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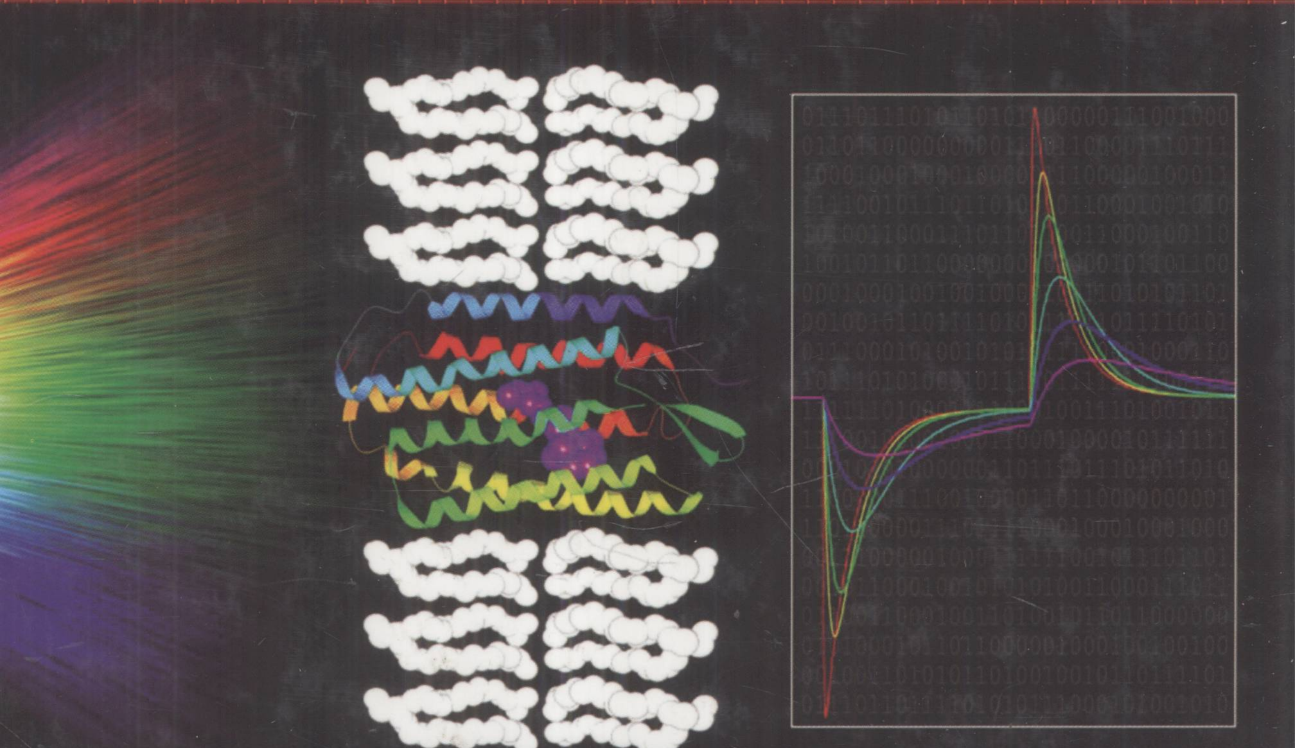

EDITED BY

George K. Knopf
Amarjeet S. Bassi

Smart Biosensor Technology

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GEORGE K. KNOPF
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Foreword

The topic of this book is smart biosensors, analytical devices that combine a biological or biomimetic sensing element with a separate signal transducer system. These biosensors have ultimate applications in biological research as well as medical and environmental monitoring. The range of applications is so extensive that it is hard to find one involving the monitoring of an external chemical or biological agent that would not benefit from the availability of a smart biosensor. However, such sensors are rarely available as commercial devices except in the field of medical monitoring (e.g., blood oxygen and glucose sensors). Current efforts in this field are limited primarily to academic, government, and a few commercial research laboratories. Much remains to be done before smart biosensors advance to the point where they have more global comparative advantage. Thus, the present volume is both timely and important as it will further research and interaction among the groups working in this important field.

