"Biomedical nanosensors have a wide range of applications in human, animal, and plant health for diagnostics and therapeutics. Assembled by Prof. Joseph Irudayaraj, this book is an important reference in the exciting, important, and rapidly evolving field of biomedical nanotechnology. The chapters are detailed and thorough, and rich with references. It is an interdisciplinary collection of contributions from experts with diverse backgrounds, and therefore a very interesting and educational read for students and faculty researchers in bionanotechnology."

Prof. Rashid Bashir
University of Illinois at Urbana-Champaign, USA

Biomedical nanosensors play a central role in the development of diagnostics and therapeutics for early detection and treatment of diseases. Bringing a nanoscale perspective to sensing is expected to allow interrogation of biological systems; detection of ultrasmall concentration of biomolecules, ions, and molecular interactions; exploration of cellular mechanisms; and integration of nanosensors into many other devices, including implantable ones.

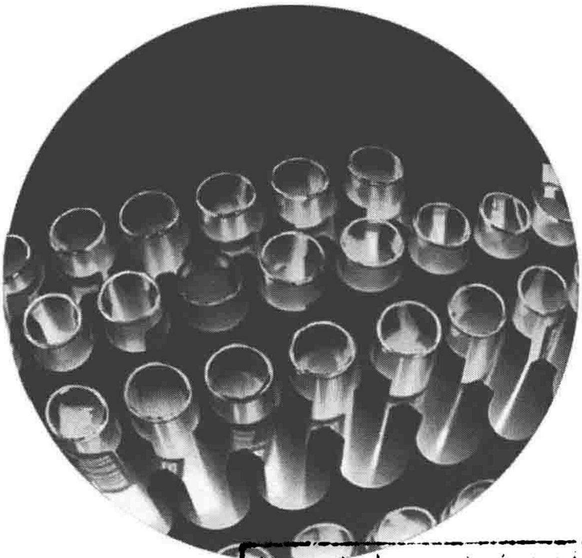
This book specifically addresses the use of nanomaterials as sensing and therapeutic agents. Nanoparticles, nanowires, and nanotubes of inorganic as well as polymeric composition of nano- and microscale dimensions constitute a major direction in nanomedicine. The volume also discusses selected technologies involving single-molecule and single-particle methods for tracking. A comprehensive treatise on sensors and biomedicine, this impressive compilation is destined to be of immense value to scientists and engineers interested in the field of medicine, sensor development, and nanotechnology. Even graduate students and consultants wanting to obtain a quick introduction to biosensors for biomedicine with a focus on materials, properties, devices and technologies, and real-world applications can use this book as a solid introductory text.

Joseph Irudayaraj has BS and MS degrees in biosystems engineering and computer sciences. He obtained his PhD from Purdue University and held faculty positions at Penn State and Utah State before coming to Purdue in 2005. The primary focus of Dr. Irudayaraj's group is on single-cell technology development for the detection and quantification of epigenetic modifications, transcripts, and phosphorylation. The group is also interested in nanoparticle-based targeting and drug delivery for diagnostics, and the technologies it has developed and applied in the laboratory include surface-enhanced Raman spectroscopy, hyperspectral plasmon imaging, second-harmonic super-resolution microscopy for deep-tissue imaging, and single-molecule fluorescence spectroscopy. Dr. Irudayaraj has published over 200 refereed journal articles in areas covering nanosensors, intracellular drug localization, surface-enhanced Raman spectroscopic approaches for cancer detection, tracking biomolecule dynamics in single cells, spectroscopic (Raman and FTIR) characterization of biomaterials, and numerical modeling of thermodynamic and mechanical behavior of biomaterials. He is a member of American Chemical Society, Institute of Biological Engineering, Biophysical Society, and the American Society of Agricultural and Biological Engineers.

V145
ISBN-13 978-981-4303-03-3
9 789814 303033

PAN STANFORD PUBLISHING
www.panstanford.com

Biomedical Nanosensors



Joseph Irudayaraj
Editor

PAN STANFORD PUBLISHING

Published by

Pan Stanford Publishing Pte. Ltd.
Penthouse Level, Suntec Tower 3
8 Temasek Boulevard
Singapore 038988

Email: editorial@panstanford.com
Web: www.panstanford.com

British Library Cataloguing-in-Publication Data
A catalogue record for this book is available from the British Library.

