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Review

Utilization of nanoparticle labels for signal amplification in ultrasensitive electrochemical affinity biosensors: A review

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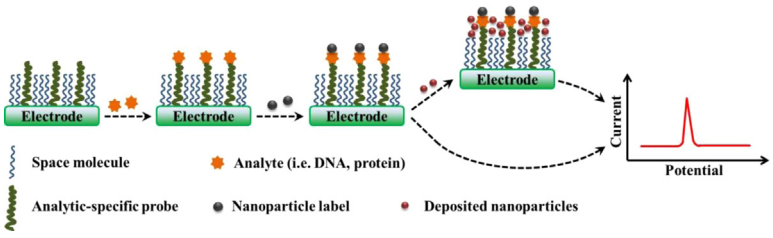
HIGHLIGHTS

- Basic principle of ultrasensitive electrochemical affinity biosensors for the detection of DNA and proteins.
- Applications of nanoparticles for signal amplification in electrochemical affinity biosensors.
- Principles of signal amplification strategies involving nanoparticles.
- Critical assess the potential drawback associated with each sensing strategy.
- Future perspectives for signal simplification in biosensors based on nanoparticles.

GRAPHICAL ABSTRACT



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ABSTRACT

Nanoparticles with desirable properties not exhibited by the bulk material can be readily synthesized because of rapid technological developments in the fields of materials science and nanotechnology. In particular their highly attractive electrochemical properties and electrocatalytic activity have facilitated achievement of the high level of signal amplification needed for the development of ultrasensitive electrochemical affinity biosensors for the detection of proteins and DNA. This review article explains the basic principles of nanoparticle based electrochemical biosensors, highlights the recent advances in the development of nanoparticle based signal amplification strategies, and provides a critical assessment of the likely drawbacks associated with each strategy. Finally, future perspectives for achieving advanced signal simplification in nanoparticles based biosensors are considered.

Contents

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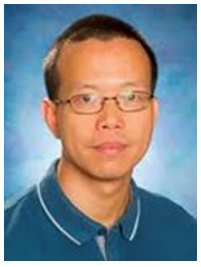

Dr. Jie Zhang is currently an Australian Research Council Future Fellow at the School of Chemistry, Monash University. Dr. Zhang obtained his PhD degree in electrochemistry in 2002 at the University of Warwick, UK. He has published 3 book chapters, 5 international patents and more than 100 refereed journal articles. His work has received more than 1500 citations with an H index of 25. Dr. Zhang has been awarded two medals from both the Electrochemistry Division and the Analytical and Environmental Chemistry Division of Royal Australian Chemical Institute for his contributions to electrochemistry and analytical chemistry.

1. Introduction

There is an increasing need for the development of simple, reliable and ultrasensitive biosensors with rapid response for the detection of DNA and proteins [1–4]. These biosensors are potentially highly beneficial for a range of key applications that include clinical diagnostics, detection of biological threats, drug screening, forensic analysis and environmental monitoring [5,6]. A wide variety of highly sensitive DNA and protein biosensors have been developed based on piezoelectric, optical and electrochemical detection principles [7–10]. Among all catalogues of biosensors, the electrochemically based ones are of particular interest due to their simplicity of fabrication, short response time, low cost, high sensitivity, high selectivity and amenability to miniaturization [11,12]. The general procedures involved in the fabrication of electrochemical biosensors and their application in the detection of target DNA/protein, when nanoparticle labels are used for signal amplification, are shown schematically in Fig. 1 and explained as follows:

Procedure (a): Immobilization of capture probes on the electrode surface at an optimal density

Exhibiting high selectivity towards the target analyte is the basic requirement for a biosensor. In order to achieve this goal, the surface of the electrochemical biosensor (an electrode) is modified with an analyte-specific probe, such as DNA (with the sequence complementary to that of the analyte DNA) or antibodies of the analyte proteins (protein affinity biosensors are therefore also called immunosensors), which can selectively capture the target analyte, such as a DNA molecule or a protein cancer biomarker. The density of the capture probe needs to be optimal in order to capture the maximum quantity of analyte. This certainly cannot be achieved when the density of the capture probes is too low. However, it cannot be achieved either when the density of the probe is too high, due to the spatial hindrance effect [13].

Procedure (b): Capture of a target analyte

The analyte will bind to the surface of a biosensor when it is placed in contact with analyte solution in cases where a high binding affinity of capture probes to the analyte applies. The relationship between the surface coverage of the analyte (θ) and its bulk concentration (c) can be described by the Langmuir isotherm (Eq. (1)) under ideal conditions where the surface is assumed to be homogeneous and the interaction between the analyte on the surface is negligible (Fig. 2) [14],

$$\theta = \frac{Kc}{1 + Kc} \quad (1)$$

where K is the binding affinity constant of the analyte used to capture the probe. In this case, the surface coverage vs log(c) curve has a linear range (the concentration range between A and B in Fig. 2) over 3–4 orders of magnitude for the analyte concentration.