The classical meaning of the term "biosensor" references the sensory apparatus of a living organism. It is useful to examine the evolution of such biosensors as it provides some insight into the current effort of scientists and engineers to make artificial or biomimetic biosensors. Evolutionary biologists have concluded that archaea and bacteria evolved from a common ancestor. While there is no fossil record of this ancestor, a comparison of the genetic codes of archaea and bacteria provides little doubt. Such studies indicate that many if not most of the "biosensors" that are expressed in modern prokaryotes and eukaryotes were present in a common form in this early ancestor. An important exception is lens-based image-resolving eyes, which require a more complex skeleton than is possible within the single-cellular domain of the early prokaryotes. Nevertheless, more recent studies have identified similarities in the genetic information associated with complex eye development that suggests a monophyletic origin. This remarkable continuity of developmental genes suggests that even the most complex of the biosensors in living organisms have a common ancestor that dates back to the archaeal era, 3.5 billion years ago. The inescapable conclusion is that life requires a complex and highly evolved biosensor network to succeed, and that much of the early work of evolution was dedicated to the exploration and optimization of these biosensors. It was only after the key biosensors had evolved that life was able to expand into the complex domains that are present today.

The development of biosensors by scientists and engineers is a recent endeavor that has progressed for less than one hundred millionth the time period that nature has devoted to the optimization process. It would therefore be logical to assume that nature is better at creating biosensors than we are. And indeed this is true in many areas. The most impressive sensors of visual or chemical information are biological, not human engineered. In contrast, human engineering has created more accurate sensors of temperature, position, and time. But the presumption is that if biology needed more accurate measurement of these three variables, it could provide the necessary resolution. Natural selection only seeks comparative advantage, not perfection. Nevertheless, natural sensors of the environment are exquisitely sensitive and approach perfection in terms of efficiency, sensitivity, and longevity.

This book explores the world of "human-engineered" biosensors. In most cases, success is due in part to taking advantage of what nature has provided, either in the form of materials or through biomimetics. Biomimetic sensors are devices that are modeled after biological sensory architectures or involve the use of natural materials that have been modified via chemical or genetic manipulation. It is a blurry line that separates biomimetic from biological sensors, and it is best not to waste energy trying to make a formal distinction. Improved methods in genetic engineering now allow more efficient and directed modification of biological molecules to enhance their performance in sensor applications. These capabilities increase the importance of biomimetics in the creation of biosensors.

Nanotechnology is also having an increasingly important role in current biosensor development. It is now possible to make insulating or semiconducting nanoscale structures with spherical or cylindrical geometry. These structures can be inserted into cells to monitor localized ionic strength or electrostatic charge. Alternatively, reporter molecules can be attached to the tip of cylindrical nanostructures and inserted inside a cell to provide photovoltaic, fluorescent, or electrochemical reporting of local conditions. The coupling of nanotechnology and bioelectronics has generated a new field of study called nano-bioelectronics. We anticipate that biosensors will benefit significantly from the exploration of nano-bioelectronics.

The chapters included in this volume provide an excellent introduction to and perspective on current research and developments in biosensors. A question that people might want to ponder as they read these chapters is the extent to which we have been successful in making "smart" biosensors. As noted above, a smart biosensor is defined as an analytical device that combines a biological, or biologically derived, sensing element with an electrical or optical signal transducer system. But when these sensors achieve their design goals, are they really "smart"? I suggest that in many cases of biosensor design, the "smart" derives from the use of biological molecules that have an elegance of structure and function that would only be possible after billions of years of evolutionary optimization.

