

Biosensor Technology: Current Advances and Potential Applications

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Abstract

The development of various new kinds of sensors for the accurate detection of biomarkers in biological fluids and environmental samples are of greatest importance for the early diagnosis of diseases and to avoid the contamination of environment through pollutants, toxic and biohazardous materials. Sensitivity limits of biosensor have increased due to developments of new biological methods like tagging of fluorescence molecule with nanomaterials. Moreover, usage of peptide arrays, aptamers, antibodies, nucleotides and molecule fixed polymers, facilitate to improve advanced biosensors over conventional approaches. Several biosensors ranging from nanomaterials, polymers to microbes have broader potential applications. Generally, biosensor has been organized into several categories containing diverse sensing arrangements such as mechanical, optical and electrical transducers and modern biosensors use micro- and nanofabrication tools, as either label-free or labeled. This review provides an overview of recent developments and applications of biosensors in the fields of biomedical sciences and environmental monitoring, along with the better detection limit and improved sensitivity of the biosensors.

Keywords: Biosensors; DNA; Detection; Biomarkers; Drugs; Nanomaterials

Recently, Wang et al. (2018) have developed an effective controlled-release biosensor based on gold (Au) nanocages (AuNCs) capped

Introduction

In recent times, biosensor technologies have progressively expended for constant examining in numerous ways, such as synthetic and biological procedures used in clinical and industrial chemistry. In addition, use of biosensor is becoming common in the field of food analysis [1], environmental monitoring [2,3], bioterrorism [4], and in the field of medical sciences for monitoring the health and diagnostics [5-7].

A biosensor is used for the detection of an analyte that combines a biological component with a physicochemical sensor [8]. The basic compounds used in biosensor are nucleic acids, cell receptors proteins, antibodies, tissue, microorganisms, and enzymes, which interact with the analyte. Biosensors have great significance in the several areas like security, environmental monitoring, biomedicine, defense, drug discovery and food safety standards [9]. There is a great potential of biosensors, because it does not require sample preparation and therefore it is a tool for easy, rapid and cheaper measurements [10].

Detection of very low amounts of prohibited drugs such as cocaine in clinical fluids like serum continues to be important for many areas in the fight against drug trafficking. Rauf et al. [11] have detected the cocaine in human saliva and serum samples with great selectivity by using the aptamer-based sensor. In another study, Liu et al. [12] have constructed fluorescence based biosensor using 2-aminopurine (2-AP) and thioflavin T (ThT) as detection signal sources for the determination of microRNA-122 (miRNA-122). Measurements on cell lysates from 100, 1000, and 10 000 cells of three different cell lines, provided increasing signal ratios, which demonstrated the potential of the sensor for miRNA determination in actual samples.

Zhao et al. [13] have developed a label-free nanopore based biosensor for detection of DNA target, which uses hybridization chain reaction (HCR) approach for signal amplification. The developed biosensor has been shown a sensitivity of 30fM with a range from 0.1 to 10 pm with good application for real sample analysis.

with disulfide-containing DNA molecular gates for ultra-sensitive and highly selective detection of glutathione (GSH). The strength of GSH has been detected, which reached from 1.0×10^{-12} to 6.0×10^{-10} M.

Exploitation of biosensors in Diagnosis and Prognosis of Diseases

Due to world-wide prevalence of infectious diseases, there is an urgent need to develop a biosensor based diagnosis of infectious diseases to start effective and rapid treatment and to control the further spread of the diseases into the community. Existing laboratory tools and techniques (laboratory-based tests including microscopy, immunoassays, culture, and nucleic-acid amplification) are not high throughput for diagnosis of infectious diseases caused by bacteria, virus, fungi and parasites. However, it has well recognized limitations. Conventional microscopy and cultures methods lack sensitivity, are laborious and also time consuming. However, rapid immunoassay detection methods involving antigen and antibody based diagnosis are highly sensitive but challenging to implement in multiplex detection. While, nucleic-acid based diagnosis such as PCR, RT-PCR, and probe hybridization offer molecular specificity but have difficult sample preparation or laborious and requires skilled person to perform the test [14,15].

The development in biosensor technologies has great potential to carry point-of-care diagnostics over the conventional microscopy and cell culture based methods [15]. To avoid the delay in diagnosis, DNA based biosensors are one of major consideration because of sequence-

specific information is detected in a rapid manner compared to the conventional hybridization [16].

