Analytica Chimica Acta 825 (2014) 1–25

Contents lists available at ScienceDirect

Analytica Chimica Acta

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

Review

Silicon nanowires as field-effect transducers for biosensor development: A review

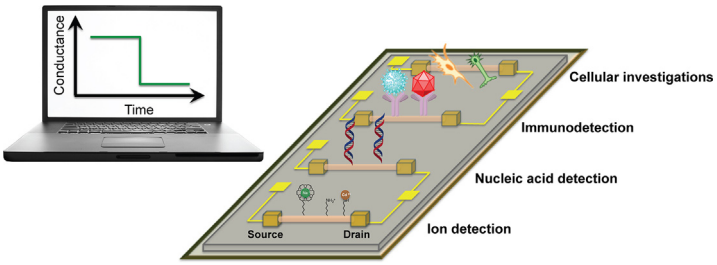
M. Omair Noor, Ulrich J. Krull *

Chemical Sensors Group, Department of Chemical and Physical Sciences, University of Toronto Mississauga, 3359 Mississauga Road North, Mississauga, ON L5L 1C6, Canada

HIGHLIGHTS

- Nanoscale field-effect transducers interrogate surface charge by conductivity changes.
- The nanometer dimensions of SiNWs facilitate sensitive detection of biomolecules.
- SiNWs can be fabricated by bottom–up or top–down approaches.
- Device parameters and solution-phase conditions strongly influence analytical performance.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 31 December 2013
Received in revised form 11 March 2014
Accepted 13 March 2014
Available online 15 March 2014

Keywords:
Silicon nanowires
Field effect transistors
Surface functionalization

ABSTRACT

The unique electronic properties and miniaturized dimensions of silicon nanowires (SiNWs) are attractive for label-free, real-time and sensitive detection of biomolecules. Sensors based on SiNWs operate as field effect transistors (FETs) and can be fabricated either by top–down or bottom–up approaches. Advances in fabrication methods have allowed for the control of physicochemical and electronic properties of SiNWs, providing opportunity for interfacing of SiNW-FET probes with intracellular environments. The Debye screening length is an important consideration that determines the performance and detection limits of SiNW-FET sensors, especially at physiologically relevant conditions of ionic strength (>100 mM). In this review, we discuss the construction and application of SiNW-FET sensors for detection of ions, nucleic acids and protein markers. Advantages and disadvantages of the top–down and bottom–up approaches for synthesis of SiNWs are discussed. An overview of various

Abbreviations: 1 BPM, 1 base pair mismatch; 1-D, 1-dimensional; 2-MEA, 2-mercaptoethylamine; 3-D, 3-dimensional; Act-D, actinomycin-D; Ad, adamantane; AIV, avian influenza virus; AMPs, antibody mimic proteins; anti-cTnI, antibody for cTnI; anti-hIgG, antibody for human IgG; APTES, 3-aminopropyltriethoxysilane; ASIC, application specific integrated circuit; β-CD, β-cyclodextrin; BB, blown–bubble; BG, back-gate; BIT-FET, branched intracellular nanotube FET; BP, base pair; BSA, bovine serum albumin; CaM, calmodulin; CEA, carcinoembryonic antigen; CK-MB, creatine kinase MB; CK-MM, creatine kinase MM; CMOS, complementary metal oxide semiconductor; cTnI, cardiac Troponin I; cTnT, cardiac Troponin T; CVD, chemical vapor deposition; D, drain; DG, double-gate; DMPC, 1,2-dimyristoyl-sn-glycero-3-phosphocholine; DNA, deoxyribonucleic acid; DTT, dithiothreitol; ECG, electrocardiogram; EDTA, ethylenediaminotetraacetic acid; ELISA, enzyme-linked immunosorbent assay; FC, fully-complementary; FET, Field effect transistor; FG, front-gate; G, gate; GSH, glutathione; GST, glutathione S-transferase; H-terminated, hydrogen terminated; hIgG, human IgG; His-tag, histidine tag; I_{sd}, source–drain current; LB, Langmuir–Blodgett; LOD, limit of detection; mAb, monoclonal antibody; mES, mouse embryonic stem; MPTES, 3-mercaptopropyltriethoxysilane; MPTMS, 3-mercaptopropyltrimethoxysilane; NC, non-complementary; NTA, nitrilotriacetic acid; NW, nanowire; PBS, phosphate buffered saline; PDMS, polydimethylsiloxane; PNA, peptide nucleic acid; PSA, prostate specific antigen; PSAα1, PSA-α1-antichymotrypsin; RCA, rolling circle amplification; RE, reference electrode; S, source; SEM, scanning electron microscope; SiNW, Silicon nanowire; siRNA, small interfering RNA; SNP, single nucleotide polymorphism; SOI, silicon-on-insulator; SSC, saline sodium citrate; ssDNA, single-stranded DNA; TCEP, *tris*(2-carboxyethyl) phosphine; TEM, transmission electron microscope; TNF-α, tumor necrosis factor-alpha; TUNEL, terminal deoxynucleotidyl transferase dUTP nick end labeling; V_{bg}, back-gate voltage; V_G, gate voltage; V_{lg}, liquid gate voltage; V_{sd}, source–drain voltage; VLS, vapor–liquid–solid.

