Nano Today (2011) 6, 131—154

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REVIEW

Silicon nanowire field-effect transistor-based biosensors for biomedical diagnosis and cellular recording investigation

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Received 31 October 2010; received in revised form 18 December 2010; accepted 7 February 2011
Available online 8 March 2011

KEYWORDS
Silicon nanowire;
Field-effect transistor;
Protein—protein interaction;
DNA hybridization;
Peptide—small molecule interaction;
Biomarker detection;
Three-dimensional localized bioprobe

Summary Silicon nanowire field-effect transistors (SiNW-FETs) have recently drawn tremendous attention as a promising tool in biosensor design because of their ultrasensitivity, selectivity, and label-free and real-time detection capabilities. Here, we review the recently published literature that describes the device fabrication and biomedical applications of SiNW-FET sensors. For practical uses, SiNW-FETs can be delicately designed to be a reusable device via a reversible surface functionalization method. In the fields of biological research, SiNW-FETs are employed in the detections of proteins, DNA sequences, small molecules, cancer biomarkers, and viruses. The methods by which the SiNW-FET devices were integrated with these representative examples and advanced to virus infection diagnosis or early cancer detection will be discussed. In addition, the utilization of SiNW-FETs in recording the physiological responses from cells or tissues will also be reviewed. Finally, the novel design of a three dimensional (3D) nano-FET probe with kinked SiNWs for recording intracellular signals will be highlighted in this review.

Abbreviations: AFM, atomic force microscopy; ATP, adenosine triphosphate; CA, carbohydrate antigen; CaM, calmodulin; CEA, carcinoembryonic antigen; CgA, chromogranin A; CNT, carbon nanotube; CVD, chemical vapor deposition; DNA, deoxyribonucleic acid; EDTA, ethylenediaminetetraacetic acid; FET, field-effect transistor; GSH, glutathione; GST, glutathione S-transferase; His-tag, histidine-tag; miRNA, microRNA; MPC, microfluidic purification chip; NTA, nitrilotriacetic acid; PBS, phosphate buffered saline; PDMS, polydimethylsiloxane; PNA, peptide nucleic acid; PS, phosphate solution; PSA, prostate specific antigen; RNA, ribonucleic acid; RT-PCR, reverse transcription-polymerase chain reaction; SiNW, silicon nanowire; TnI, troponin I; VGCC, voltage-gated Ca^{2+} channel; VLS, vapor—liquid—solid.

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doi:10.1016/j.nantod.2011.02.001

Introduction

Quantification and analysis of biological processes are of utmost importance for biomedical applications and cellular programming investigation. However, it is challenging to convert the biological information into an electronic signal due to the difficulties of connecting an electronic device into a biological environment. In recent years, there has been dramatic development of electrochemical biosensors because of their applications in toxicity testing [1], chemical analysis [2], medical diagnosis [3], food industry [4], environmental monitoring, and many other areas. An electrochemical biosensor, as defined by IUPAC, is a self-contained integrated device that allows for specific analytical detection by using a biological recognition element (a biochemical receptor) in direct spatial contact with a transduction element (Fig. 1(a)) [5,6]. Different from a bioanalytical system (e.g., immunoprecipitation usually used for protein analysis) that requires a reagent addition to proceed the analysis, an electrochemical biosensor provides an attractive platform to analyze the contents of biological samples because of the direct conversion of biological events to electronic signals (that can be detected directly), thus allowing more rapid and convenient sensing detection.

Investigations of the materials and methods to construct an electrochemical biosensor have been underway for decades. Over the past 20 years, nanomaterials, such as quantum dots, nanoparticles, nanowires, nanotubes, nanogaps, and nanoscale films [7–13], have received enormous attention due to their suitable properties for designing novel nanoscale biosensors. For example, the dimension of nanomaterials of ~1–100 nm provides a perfect feature to study most biological entities, such as nucleic acids, proteins, viruses, and cells (as illustrated in Fig. 1(b)) [14]. In addition, the high surface-to-volume ratios for nanomaterials allow a huge proportion of the constituent atoms in the material to be located at or close to the surface. This characteristic makes the surface atoms play

