



Electrochemical analysis based on bioaffinity

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Keywords Electrochemistry · Voltammetry · Immunosensor · Aptasensor

Electrochemical methods have been used in various analytical fields, such as environmental water and soil quality management, agriculture and food science, medical care, and energy industry, and are permeated in modern society. Recent progress in electrochemical analysis has been detailed in excellent review articles published in *Analytical Sciences* [1–4]. The integration of electrochemical analysis with nanoscience or bioscience is an effective strategy to develop sensors with high selectivity and sensitivity. Si et al. reported recent research trends of voltammetric sensing platforms for hormone analysis in a review paper [5]. This manuscript addresses the recent development of electrochemical sensors based on bioaffinity using antibody and aptamer.

Wash-free amperometric *E. coli* immunosensor using an IgG-immobilized graphene oxide/ITO electrode was developed by Park et al. [6]. This method uses a rapid and specific proteolytic cleavage by a cell membrane endopeptidase of *E. coli*. An amplified signal can be obtained using the electrochemical-enzymatic redox cycling of electroactive species produced from the peptide substrate. Jiang et al. reported a novel sandwich-type electrochemical immunosensor for *Listeria monocytogenes*, which is a foodborne pathogen that causes various lethal diseases in humans [7]. Graphene ribbons (GNR) were modified using primary antibodies *via* the π - π stacking of 3,4,9,10-perylene tetracarboxylic acid, and the analyte was determined by an amplified signal obtained from ferrocene/gold nanoparticles (Fc/Au NPs) modified using a secondary antibody. A sensitive immunosensor with a wide linear range of 10 – 2×10^4 CFU/mL and a low detection limit of 6 CFU/mL was developed. Feng et al. reported a sensitive label-free electrochemical immunosensor for α -fetoprotein

(AFP), which is an acid glycoprotein that accumulates in human plasma at high concentrations due to liver morbidity [8]. This immunosensor was fabricated by modifying the antibody on a hierarchically flower-like gold microstructures/polyaniline/reduced graphene oxide/Prussian blue (HFG/PANI/rGO/PB) composite electrode. This unique electrode-based immunosensor was able to accurately detect AFP in human plasma samples. Ghithan et al. investigated the physical and chemical properties of redox proteins adsorbed at different interfaces in a multilayer immunoassay assembly using a single-mode, electroactive, integrated optical waveguide (SM-EA-IOW) platform [9]. The electron-transfer rate of bound species of the redox-active cytochrome c (Cyt-C) protein was quantified. The proposed system is important for understanding the mechanisms of electron-transfer rate, affinity strength of molecular binding, and associated bioselectivity, and will be useful for developing novel and advanced immunosensors.

Nucleic acid and peptide aptamers have remarkably contributed to expanding the range and enhancing the performance of bioaffinity sensors [10]. An aptasensor using an electrode modified with a synergistic nanocomposite film composed of gold nanourchins (AuNU), oxidized carbon nanohorns (CNH), and chitosan was proposed by Kurup et al. [11]. This sensor uses the voltammetric signal from $[\text{Fe}(\text{CN})_6]^{4-/3-}$ as redox maker added to the solution. The principle of detection is that the lipocalin protein (LCN-2) to be analyzed binds to the aptamer modified on the nanocomposite electrode, resulting in an increase in the electrochemical signal due to the attraction of $[\text{Fe}(\text{CN})_6]^{4-/3-}$ to the electrode surface. LCN-2 has been detected in serum samples. Jin et al. reported a simple homogeneous aptasensor based on potential-assisted Au–S deposition for thrombin, which is a serine protease involved in the blood coagulation system of the body [12]. The potential-assisted Au–S deposition eliminates the premodification process of the aptamer on the electrode. A signal hairpin probe conjugated with tetraferrocene on both ends hybridizes with a thiol-modified probe *via* thrombin to

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generate a voltammetric signal. The detection limit was as low as 0.06 pmol/L and showed high specificity. A new method for detecting epidermal growth factor receptor (EGFR) gene mutation, which is an important therapeutic effect predictor of target drugs for nonsmall cell lung cancer, was developed by Weng et al. [13]. The hybridization–digestion cycle using λ -exonuclease (λ -Exo) was used to detect trace amounts of EGFR gene status. This technique can discriminate mutant and wild genes of EGFR with high specificity.

Electrochemical impedance spectroscopy (EIS) and electrochemiluminescence (ECL) are attractive and powerful detection tools for aptasensor development. Lasserre et al. developed the SARS-CoV-2 sensor based on EIS using a low-cost gold-coated polyester substrate [14]. Wannapob et al. reported EIS detection of non-Watson–Crick base pairs of DNA using DNA/mercaptohexanol mixed self-assembled monolayer on a gold electrode [15]. Li et al. achieved a sensitive detection of aflatoxin B1 by regulating the ECL of $\text{Ru}(\text{bpy})_3^{2+}$ by tuning the length of the DNA sequence between ferrocene and the luminophore of nitrogen-doped graphene quantum dots- $\text{Ru}(\text{bpy})_3^{2+}$ -doped silica nanoparticles [16]. Ding et al. reported a signal-on supersandwich-type DNA sensor based on the poly(aniline-luminol) nanowires (PALNWs) modified electrode and enhancement of ferrocene on the ECL of luminol [17]. Kitamura et al. reported a unique nucleic acid sensing based on an electrochemical molecular beacon (eMB), fabricated by modifying both ends of stem-loop structured DNA with ferrocene and β -cyclodextrin as electrochemical signal generators and quenchers, respectively [18].

Electrochemical analysis methods, such as voltammetry, EIS, and ECL, are essential techniques for developing biosensors that provide superior and realistic cost performance, and are convenient to use. This research field will continue to grow as nanoscience and bioscience advance.

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Schematic for the diversity of electrochemical analysis (left). Example of electrochemical analytical methods based on bioaffinity; overview of electrochemical hormone sensors using various bioaffinities (right) [5]

Electrochemical analysis in various fields

