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Iron and iron-oxide magnetic nanoparticles as signal-amplification elements in electrochemical biosensing

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ABSTRACT

Growing demands for ultrasensitive biosensing have led to the development of numerous signal-amplification strategies. Based on their unique properties (i.e., electro-conductivity, bio-compatibility and ease of synthesis), various iron magnetic nanoparticles (MNPs) have proved to be an excellent nanomaterial for applications in electrochemical biosensing. This review shows how iron MNPs have made significant contributions in the development of electrochemical nanobiosensors, including immuno-, enzyme, DNA and aptamer types. More importantly, we discuss in detail different aspects of the electrochemical biosensors (e.g., modes of magnetic particles, detection techniques, analytes and the corresponding sensitivity and sample matrix, and several prominent characteristics). Accordingly, we discuss research opportunities and future development trends in these areas.

Contents

1. Introduction

1.1. Principles of biosensor function

Biosensing is based on immobilized biomolecules for detection and determination of target analytes. Such sensing biomolecules should be attached to the surface of a signal transducer. After interaction, the biological-recognition event generates an optical or electrical signal. Thus, biomolecule immobilization plays a crucial role in achieving biosensing with extended device lifetime. The substrate materials [e.g., electrodes, mesoporous materials, nanoparticles

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(NPs), nanotubes, and graphene (GN)] for biomolecule immobilization must be modified to introduce functional groups that are attached to biomolecules with high bonding strength, excellent long-term stability, biocompatibility, and high activity [1]. In general, a biosensor is an analytical device composed of two components, a bioreceptor and a transducer. First, the bioreceptor is a biomolecule that recognizes the target analyte, and, second, the transducer converts the recognition event into a measurable signal [2].

1.2. Electrochemical biosensing

Electrochemical biosensors combine the analytical power of electrochemical techniques with the specificity of biological-recognition processes [3–7]. The basic principle of electrochemical biosensors is that chemical reaction between immobilized biomolecule and target analyte produces or consumes ions or electrons, which affects the measurable electrical properties of the solution (e.g., electric current or potential). In biochemistry or electrochemistry, the reaction would generate a measurable current (amperometric), a measurable potential or charge accumulation (potentiometric) or alter the impedance (both resistance and reactance) of the medium between the electrodes [8].

2. Magnetic nanoparticles in electrochemical biosensing

2.1. Why nanoparticles?

The appearance of nanoscience is opening novel fields for the application of NPs in biosensing technology. NPs are of great interest in the world of nanoscience based on their physical and chemical properties. Such properties offer excellent prospects for chemical and biological sensing [9]. NPs were widely used in recent years as useful, sensitive tools for the electronic, optical, and microgravimetric transduction of different biomolecular recognition events [10]. NPs can therefore be seriously enhanced by incorporating them within biological systems. The signal enhancement associated with the use of NP-amplifying labels and with the formation of NP-biomolecule assemblies provides the basis for sensitive electrical and optical detection. Such procedures couple the extensive features of NP-biomolecule associations with sensitive electrochemical or optical transduction. In general, NP-based biosensors offer excellent potential for diagnostics and can have a deep impact upon bio-analytical applications.

2.2. Why magnetic nanoparticles?

The capability of magnetic NPs (MNPs) to provide biocompatibility is a benefit for the preparation of bio-(sensors). However, MNPs allow electron transfer between redox systems and bulk-electrode materials based on their unique properties (e.g., high surface energy and large surface area and functioning as electron-conducting pathways) [11]. MNPs have also established useful interfaces for the electrocatalysis of redox processes of molecules (e.g., H_2O_2, O_2 or NADH) involved in many significant biochemical reactions [12].

2.3. Why nanomaterial-based electrochemical-signal amplification?

With notable attainments in nanoscience, nano-sized material-based electrochemical-signal amplifications have excellent potential to improve both sensitivity and selectivity of electrochemical biosensors. It is recognized that the electrode materials play a serious role in preparing high-performance electrochemical-sensing platforms for detecting target molecules. Also, nanomaterials produce a synergistic effect for conductivity and biocompatibility to accelerate signal transduction but also to amplify recognition events with designed signal tags. Significantly, a great deal of research on preparing functional materials for electrode construction are extending the applications of electrochemical biosensors. For example, Walcarius et al. highlighted recent advances of nanostructured materials in the rational design of bioelectrodes and related biosensing systems [13]. The appeal of nanomaterials lies in their capability to act as an immobilization matrix and their exclusive features. These properties, combined with the functioning of biomolecules, contribute to the improvement of bioelectrode performance in terms of sensitivity and specificity.

2.4. Why iron-based magnetic nanoparticles in electrochemical biosensing?

The applications of NPs in biosensors can be classified into two categories according to their functions:

- NP-modified transducers for bioanalytical applications; and,
- biomolecule-NP conjugates as labels for biosensing and bioassays.

We intend to survey some major advances and milestones in biosensor development based upon NP labels and their roles in biosensors and bioassays for nucleic acids and proteins. Moreover, we focus on some of the key fundamental properties of certain NPs that make them ideal for different biosensing applications.

Electrochemical immunosensors, enzyme sensors, and tissue and DNA biosensors are designed through immobilizing on the working electrode surface biological-recognition elements of antibodies (Abs), enzyme, tissue and DNA, respectively [14]. The NPs could be immobilized on the surface of the transducers (e.g., physical adsorption, chemical-covalent bonding, or electrodeposition) for electrochemical-signal generation and amplification [15]. Iron-based MNPs provide a large surface area to immobilize as many biomolecules as possible, resulting in a lower limit of detection (LOD). Moreover, iron-based MNPs can play roles in concentration and purification. Iron-based MNPs are particularly efficient in detecting analytes in complex sample matrices, which may exhibit either poor mass transport to the biosensor or physical blockage of the biosensor surface by non-specific adsorption [16]. Iron-based MNPs can remove the need for sample pretreatment by centrifugation or chromatography, thus shortening the handling time [17]. Also, most iron-based MNPs, especially iron oxides, are biocompatible and non-genotoxic; they can be applied for simple adsorption of biomolecules, functionalized or encapsulated in polymers, metal or silica NPs, or carbon materials to enhance the biocompatibility and increase the functionalities [18]. Thus, iron-based MNPs provide a promising experimental platform for developing both types of electrochemical biosensor.

This review emphasizes more recent progress in electrochemical sensors, biosensors and immunosensors, based on iron and iron-oxide MNPs (i.e., in the period January 2014 to January 2015). The purpose of this review is to illustrate new progress in areas ranging from novel electroanalytical techniques to electrochemical-signal amplification based on iron and iron-oxide MNPs. We also attempt to introduce the significant development of electrochemical biosensors based on iron and iron-oxide MNPs. Therefore, based on the previous review articles [14,19] and selected research articles from January 2014 to January 2015, we comprehensively summarize various iron and iron-oxide MNP-based electrochemical biosensors including immunosensors, enzyme sensors, DNA sensors and aptamer sensors. More importantly, we discuss in detail different aspects of the biosensors (e.g., modes of MNPs, injection and detection techniques, labels, analytes and the corresponding sample matrix, and sensitivity). Consequently, we discuss several outstanding properties of the biosensors, research opportunities and the development potential and prospects.