Biomedical Nanosensors

ISBN 978-981-4303-03-3 (Hardcover)
ISBN 978-981-4303-04-0 (eBook)

Printed in the USA

Biomedical Nanosensors

Pan Stanford Series on Biomedical Nanotechnology

Series Editors

Vladimir Torchilin and Mansoor Amiji

Titles in the Series

Vol. 1
Handbook of Materials for Nanomedicine
Vladimir Torchilin and Mansoor Amiji, eds.
2010
978-981-4267-55-7 (Hardcover)
978-981-4267-58-8 (eBook)

Vol. 2
Nanoimaging
Beth A. Goins and William T. Phillips, eds.
2011
978-981-4267-09-0 (Hardcover)
978-981-4267-91-5 (eBook)

Vol. 3
Biomedical Nanosensors
Joseph Irudayaraj, ed.
2013
978-981-4303-03-3 (Hardcover)
978-981-4303-04-0 (eBook)

Vol. 4
Nanotechnology for Delivery of Therapeutic Nucleic Acids
Dan Peer, ed.
2013

Vol. 5
Inorganic Nanomedicine
Bhupinder Singh Sekhon, ed.
2014

Vol. 6
Nanotechnology for Cancer
Julia Ljubimova, ed.
2014

Vol. 7
Nanotechnology for Delivery of DNA and Related Materials
Bengt Fadeel, ed.
2015

Vol. 8
Translation Industrial Nanotechnology
Thomas Redelmeier, ed.
2015

Preface

The overall theme of *Biomedical Nanosensors* is to compile a comprehensive treatise on sensors for biomedicine. Specifically, we address the enthusiasm that nanotechnology and relevant tools have provided to medicine and biology in order to address diagnostics and therapeutics. The infusion of the nanoscale perspective to sensing is expected to allow the interrogation of biological systems, detection of ultrasmall concentrations of biomolecules, ions, and molecular interactions, exploration of cellular mechanisms, and integration of nanosensors into many other devices, including implantable devices and drug delivery vehicles. In this book, we will specifically address nanomaterials, constituting nanoparticles and nanotubes of inorganic as well as of polymeric composition of nano- and microscale dimensions, as these constitute a major direction in nanomedicine. Considering the diversity and the wealth of information in this field, we have attempted to focus on the basic concepts of fundamental and more recent materials and sensing paradigms leading to applications, including implantable devices, as these are central to micro- and nanoscale biomedical technology development.

In Chapter 1, we provide the fundamentals of biosensors, including the different transduction modes, biosensor elements, and bioconjugation strategies. A detailed account of molecular recognition is given in Chapter 2 in the context of molecular-imprinted polymer design, imprinting, and applications. Chapters 3 and 4 discuss the use of gold nanoparticles as plasmonic and Raman sensors. A comprehensive treatment of the fundamentals of gold nanoparticles as biosensors for ultrasensitive detection *in vitro* and *in vivo* can be found in these chapters. Chapters 5 and 6 discuss carbon nanotubes and graphene sensors. The physics of these versatile materials and their integration in sensor technology development, with a comprehensive survey of the work done in this field, is provided. The book will not be complete without a discussion on the use of single-molecule tools (Chapter 7), as these are becoming fundamental to understanding the mechanisms in biomedicine. In Chapter 8, recent advances in creating micro- and nanoparticles for inhalation drug delivery are addressed. Chapters 9 to 11 address *in vivo* therapeutics constituting bioelectric monitoring and stimulation, microelectromechanical systems, and implantable electrochemical biosensors. All of the chapters provide a detailed narrative on the future outlook.

Since the treatment is comprehensive, we expect this compilation to be valuable to scientists and engineers interested in the field of medicine, sensor development, and nanotechnology. Thus, this book could be used as an introductory text by graduate students and consultants wanting to obtain a quick introduction to biosensors for biomedicine with a focus on materials, properties, devices and technologies, and real-world applications.