Robert R. Birge
Coventry, Connecticut

Preface

A smart biosensor is a compact analytical device that combines a biological, or biologically derived, sensing element with an electrical, optical, or chemical transducer. Early biosensors had simple designs that affixed soluble enzymes or enzyme membranes to the surface of electrochemical transducers. Many of these systems exploited the direct covalent bonding of organized biomolecular monolayers on the surface of semiconductor devices and optical waveguides. In recent years, however, the functionality and design of the biosensor have greatly changed with the introduction of new intelligent materials and rapid advances in computing technology and microfabrication techniques.

Biosensors are now integrated devices that closely connect the biomolecular recognition element with a physical transducer to create an electrical or optical signal that is proportional to the concentration of a specific chemical or biological agent being measured. These microsystems include numerous sensors, transducers, and microfluidic actuators on a single integrated chip. The technology has evolved to sophisticated biochips where a collection of microarrays, or miniature test sites, can be fabricated on a single solid substrate to allow a large number of tests to be performed simultaneously at multiple sites. This design principle has greatly increased the speed of biochemical analysis. These biochips have been able to perform and gather data on thousands of biological reactions in only a few seconds permitting scientists to undertake previously impossible tasks such as decoding genes.

Modern biosensor design stresses technology integration and smart function for enhanced system performance. In essence, it is not a single technology or specific material that makes a biosensor smart or intelligent, but the synergistic interaction between the constituent components that comprise the sensory system. Seamless functional integration requires the development team to understand fundamental scientific and design principles derived from chemistry, physics, biology, material science, electronics and optics, and informatics. These seemingly diverse branches of science, engineering, and information science all provide unique perspectives on the meaning of "intelligent biosensors," their design, and potential applications.

This volume of *Smart Biosensor Technology* provides a multidisciplinary, multiple-author perspective of this rapidly evolving field. The scope of this book is to provide both the essential background to understanding biosensors and introduce new ideas of intelligent biosensor design and the leading-edge technologies used for realizing solutions in a wide variety of applications. This book is a collection of 23 chapters organized in five parts covering the fundamentals of smart biosensor technology, issues related to material design and selection, bioelectronics, and applications. The chapters are written by an international group of leading experts from academia and industry representing North America, Europe, and Asia.

Part I: Overview and Fundamentals

Part I is composed of six chapters that provide the reader with key definitions, and an overview of the fundamental functions and characteristics of smart biosensors. The discussion focuses on different perspectives of intelligence and how smart functions can be incorporated into sensors or sensor systems. The contributing authors represent a variety of scientific and engineering disciplines with backgrounds as diverse as engineering design, informatics, theoretical chemistry, and biological sciences. Topics include an introduction to the fundamental characteristics of smart biosensors, understanding and exploiting the intelligent properties of biological macromolecules, nanoscale optical methods for detecting single molecules, the design of BioFET sensors, the role that machine learning can play in analyzing biosensor data, and an introduction to innovative neural network biosensor designs.

Part II: Material Design and Selection I

Future advances in smart biosensors are dependent upon rapidly evolving materials that broaden bioreceptor selectivity, enhance sensitivity to diverse chemical compounds, enable biosensors to be seamlessly interfaced with the environment being monitored, and permit sensor system designs that have never been previously envisioned. This part contains four chapters that introduce and explore material-dependent technologies that will lead the development of functionally intelligent biosensors. Specific issues related to smart material design, molecular film assembly, nanostructured organic matrices, and biotic/abiotic interfaces are discussed in this part of the book.

Part III: Material Design and Selection II

Advances in microfabrication techniques have also led to the development of new biosensor designs and previously unheard-of technologies. This part presents three chapters that describe new nanotechnologies that will greatly change the functionality of biosensors, including porous silicon, carbon nanotubes and nanowires, and electrochemical biosensor designs that exploit innovative nanotubes.

