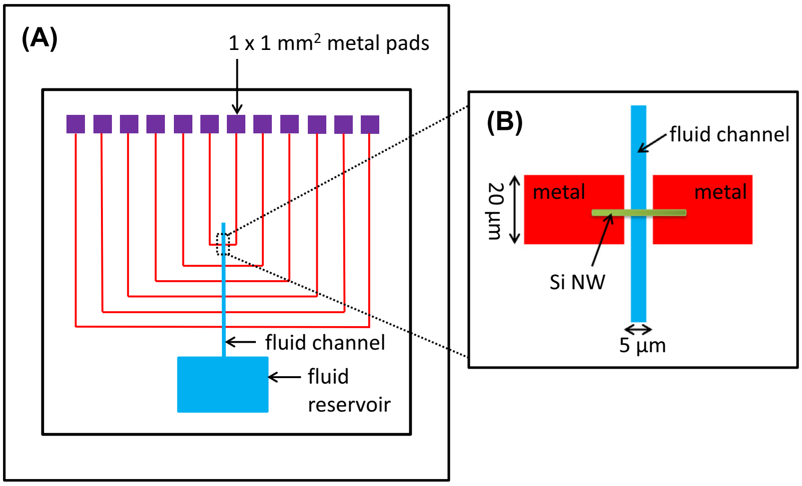

Fig. 1. (A) The design schematic of the Si NW sensor chip. The chip contained six two-terminal NW devices, a fluid channel, and a fluid reservoir. (B) An enlarged region of one of the six NW devices.

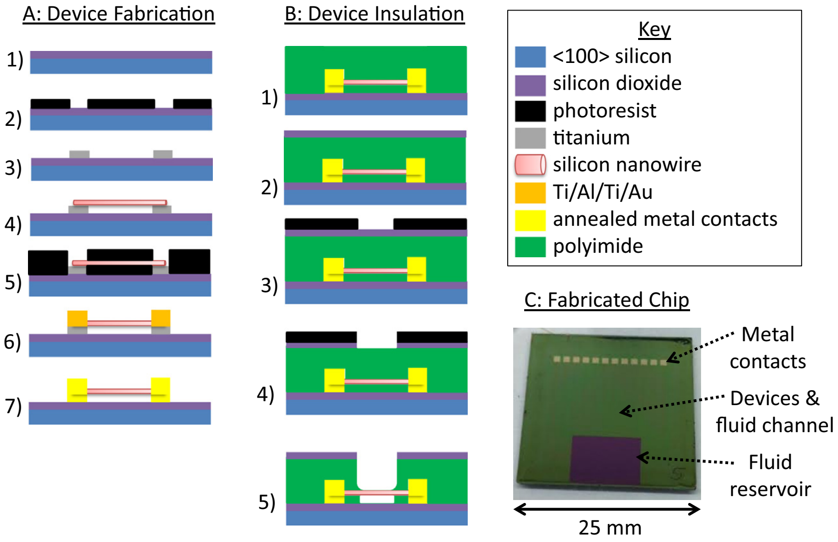

Fig. 2. Si NW sensor chip fabrication (A) and insulation (B) steps. An optical image of a fabricated and insulated sensor chip is shown in (C).