Joseph Irudayaraj
Purdue University
June 2012

Contents

Chapter 1

Biomolecular Components of a Biosensor: Fundamentals

Kaustubh D. Bhalerao[a] and Goutam J. Nistala[b]

[a]*Agricultural and Biological Engineering, University of Illinois at Urbana-Champaign, 1304 West Pennsylvania Avenue, Urbana, IL 61801, USA*

[b]*Department of Chemical Engineering, Stauffer III, 381 North-South Mall, Stanford University, Stanford, CA 94305, USA*

bhalerao@illinois.edu

Biorecognition, the ability to recognize a specific biomolecular analyte from a complex sample, is key to the detection and quantification of biomolecules. Often, the physiological role of these analytes is well understood in terms of their interactions with other biomolecular components. This knowledge can be exploited to identify biomolecular elements that can serve as recognition components in a sensing system.

Analytes of interest are diverse in nature and include nucleic acids, proteins or peptide fragments, polysaccharides, or even small molecules. Several methodologies have evolved to recognize different kinds of analytes, some of which are based directly on the role of the analyte in the living system (in cases where the analyte is native to the living system) while others are based on imitating the immunological response of the analyte (in cases where the analyte is extraneous to the living system). Complementary to detection methodologies, there have been numerous developments in experimental and computational techniques to identify and produce such biomolecules in an efficient manner, as well as to conjugate these biomolecules with artificial sensing platforms.

While the field of biorecognition is not new in the strict sense of the term, it deserves to be recognized as an important subdiscipline of engineering. As biosensing and targeted therapeutics increase in relevance, the availability of a framework around organizing the information relevant to biorecognition will simplify and streamline the development process.

Biomedical Nanosensors
Edited by Joseph Irudayaraj

ISBN 978-981-4303-03-3 (Hardcover), 978-981-4303-04-0 (eBook)
www.panstanford.com

1.1 What Makes a Biosensor a Biosensor?

A sensor is a device that measures the presence or amount of substance and converts it into an interpretable signal. A biosensor is a class of sensor devices or systems in which a biochemical interaction is exploited as the basis of detecting the presence or level of a known analyte. This analyte may be an inorganic compound such as a salt, a small biological molecule such as a vitamin or sugar molecule, or even the concentration of larger biological macromolecules such as proteins or nucleic acids. The biochemical interaction between the sensor system and the analyte provides a biological context to the sensing event as often the sensing mechanism used by the biosensor is functionally analogous to the interaction between the analyte and its biological environment.

Consider the example of the commercially successful glucose monitors used by diabetes patients. These biosensors analyze droplet-sized blood samples for blood glucose level and provide an output in terms of milligrams of glucose per deciliter of blood. This information can be used for diagnostic purposes or to inform therapeutic actions. The level of glucose in the droplet is inferred through a biochemical reaction that occurs between the glucose in the sample and an enzyme (glucose oxidase or hexokinase) in the sampling strips. The progress of this reaction is measured either optically, as a change in the color of the strip, or electrically, by measuring the electrical current produced by the reaction. The biochemical reaction rate is converted into a number that can be interpreted by medical professionals. The glucose oxidase enzyme directly interacts with glucose in a manner and rate analogous to its interaction *in vivo*. Therefore, this biosensor system provides a way to measure the biologically relevant level of glucose in the sample and thus provides a more realistic assessment for diagnostic or therapeutic purposes.

The growing interest in the development of biosensors for biomedical applications is the result of two intertwined arcs of progress. Firstly, researchers in the life sciences continually push the boundaries of understanding life and disease at the molecular level. Cancer, cardiovascular diseases, diseases of the immune system such as AIDS and degenerative diseases such as Alzheimer's or Parkinson's are now described in terms of genetic mutations or the interplay between various biomolecules. Elucidating the molecular etiology of disease is a deterministic route to conceive of monitoring and intervention strategies directed specifically to detect or modulate the interaction between these biomolecules. Secondly, the progress in miniaturization of technology has allowed the manufacture of devices and systems comparable in size to biomolecules that can be leveraged as a therapeutic by directly intervening in the disease at the biomolecular level. Of course, these two developments are not altogether unrelated. The advances in understanding life at the molecular level have been enabled by advances in technology, while the drive of the life science community has been a motivating factor in developing these technologies.

Figure 1.1 shows an abstraction of a typical biosensor. Each biosensor can be said to be composed of three layers: recognition, transduction, and representation. The recognition layer, the subject of this chapter, is responsible for physically detecting the analyte by means of a biomolecular interaction. This recognition event is then transmitted to the transducer, which converts it into a machine-readable (typically electrical) signal. The representation layer takes this machine-readable signal and converts it into a form readily interpreted by humans.