Part IV: Bioelectronics

Bioelectronics is an emerging discipline that exploits the signal detection and processing capabilities of biological materials. In general, biomolecular electronics is defined as a technology that uses chromophore and protein molecules to encode, manipulate, and retrieve information at the molecular or macromolecular level. Biomolecular electronics provides an opportunity for product designers to create new hybrid technologies and computing architectures that can perform sophisticated information processing tasks faster and more energy efficiently. This part presents four chapters that explore the scientific basis of photoelectric biosensors, discuss the role of bacteriorhodopsin as a biophotonic material and its application to chemical sensing, how this bioelectric material can be used for color-sensitive imaging, and the design and fabrication of new bioelectronic sensing arrays on flexible substrates.

Part V: Applications in Detection and Monitoring

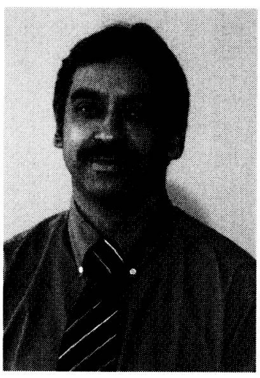
Although biosensor technology has been utilized over the past several decades, it was not until the introduction of new biomaterials and nanofabrication technologies that "smarter," more effective biosensors were developed. This part consists of six chapters that describe the application of biosensors to solving real-world problems in analyte detection and environment monitoring. The chapters include a discussion on how optical biosensors can be used for detecting foodborne pathogens, a multiarray biosensor is utilized for monitoring toxicity, aptasensors are used to detect allergens, and biosensors can be used for detecting and identifying viruses. The book concludes with a chapter that gives the contributing authors an opportunity to provide their viewpoints as to the future prospects of biosensor technology and innovative applications. It is hoped that this more speculative chapter will spur discussion and provide young researchers with insight on future directions. This presentation may also be of interest to individuals who wish to see a snapshot of views of a rapidly changing technology in the early part of the twenty-first century.

Editors

George K. Knopf is the associate dean (academic) in the faculty of engineering at The University of Western Ontario, and professor in the Department of Mechanical and Materials Engineering. He received his B.A. degree in humanities and B.E. degree in mechanical engineering in 1984, and then obtained his M.Sc. and Ph.D. degrees in 1987 and 1991, respectively, from the University of Saskatchewan.

Dr. Knopf's teaching and research interests lie in the general area of product design and manufacturing. His main fields of expertise are 3D shape reconstruction, adaptive geometric modeling, interactive data visualization, optical sensors and actuators, and bioelectronics. He has authored and coauthored numerous journal and conference papers, and coedited an IEEE Press volume entitled *Neuro-Vision Systems: Principles and Applications* and several SPIE *Proceedings on Optomechatronic Systems.* His recent work on an innovative three-dimensional scanning system has led to a US patent (No. 6,542,249).

He has acted as a technical reviewer for a variety of refereed journals, conferences, and granting agencies and has cochaired several international conferences. Over the past several years, he has been on the Canadian Advisory Committee (CAC) on Robots for Manufacturing Environment (TC 184/SC2) for the Standards Council of Canada (SCC).



Amarjeet S. Bassi is a professor of chemical and biochemical engineering in the faculty of engineering at The University of Western Ontario. He received his B.Tech degree in chemical engineering from the Institute of Technology, Banaras Hindu University, Varanasi, India in 1980, an M.E.Sc. degree in chemical engineering from the University of Saskatchewan in 1989, and a Ph.D. from the University of Western Ontario in 1993. He was a post-doctoral fellow at the University of California, Riverside, 1993 to 1994.

Dr. Bassi's teaching and research interests are environmental biosensor design and biocatalysis. His main fields of expertise are biosensors and nanosensors, enzymatic biocatalysis, and bioseparations. He has authored and coauthored over 75 refereed journal and conference papers, and several book chapters, and holds two patents on his recent work. Over the past several years, he has graduated a large number of M.E.Sc. and Ph.D. students and currently supervises a large group.

He has acted as a technical reviewer for numerous refereed journals, conferences, and granting agencies and has been involved in organizing several conferences, including the Canadian Conference in Chemical Engineering.

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George K. Knopf
Amarjeet S. Bassi

Contents