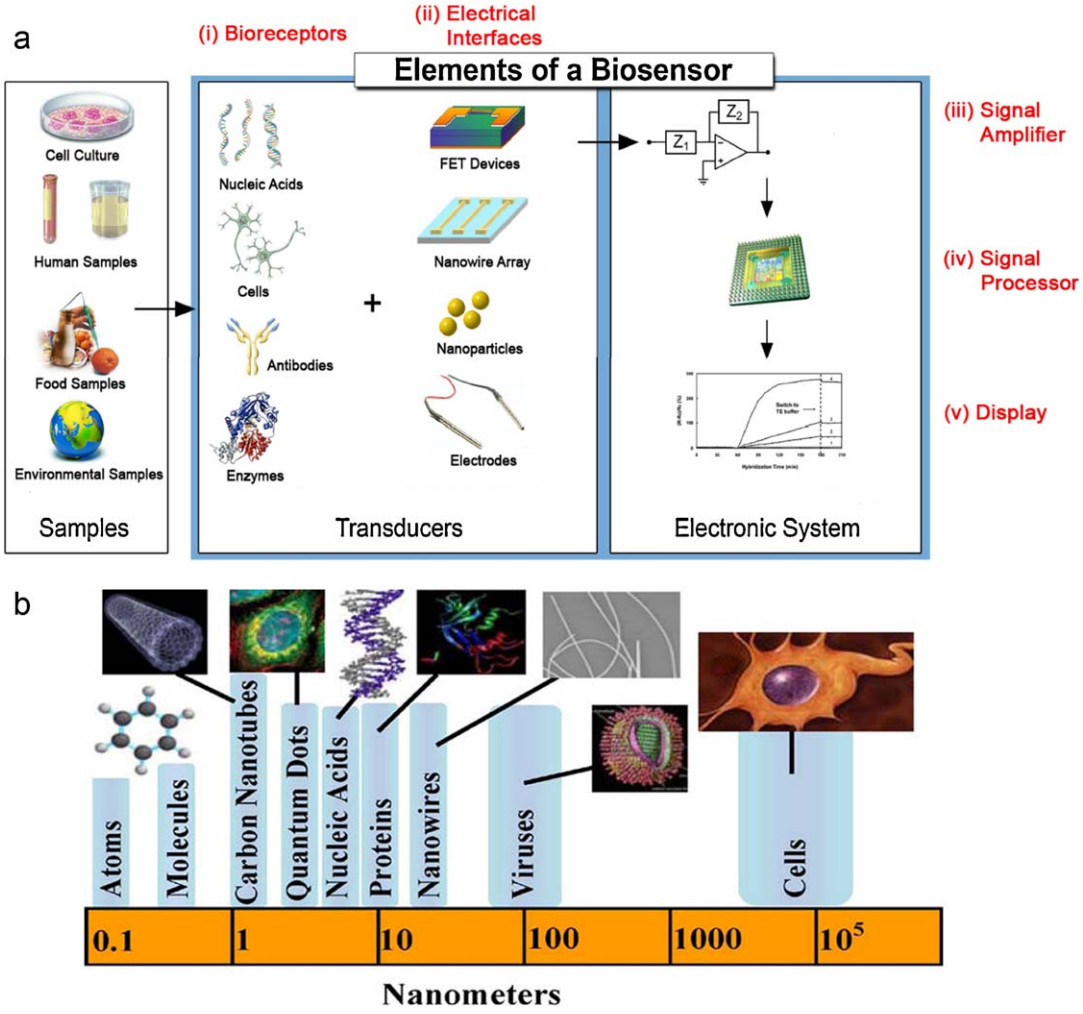

Figure 1 (a) The construction of typical biosensors with elements and selected components. The procedures are described as follows: (i) receptors specifically bind the analyte; (ii) an interface architecture where a specific biological event takes place and gives rise to a signal recorded by (iii) the transducer element; (iv) computer software to convert the signal into a meaningful physical parameter; finally, the resulting quantity is displayed through (v) an interface to the human operator. (b) The sizes of nanomaterials (NW and NT) in comparison to some biological entities, such as bacteria, viruses, proteins, and DNA.
Reprinted from [6,14].