

Chapter 11

Advances in Biosensors for In Vitro Diagnostics

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ABSTRACT

The array of tools available to the medical practitioner for diagnosis of disease has experienced extremely rapid expansion over the past decades. Traditional “blood chemistries” and hematological testing have been augmented with immunoassays for serological testing and PCR-based assays for genomic screening. Rapid, inexpensive point-of-care assays with enhanced sensitivity and specificity have the potential for altering the manner in which medicine is practiced; pharmacogenomics and the advent of “personalized medicine” permit the tailoring of therapeutic pharmacologic regimens to the genetic makeup of an individual. Facilitating this are novel biosensing approaches for in vitro diagnostics, developed at the interface of engineering, physics, chemistry and biology. New discoveries promise to sustain the high rate of growth of this important field of research and development. This chapter examines recent advances in techniques for biosensing and in vitro biomedical diagnostics, building on progress in materials science, nanotechnology, semiconductor devices, and biotechnology. The importance of this topic is motivated through the presentation of case studies of biosensing applications within various medical specialties.

INTRODUCTION

It is difficult to craft a precise definition of a “biosensor,” given that the concept of biosensing is very broad in scope, involving a wide range of implementations. At the most fundamental level, biosensors are devices which are capable of pro-

viding qualitative and/or quantitative information about biologically-relevant entities or components. These entities can span the dimensional scale from ions to complete organisms. For example, an optical probe which measures hydrogen ion concentration (pH) using colorimetric dyes can be considered a biosensor, used to detect and quantify urea or glucose. For that matter, an even simpler biosen-

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sor might consist of a strip of pH paper! At the other extreme, sentinel animals such as chickens may also be considered biosensors, frequently used to detect the presence of viruses and larger microorganisms responsible for epidemics of infectious disease over a large geographical region (Rizzoli, 2007). Indeed, the proverbial “canary in a coal mine” served as a sensor for toxic chemical species which could endanger life—a living “biosensor” used in centuries past.

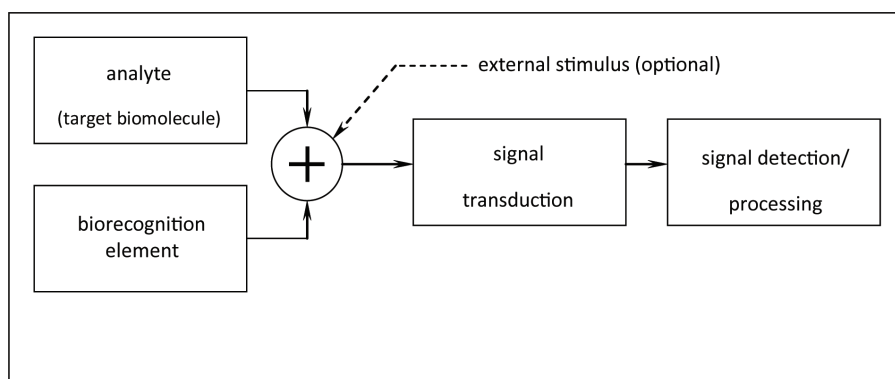
In this chapter, we will limit the scope of our discussion of biosensing, considering only sensors that are designed to identify and quantify the presence of biomolecular species of interest. In addition, we will focus our attention on sensors which perform measurements of an analyte outside the human body, so-called *in vitro* sensing or *in vitro* diagnostics. This is the type of sensing that a general practitioner may be interested in when drawing a blood sample from a patient in a family medicine clinic. In the discussion which follows, we will not address the type of sensing accomplished, for example, using a radioactively labeled “molecular probe” injected into the body and used to detect the presence of cancer using a PET (positron emission tomography) scanner. Although this *in vivo* approach to diagnostics based on biomedical imaging is of great interest, such techniques fall outside the scope of this chapter.

BIOSENSING TECHNIQUES AND EXAMPLES

It is helpful to develop a framework to organize a discussion of biosensors. The basic schematic block diagram of a biosensor is shown in Figure 1. The sensing platform typically consists of a molecule—often termed a “biorecognition element”—which has a particular affinity for another biomolecule to be detected (Prasad, 2003). Of the four principal families of organic biomolecules which contribute to life (proteins, nucleic acids, saccharides and lipids), proteins and nucleic acids have received a great deal of attention as biorecognition elements, given their high specificity of intermolecular interactions. Binding of the recognition element to a target biomolecule is transformed into a measurable signal via a transduction process; this process may be facilitated by an external excitation or stimulus. As an example, consider a target biomolecule which is tagged with a fluorescent molecule and bound to a biorecognition probe molecule immobilized onto a biosensor. In this case, an ultraviolet excitation signal might be used to excite a fluorescence emission which is sensed using a photodetector and transduced into an electrical current. The current is then converted to a detected voltage, processed and used for further analysis or display.

Biosensor implementations can be organized and classified using various schemas, based on the

Figure 1. Conceptual framework for biosensor implementation



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