Preface

It is interesting to note that the first biosensor which emerged involved the use of an enzyme, while the most recent bioreceptor molecule is the aptamer. Therefore, the title and subject of this volume reminds us not only to look back to the history of biosensor development, but also to foresee the future of biosensors. We are really delighted to present this volume, even if it is true that a single volume cannot show all the progress in the biosensor development since it started. In this volume, therefore, after a brief introduction to the latest technology in biosensors, topical reviews are followed for the most recent advances in aptamer and enzyme biosensors. These contributions are by world renowned biosensor scientists and engineers who share their broad and deep experience and knowledge.

"Future of Biosensors: A Personal View" (Frieder W. Scheller, Aysu Yarman, Till Bachmann, Thomas Hirsch, Stefan Kubick, Reinhard Renneberg, Soeren Schumacher, Ulla Wollenberger, Carsten Teller and Frank F. Bier) gives a general overview of biosensors, which is a personal view on the future of biosensors. The chapter highlights that biosensors will be a very useful tool for decentralized and personalized online patient control or health check-ups in the future healthcare technology. They can also be widely used as a simple and rapid *on-site* measurement system, as a complement to the instrumental analysis methods, and for several applications including safety checks of drinking water and foods.

Since their first discovery in 1990, aptamers have received tremendous attention not only in academia but also from industrial sectors. During the last two decades, thousands of publications on aptamers or SELEX have been reported, numerous patents have been filed and granted, and several companies in pharmaceutical and diagnostic fields are now dealing with aptamers. Since the first FDA approved aptamer-drug (Macugen) entered onto the market, aptamers have become increasingly important as molecular probes for diagnostics and therapeutics. Especially, several advantages of aptamers, compared to natural receptors such as antibodies or enzymes, have attracted researchers to develop aptamer-based biosensors. Recently, various novel aptasensors have been developed from their intrinsic properties as nucleic acids, these show remarkable flexibility and convenience in the design of their structures. Moreover, a considerable understanding of aptamers' conformation and their ligand-binding properties combined with functional nanomaterials, such as gold nanoparticles or quantum dots, has led

to the emergence of a range of different styles of bioassay platforms. These issues are included in a different chapter of this book.

"Advances in Aptamer Screening and Small Molecule Aptasensors" (Gu and Kim) introduces the recent advances in aptamer screening methods, including a modified SELEX processes using graphene oxide (GO) from their own study, which enables aptamer isolation with higher affinity and selectivity through a less labor-efficient and time-efficient manner. This chapter also reviews aptasensors, especially for low-weight molecular targets, which have not been studied sufficiently, despite the increasing need in the fields of environmental monitoring, food safety, and defense and security.

In "Exploration of Structure-Switching in the Design of Aptamer Biosensors", Lau and Li review the recent progress on engineered structure-switching aptamer sensors. In this chapter, the authors introduce the origin and design of structure-switching aptamers and summarize their key applications for aptasensor development with the integration of fluorescent, electrochemical and colorimetric detection methods.

In "DNAzyme-Functionalized Gold Nanoparticles for Biosensing", Xiang, Wu, Tan, and Lu review the recent progress on analytical methods using DNAzyme and gold nanoparticles (AuNPs). In this chapter, various sensing methods using DNAzyme functionalized AuNPs are summarized. In addition, the intracellular applications of DNAzyme functionalized AuNPs are discussed.

In "Aptamer-Modified Nanoparticles as Biosensors" (Lonne, Zhu, Stahl, and Walter), the authors review both the utilization of aptamers in combination with various nanoparticles and discuss the analytical applications of aptamer-modified nanoparticles. Also, the authors address the medical applications of these aptamers in the detection of biomarkers and pathogens, cell targeting and imaging, and targeted drug delivery.

"Electrochemical Aptasensors for Microbial and Viral Pathogens" (Labib and Berezovski) summarizes the recent developments in electrochemical aptasensors for the detection of microbial and viral pathogens. In addition, the authors give a viability assessment of microorganisms, bacterial typing, identification of epitope-specific aptamers, and affinity measurement between aptamers and their respective targets.

