Biosensors and Bioelectronics 94 (2017) 207–218

Contents lists available at ScienceDirect

Biosensors and Bioelectronics

journal homepage: www.elsevier.com/locate/bios

Quantum-dots-based photoelectrochemical bioanalysis highlighted with recent examples

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ARTICLE INFO

Keywords:
Photoelectrochemical
Bioanalysis
Quantum dots
Recent advances
Review

ABSTRACT

Photoelectrochemical (PEC) bioanalysis is a newly developed methodology that provides an exquisite route for innovative biomolecular detection. Quantum dots (QDs) are semiconductor nanocrystals with unique photophysical properties that have attracted tremendous attentions among the analytical community. QDs-based PEC bioanalysis comprises an important research hotspot in the field of PEC bioanalysis due to its combined advantages and potentials. Currently, it has ignited increasing interests as demonstrated by increased research papers. This review aims to cover the most recent advances in this field. With the discussion of recent examples of QDs-PEC bioanalysis from the literatures, special emphasis will be placed on work reporting on fundamental advances in the signaling strategies of QDs-based PEC bioanalysis from 2013 to now. Future prospects in this field are also discussed.

1. Introduction

With the ever-growing demands for ultrasensitive biomolecular detection, there have long been substantial efforts on developing new bioanalytical methods with different modalities (Liu et al., 2015a; Szunerits et al., 2012; Guan et al., 2015; Zheng et al., 2015; Sun et al., 2016). Among various techniques, photoelectrochemical (PEC) bioanalysis represents a recently emerged methodology that provides an exquisite route for innovative biomolecular detection with high sensitivity and specificity (Zhao et al., 2014b, 2015b). In a typical PEC bioanalysis, light is used as the excitation source and the electricity as the detection signal. Upon illumination, through properly steering of the energetic electron transfer in the rationally designed PEC nanobiosystem, the photo-to-electric conversion of the photoactive species could intimately associate with particular biorecognition events or biocatalytic transformations. When in presence of the biomolecular targets, the change of specific physicochemical factors related to the PEC nanobiosystem could induce the signal variation to reflect the studied biochemical information of targets concentrations. Compared with various optical techniques (e.g. fluorescent sensors, LSPR sensors, SERS techniques) that need complicated and expensive instrument, the utilization of an electronic readout makes instrumentation simpler, cheaper and easier to miniaturize. Besides, the separated energy forms between the excitation source and the detection signal would reduce the background signal of PEC bioanalysis, thus making it more sensitive than conventional electrochemical sensors. (Wei et al., 2011; Lisdat et al., 2013; Zhou et al., 2015a;). Due to its obvious advantages, PEC bioanalysis has been extensively studied for the advanced detection of numerous biochemical species of clinical and environmental significance (Zhang et al., 2013; Devadoss et al., 2015; Tang et al., 2015;).

Quantum dots (QDs), also called colloidal semiconductor nanocrystals, are semiconductor nanocrystals with unique photophysical properties that have rapidly come to the forefront of nanoscience and nanotechnology since their discovery in 1980s (Rossetti et al., 1983; Brus et al., 1983). In 1998, the debut of QDs for bioassay has inaugurated a new era in bioanalytical fields (Bruchez et al., 1998; Chan et al., 1998). The coupling of functional QDs with various biomolecules has opened almost unprecedented possibilities for novel fluorescent, spectroscopic, electrical and electrochemical bioanalysis (Xiao et al., 2014). In the early 2000s, QDs–biomolecule hybrid nanoarchitectures have initially been exploited for PEC bioanalysis, and these pioneering works then stimulated broad interest in using QDs as signal reporters or light-harvesting species for novel PEC bioanalysis (Willner et al., 2001; Curri et al., 2002; Pardo-Yissar et al., 2003; Vastarella et al., 2005). Among numerous photoactive species, QDs have excellent PEC activity, chemical stability as well as easy processability in size, composition and surface modification. In addi-

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http://dx.doi.org/10.1016/j.bios.2017.03.011
Received 12 January 2017; Received in revised form 25 February 2017; Accepted 6 March 2017
Available online 07 March 2017
0956-5663/

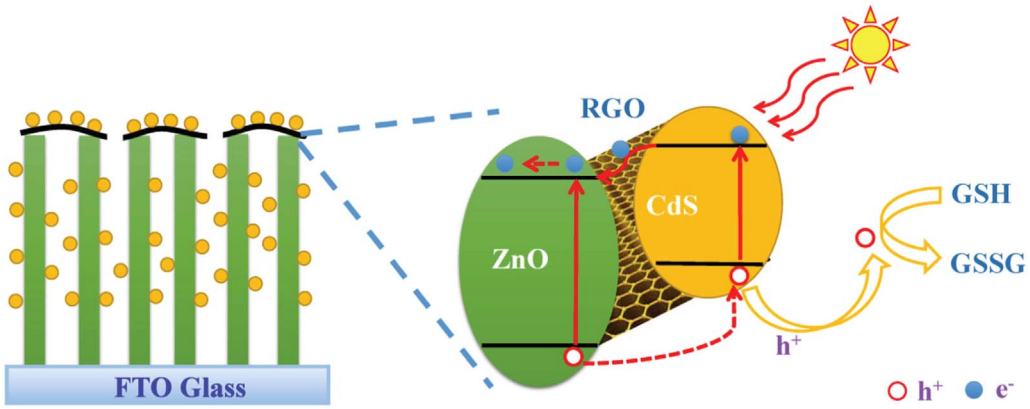

Fig. 1. Schematic illustration of the mechanism for the PEC detection of GSH (reprinted with permission from (Zhao et al., 2016a)).

tion, due to their comparable dimensions to many biomolecules and nanometer-size surfaces with advantageous physical properties, QDs could be easily applied as versatile building blocks for constructing various QDs-biomolecules architectures for elegant PEC bioanalysis. Despite these advantages, some hurdles still remain. For example, the commonly used inorganic QDs, mainly Cd-chalcogenide (CdC, C=S, Se, Te) QDs, suffer from the toxicity issues. The potential leakage of metal ions (e.g., Cd and Se) from the QDs may produce severe toxicity against many biomolecules and cells, and thus prohibit their specific application. In all, as evidenced by increasing academic articles, the impetus for advanced QDs-based PEC bioanalysis has still been growing much faster.

