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Review

Optical Biosensors for the Detection of Pathogenic Microorganisms

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Pathogenic microorganisms are causative agents of various infectious diseases that are becoming increasingly serious worldwide. For the successful treatment of pathogenic infection, the rapid and accurate detection of multiple pathogenic microorganisms is of great importance in all areas related to health and safety. Among various sensor systems, optical biosensors allow easy-to-use, rapid, portable, multiplexed, and cost-effective diagnosis. Here, we review current trends and advances in pathogen-diagnostic optical biosensors. The technological and methodological approaches underlying diverse optical-sensing platforms and methods for detecting pathogenic microorganisms are reviewed, together with the strengths and drawbacks of each technique. Finally, challenges in developing efficient optical biosensor systems and future perspectives are discussed.

Trends

Rapid and accurate pathogen diagnosis is important for saving lives from infection.

Various optical sensors have been developed for the detection of pathogens.

Microfluidic-integrated optical sensors are useful for point-of-care diagnostics.

Smartphone-based optical sensors provide a simple user interface for rapid sensing at reduced cost with ubiquitous capabilities.

Improvement is needed for more rapid, accurate, and multiplex sensing of pathogens.

Pathogenic Microorganisms as Causative Agents of Infectious Diseases

Pathogenic microorganisms cause various infectious diseases and even death. Despite early triumphs over infectious diseases with the development of vaccines and antibiotics, new and multidrug-resistant pathogens are continuously emerging [1]. Furthermore, current pathogen-diagnostic methods are inefficient and slow, especially in resource-limited regions, which remain hard pressed for appropriate solutions. Thus, there is a greater need for developing faster, more accurate, and multiplex diagnostic methods that do not require complicated and expensive assay steps.

Conventional culture-based assays, the gold standard method, are inherently time consuming and labor intensive. This problem is compounded by the expanding spectrum of pathogens, which markedly reduces the sensitivity of culture-based systems for detecting pathogens, causing serious healthcare problems throughout the world [2–4]. Thus, successful pathogen-diagnostic systems with enhanced multiplex capacity, sensitivity, selectivity, speed, and cost-effectiveness need to be developed to overcoming these problems.

Biosensors integrated with nanobiotechnology offer several advantages over conventional methods, including high-throughput screening, low limit of detection (LOD), real-time analysis, label-free detection, and the small sample volume required, among others. As nanobiotechnology advances rapidly, various types of binding receptors and ligands, physicochemical methods, and nanoplatforms have been exploited, creating novel strategies for enhancing detection performance. These biosensors hold great promise for addressing the analytical needs in practical pathogen diagnostics, as described below.

Various pathogen-detecting biosensors have been developed by using electrical [5], electrochemical [6], mechanical [7], nuclear magnetic resonance (NMR) [8], and optical-sensing [9]

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methods. Among these, optical sensors, especially colorimetric sensors, allow easy-to-use, rapid (within 15 min), portable, and cost-effective diagnosis. Additionally, plasmonic biosensors, which are also optical biosensors, offer superior sensitivity and multiplexing capability. These distinct advantages have led to the development of several ingenious optical sensors, some of which are currently available on the market (Table 1). Furthermore, optical sensors integrated with microfluidic system are under active commercial development, and some are ready to be launched on the market by several companies, such as LAMDAGEN. Furthermore, much effort has been exerted to develop smartphone-based system that have both a light source and a light detector, providing a simple user interface for rapid sensing at reduced cost. Thus, it can be envisioned that optical sensors will have increasingly important roles in pathogen diagnostics and point-of-care (POC) monitoring under various clinical and environmental settings.

Here, we review recent advances in optical biosensors for pathogen diagnosis, especially colorimetric and plasmonic sensors, and introduce technologies and strategies that constitute those optical biosensors with such sensing performances. Recent examples of optical biosensors are reviewed and their advantages and limitations are discussed. Finally, future perspectives on enabling strategies for the development of desirable biosensors with rapid, accurate, and multiplexing capability are provided. All the examples of optical biosensors, including those described here together with others that have been developed and used for the detection of pathogenic microorganisms are summarized in Table 2. Their advantages and limitations, together with strategies to overcome the latter, are summarized in Table 3.

Optical Biosensor: A Trend Toward POC Pathogen Detection

An ongoing trend in the area of pathogen diagnostics is the development of biosensor for POC testing. Some of the driving forces for developing POC systems include the increasing need for a patient-centered medical system and for more convenient, inexpensive, and efficient diagnostic systems applicable in underdeveloped and developing countries, and to eliminate the need for sample transportation for medical and environmental monitoring. Also, developing POC systems has become more feasible thanks to recent advances in technologies related to the integration of microfluidics and optics, the miniaturization of devices and communication, and the advent of simplified fabrication technologies, among others. The key advantages of POC biosensors include reduced test and therapeutic turnaround times resulting from immediate diagnostic test results, the reduction and/or elimination of sample transport, and reduced sample volume and data management, and easy integration with information processing [10]. Thus, the successful establishment of POC biosensors would enhance patient survival and treatment outcomes through rapid decision-making at the hospital bedside, in ambulatory care settings (including clinics and physician offices), and for acute care in emergency rooms. Also, applications can be easily extended to food, beverage, and drinking water safety testing [10–12]. It is desirable to develop POC sensors that allow rapid, label-free, multiplexed detection with high sensitivity and specificity, thereby improving healthcare through real-time and remote monitoring [10–12]. Various components for the development of advanced optical biosensors are illustrated in Figure 1. The following sections highlight some of the important optical biosensors that have been applied to pathogen detection. Also, recent trends in the integration of optical biosensors with microfluidics are described.

Current Optical Biosensors for Pathogen Diagnostics

Colorimetric biosensors are an attractive optical biosensor system because one can easily and instantly observe with the naked eye the presence of pathogenic microorganisms in the sample through a color change without the need for any analytical instrument. Colorimetric biosensor can be divided into two system formats: flat substrate based and solution based. Flat substrate-based sensors that generally use paper and glass are favored for their simple use and small volume of sample analyzed. As a representative example, some lateral flow assay (LFA)-based