Li et al. [16] proposed a novel electrochemiluminescence (ECL) based biosensor for ultrasensitive detection of laminin (LN), in which DNA dendrimer (D) as a promising nanocarrier for luminophore and DNA nanomachine as approach for target recycling. The proposed ECL biosensor realized the ultrasensitive detection of LN with a linear range from 0.1 pg/mL to 100 ng/mL and a low detection limit was 0.0661 pg/mL. Remarkably, the application of this ECL biosensor would provide the great potential for analysis of other proteins, revealing a new way for early diagnosis and prognosis of numerous diseases.

Hong et al. [17] have developed, a convenient personal glucose meter (PGM) combining a catalytic and molecular beacon (CAMB) system with a cation exchange reaction for ultrasensitive platelet-derived growth factor BB (PDGF-BB) assay. It is the sensitive and rapid detection of PDGF-BB, a cancer-related protein that could have helped in early diagnosis, treatment, and prognosis of cancers. The enhanced signal of the PGM has a relationship with the concentration of PDGF-BB in the range of $3.16 \times 10^{-16} \text{M}$ to $3.16 \times 10^{-12} \text{M}$, and the detection limit was 0.11 fM.

Xiong et al. [18] have proposed, an ultrasensitive "off-on" electrochemiluminescence (ECL) biosensor for the determination of telomerase activity by using a self-enhanced ruthenium polyethylenimine (Ru-PEI) complex doped zeolitic imidazolate framework-8 (Ru-PEI@ZIF-8) with high ECL efficiency as an ECL indicator and an enzyme-assisted DNA cycle amplification strategy. The ECL biosensor demonstrated telomerase activity detection from 5×10^1 to 10^6 Hela cells with a detection limit of 11 cells. Furthermore, this method was applied in the detection of telomerase activity from cancer cells treated with an anticancer drug, which indicated the proposed method assumed potential application value as an evaluation tool in anticancer drug screening.

Wang et al. [19] have developed, a colorimetric based biosensor for DNA screening that is based on the conformational changes of the horseradish peroxidase (HRP)-mimicking DNAzyme. It has been used to screen elements from genetically modified organisms (GMOs) and covered more than 90% of all totally authorized events in the world. In addition, the colorimetric based biosensor is a rapid, portable and versatile tool for nucleic acids detection and diagnosis in the field.

A fluorescent carbon nanoparticle (FCN)-based lateral flow biosensor for ultrasensitive detection of DNA has been developed. After systematic optimizations of experimental parameters the biosensor has been found capable of detecting a minimum concentration of 0.4 fM DNA. This study provided a rapid and low-cost approach for DNA detection with high sensitivity, showing great promise for clinical application and biomedical diagnosis [20].

Zhang et al. [21] have developed a sandwich-type electrochemical immunosensor for the detection of C-reactive protein (CRP), in which, copper nanoparticles (Cu NPs) were used for signal tag and hybridization chain reaction (HCR) amplified output signal. The applied application of immunosensor has been evaluated by investigating CRP in actual human serum samples, the retrievals obtained were within 95.3%-103.8%, demonstrating the immunosensor possessed potential application ability for real disease diagnosis

Exploration of Biosensor in Tuberculosis Disease

Tuberculosis (TB) is a most contagious disease, which is caused by

Mycobacterium tuberculosis. The global incidence rate of TB is growing by 0.4% per year; however, the prevalence rate is much higher in South East Asia and Sub-Saharan Africa [22]. In 2014, there were about 9.6 million developing cases of TB (among which 12% were HIV-positive) and 1.5 million people died from the disease. The burden of TB is very high in the South-East Asia and Western Pacific regions where more than half (58%) of the world's TB affected population is found. India, China and Indonesia globally contributed for 23%, 10% and 10% of the total TB cases, respectively [23].

Delayed detection of tuberculosis disease due to lack of rapid detection methods and long duration of treatments/therapy, the patients develop multidrug-resistance tuberculosis (MDR-TB) and extensively-drug resistance tuberculosis (XDR-TB). The treatment of drug resistant TB has always been more difficult than the treatment of drug susceptible TB. Emergence of drug resistant TB remains a great risk to control the disease, mainly with the MDR strains. In 2014, about 3.3% of new and 20% of previously treated TB cases were estimated to have had MDR-TB and on an average 9.7% of MDR-TB patients had XDR-TB globally [23]. In such grave scenario, there is an urgent need to develop rapid, sensitive and cheap methods like biosensor techniques, required to early diagnosis of tuberculosis leading to better therapeutic.