Given the rapid progress in this field, this review will cover the most recent advances in QDs-based PEC bioanalysis from 2013 to now. We earlier have summarized recent advances in the use of QDs for PEC bioanalysis (Zhao et al., 2016b). However, in choosing scholarly articles to contribute to this article, special emphasis was placed on the work reporting the important advances in the signaling strategies of QDs-based PEC bioanalysis. We want to remind our readers that this work is not intended to provide comprehensive coverage of QDs-based PEC bioanalysis development but rather to provide a clear and concise snapshot of the available depth of knowledge published in the past 3 years or so. Moreover, the authors have attempted to highlight the significant developments that inspire further works in this area. Such novel advances are important for the development of (QDs-based) PEC bioanalysis that open up new sensing avenues for future research. For readers seeking more information on the general principles about PEC bioanalysis, we recommend them to refer to other reviews for a broad scope in this area (Gill et al., 2008; Freeman et al., 2013; Yue et al., 2013; Zhao et al., 2013, 2014b; Zhou et al., 2015a). This work represents the author's subjective view of the important advances in the cited references, and some articles detailing important advances in the field may have been unintentionally left out. We sincerely apologize to the authors of QDs-based PEC bioanalysis publications that were inadvertently overlooked.

2. Recent advances from the perspective of signaling strategies

The applications of QDs for PEC bioanalysis are very dynamic, with increasing explorations in the development of various ingenious detection protocols with novel signaling strategies. Generally, for QDs-based PEC bioanalysis, the signaling strategies depend closely on how the biocatalytic/bioaffinity events interact with the QDs-based PEC nanosystems. They might be classified into the four main categories: (a) direct charge-transfer and how the bioaffinity events affect (b) the solution species, (c) the interfacial electron/mass transfer, and (d) the QDs associated electrode or QDs reporters.

2.1. On direct charge-transfer

Among the aforementioned four strategies, on direct charge-transfer is the simplest way for the QDs-based PEC bioanalysis. Namely, the direct redox reactions of the QDs toward biochemical species in solution enables the simplest PEC method for biomolecular detection. More specifically, in this strategy, photogenerated charge carriers communicate directly with the solution-solubilized electron donor or acceptor, leading to the changed photocurrent recorded as the signal. Numerous PEC bioanalytical studies on direct charge-transfer have been established for PEC detection of various biomolecules such as cysteine (CYS) and glutathione (GSH). CYS is a sulfur-containing nonessential amino acid that helps to fold and maintain a stable structure of protein, contributes towards enzymatic reactions and detoxification processes, and participates in numerous posttranslational modifications, while GSH is an important thiolated tripeptide and endogenous antioxidant that widely exists in the intracellular environment and its level associates with many diseases including aging and cancer (Tu et al., 2010, 2011; Long et al., 2011; Zhao et al., 2012d; Tang et al., 2013). Recently, Shen and Huang et al. reported the use of Au–SnO_2/CdS for PEC detection of CYS, in which Au NPs are able to trap electrons, improve the separation efficiency of electron–hole pairs and enhance the visible light absorption intensity. And the biosensor could achieved the CYS detection with a broad linear range from 0.4 mM to 12 mM and a low detection limit of 0.1 mM (Shen et al., 2014). Using optically transparent electrodes modified with S^{2-}-covered CdS QDs, Lin and Zhou et al. found that the weakly bound S^{2-} ions could be easily replaced by a sulphydryl-containing analyte, and the photocurrent decrease is proportional to the CYS concentration, and the linear range is 1.0–100.0 nM with a detection limit of 0.4 nM (Zhang et al., 2015). For GSH, N-doped graphene QDs/BiOBr nanohybrids has been used for the novel PEC detection of GSH (Yin et al., 2016), during which the GSH serves as the electron donor to the photogenerated holes and GSH is oxidized to glutathione disulfide (GSSG) in this process. As shown in Fig. 1, Zhang et al. proposed the use of CdS/RGO/ZnO nanowire array heterostructure for innovative self-powered PEC detection of GSH, and the sensor demonstrated satisfactory sensing performance of a wide detection linear range from 0.05 to 1 mM and an detection limit of 10 mM (Zhao et al., 2016a).

Glucose has also been used as model molecules. With CdS QDs modified CuO inverse opal electrodes, the PEC detection of glucose has also been reported (Xia et al., 2015). More recently, Xu et al. exploited the use of Ni/CdS/TiO_2 NTs array heterostructures for high performance PEC detection of glucose (Huo et al., 2015). Especially, Zhang et al. proposed a visible-light induced self-powered sensing platform based on a photofuel cell. As shown in Fig. 2, glucose in the anodic chamber is facilely oxidized on Ni$(OH)_2$/CdS/TiO_2 while H_2O_2 in the cathodic chamber is catalytically reduced by hemin-graphene, which