* Corresponding author. Tel. +1 905 828 5437; fax: +1 905 828 5425.
E-mail address: ulrich.krull@utoronto.ca (U. J. Krull).

http://dx.doi.org/10.1016/j.aca.2014.03.016
0003-2670/

Gating
Debye length

methods for surface functionalization of SiNWs for immobilization of selective chemistry is provided in the context of impact on the analytical performance of SiNW-FET sensors. In addition to *in vitro* examples, an overview of the progress of use of SiNW-FET sensors for *ex vivo* studies is also presented. This review concludes with a discussion of the future prospects of SiNW-FET sensors.

Contents

Omair Noor received his Hon. B.Sc. degree in Biotechnology specialist program, in 2008, and M. Sc. degree in Bio-Analytical Chemistry, in 2010, from the University of Toronto Mississauga, Mississauga, ON, Canada. He is currently working towards his Ph. D. degree in the department of Chemistry at University of Toronto with the Chemical Sensors Group under the supervision of Prof. Ulrich J. Krull. His research interests focus on the integration of quantum dots and FRET based assays for nucleic acid detection using microfluidic channels and paper as a solid support. Omair currently holds an Ontario Graduate Scholarship (OGS) from the Ontario Ministry of Training, Colleges and Universities (MTCU). He was also a recipient of Undergraduate Student Research Award (USRA) from the Natural Sciences and Engineering Research Council of Canada (NSERC).

Ulrich Krull is appointed as a Professor of Analytical Chemistry at the University of Toronto, and holds the endowed AstraZeneca Chair in Biotechnology. His research interests are in the areas of biosensor and diagnostic technologies, and applications to biotechnology, forensic, clinical and environmental chemistry. His research work is exploring the use of luminescent nanoscale materials and microfluidics technologies to build devices for detection of DNA and RNA targets. Krull is an editor for Analytica Chimica Acta, and serves on a number of Scientific Advisory Boards for industry.

1. Introduction

The integration of nanomaterials into device structures for biosensing applications has played a central role in the development of new strategies for signal transduction [1,2]. Due to comparable sizes of biological macromolecules and nanomaterials (nanotubes, nanowires and nanoparticles), the combination of nanomaterials with biomolecules offers potential for development of sensing technologies of molecular size scale for sensitive detection of biomolecules [2]. Silicon nanowires (SiNWs) are a class of 1-dimensional (1-D) nanomaterial that was introduced in 2001 by the Lieber group [3]. Since this time SiNWs have been described in numerous studies as electrical field-based sensors that are suitable for a variety of applications that include detection of ions [4,5], small molecules [6,7], nucleic acids [8], proteins [9] and the investigation of the electrophysiology associated with single cells [10–13] and tissues [14,15]. SiNWs can be synthesized as single crystals, and owing to their 1-D morphology and resulting increase in surface area-to-volume ratio, they provide improved analytical sensitivity as compared to planar field effect transistor (FET) devices for chemical and biosensing [16,17]. Advances in synthetic approaches for fabrication of SiNWs have allowed for the control of morphology and doping levels of SiNWs [18], enabling SiNW-FETs for cellular studies with high spatial and temporal resolution [19]. Additionally, SiNWs offer label-free, real-time and ultrasensitive detection of biomolecules to sub-fM detection limits [20]. These detection limits are 2–3 orders of magnitude lower than those that have been reported with quantum dots and carbon nanotubes for ensemble compatible measurements [1]. Top–down fabrication of sensors based on silicon nanostructures offers the practical advantage of compatibility with the established fabrication