Molecular typing of *Mycobacterium tuberculosis* has greatly enhanced the understanding of the population structure of MTB isolates and epidemiology of tuberculosis (TB). Microarrays-based spoligotyping has been used to characterize prevalent genotypes of MTB, for 80 isolates collected from primary health care facilities in Tanga, North-eastern Tanzania [24]. In another study, using an electrochemical technique has used the composite nanofibers with an immobilized DNA probe for the detection of *Mycobacterium tuberculosis*. The detection range of DNA biosensor was obtained from 10^{-6} - 10^{-9}M with the detection limit of $7.853 \times 10^{-7} \text{M}$ under optimum conditions. The results indicated that the composite nanofibers have a great potential in a range of applications for DNA sensors [25].

Bizid et al. [26] have developed a new redox oligomer "oligo-methoxy-phenyl-acetonitrile" (Fc-acid-OMPA) based biosensor. This biosensor has shown significant sensitivity to PCR of genomic DNA from *Mycobacterium tuberculosis*, and has also been able to detect a single mutation, which confers resistance of *M. tuberculosis* to rifampicin antibiotic [27].

Exploration of Biosensors in Environmental Studies

Yu et al. [28] have developed lead ions (Pb^{2+}) based biosensor. It is based on a target-triggered nuclear acid cleavage of Pb^{2+} -specific DNAzyme as a selectivity interface combined with Pd-Pt alloys modified Fe-MOFs (Fe-MOFs/PdPt NPs) hybrids acting as the signal tag. This biosensor has shown high sensitivity and selectivity for Pb^{2+} detection in naturally contaminated sewage and spiked drinking water samples. Furthermore, the developed biosensor could be utilized for the sensitive detection of Pb^{2+} , which indicated that it can be potentially used in field for environmental analysis and monitoring. Consequently, recommending a new modular platform for the construction of functional DNA nanomachines in the ultra-high sensitive analysis of promising biomarkers and toxic metals [27].

Cai et al. [27] have developed an electrochemical impedance biosensor for highly sensitive detection of Hg^{2+} which was made accessible by coupling with Hg^{2+} -induced activation of Mg^{2+} -specific DNAzyme (Mg^{2+} -DNAzyme) for target cycling and HCR connected DNA hydrogel for signal amplification. Under the optimal

conditions, the impedance biosensor has shown an excellent sensitivity and selectivity towards detection of Hg^{2+} in a concentration range of 0.1pM - 10nM with a detection limit of 0.042 pM. Additionally, the real sample analysis has shown that the proposed biosensor has capability of discriminating Hg^{2+} ions in reliable and quantitative manners, indicating that this method has a promising potential for preliminary application in routine tests [29,30].

Conclusion

Biosensors play a significant role in analysis of biomarkers from various sources i.e., humans, environments etc. The improvement of biosensors mainly relies on sensitivity, specificity, small molecule detection, non-toxicity, and cost-effectiveness. Currently, several kinds of biosensors have been developed ranging from nanomaterials, polymers to microbes. By taking advantage of this new biosensor platform, an extensive range of targets, involving proteins and nucleic acids, small molecules have been successfully detected with high sensitivity, selectivity and rapidly that may hold great potential for application in numerous fields. For the rapid diagnosis of infectious diseases, the developments of effective biosensors is the critical challenges, which need to be overcome in order to implement integrated diagnostic biosensors globally. In addition, translation of biosensors from research laboratories to clinical applications has remained limited to a few examples, such as the glucose sensor for diabetes.

Challenges to be overcome include sample preparation, system integration and matrix effects. Effective biosensors will not essentially function as a stand-alone detector, although will form an integral part of an analytical system. Development of compact and portable devices will constitute another forthcoming area of intensive multidisciplinary sensor research. Furthermore, for the detection of biomarkers in various life threatening diseases (infectious and non infectious) are remains a practical challenge for current research. Moreover, basic research is still essential to advance the sensor technologies, sensing strategies as well as analytical instrumentations and methods to develop cost effective and easy to use biosensors.

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