Abe, Yoshida, and Ikebukuro also present electrochemical aptasensors in "Electrochemical Biosensors Using Aptamers for Theranostics", but this time focused on the theragnostics application, in which specific patients are selected for appropriate drug administration with diagnostics. The authors summarize the electrochemical aptamer-based sensing systems and discuss their advantages for theragnostics.

In spite of extensive advances in aptasensors, the market in biosensors is dominated by antibodies which are fully matured and standardized in the industry. One bottleneck in the commercialization of aptasensors is the isolation process of aptamers by in vitro selection which prevents widespread usages of aptamers. Only a limited number of aptamers are currently available. To overcome this issue, SELEX has been continuously advanced to make it simpler and quicker.

In addition, the understanding of whether any overarching rules govern aptamer functions is also important for optimal aptamer performance in assays and detection systems. Aptasensors are now starting to show their worth as a rival of traditional immunoassays in analytical fields.

In an effort to overcome the current limitations and expand the use of enzyme biosensors, many attempts have been made. This book describes some typical examples.

First, Lim and Kim in "Enzymatic Glucose Biosensors Based on Nanomaterials" describe the innovations in glucose biosensors that account for about 85 % of the entire biosensor market. Over the last few decades, glucose biosensors based on glucose oxidase (GOx) have played a pivotal role in simple glucose detection kits in blood as well as in vivo glucose monitoring, due to its mass production and easy availability. The major issues to be addressed in enzyme biosensors include the enhancement of biosensor performance such as sensitivity, selectivity, and detection range of analytes.

In "Cascadic Multienzyme Reaction-Based Electrochemical Biosensors", Yoon et al. describe a concept of cascadic multi-enzyme reaction employing more than two enzymes in the construction of biosensors to enhance their sensitivity and accuracy. They present fundamental principles for the development of electrochemical biosensors based on cascadic multienzyme reactions and their applications in clinical and environmental fields. Essential knowledge for the development of such biosensors includes a cascadic multi-enzyme reaction-based assay method and their multi-enzyme reaction mechanisms, electrochemical signaling principles, and multi-enzyme immobilization strategies. Obviously, a key step in the construction of biosensors is the immobilization process of enzymes that specifically recognizes the analyte. This crucial process is often limited by reduction in the catalytic activity of enzymes at the solid–liquid interface, which is related to the need for the biomaterial to be well-arranged on the surface, or within, an assembly. Furthermore, the number of biomolecules immobilized is connected to the sensitivity of the whole sensing device. This gives rise to the development of immobilization procedures which move away from simple mixing of the biocomponent with a matrix to methods allowing a layered and controlled deposition of the recognition element, resulting in multilayered architectures on the transducer surface.

In "Protein Multilayer Architectures on Electrodes for Analyte Detection", Feifel et al. present an overview of the methods available for arranging biomolecules in a layer-by-layer (LBL) design. Furthermore, applications in sensor construction are illustrated with the focus on electrochemical transduction. In particular, this chapter provides an overview of different assembly methodologies used for the construction of multilayer architectures with bio-molecules for application in sensors. The use of different building blocks is introduced for the formation of multilayers with a clear preference for polymers and nanoparticles.

Finally, as a new concept of enzyme biosensors, Arduini and Aminec in "Biosensors Based on Enzyme Inhibition" introduce a biosensor based on enzyme inhibition. The measurement of analytes can be performed by means of two

different approaches. If the enzyme metabolizes the analyte, the analyte can be determined measuring the enzymatic product. If the analyte inhibits the enzyme, the decrease in the enzymatic product formation can be measured and correlated to the analyte concentration. In this context, the authors describe the detection principle and the potential application of biosensors based on enzyme inhibition.

With a growing demand for sensitive and robust biosensors in the fields of healthcare, the environment, and bioprocesses, many advances in aptamer or enzyme biosensors are in high demand. In particular, the integration of new materials and nanotechnology with current biosensor technology will accelerate the development of new biosensors with greater potential. We hope that this volume provides some insight into the possible future developments of aptamer and enzyme biosensors.

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