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Immunoassays

Current Advances in Quantum-Dots-Based Photoelectrochemical Immunoassays

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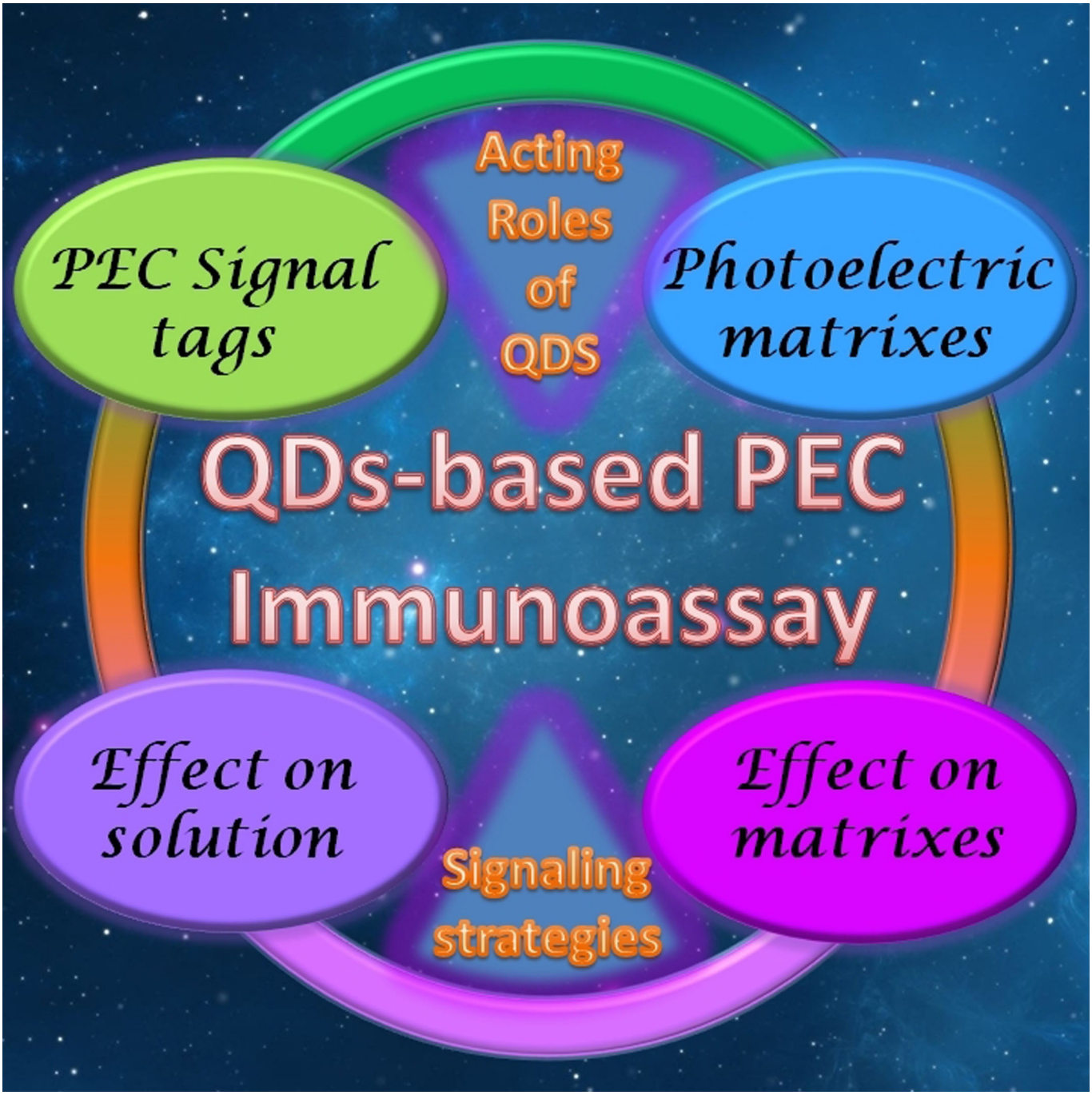

Abstract: As a newly developed technique, photoelectrochemical (PEC) immunoassays have attracted great attention in recent years because of their low cost and desirable sensitivity. Because the detection signal originates from the photoelectric conversion of photoelectric materials, the appearance and application of quantum dots (QDs), which possess unique photophysical properties and regulated optoelectronic characteristics, has taken the development of PEC immunoassays to new heights. This review concisely introduces the general mechanism of QDs-based photoelectric conversion for immunoassays and summarizes the current advances in QD applications in immunoassays. Given that signal strategies and photoactive materials are the key elements in PEC biosensor systems, we comprehensively highlight the state-of-the-art signaling strategies and various applications of QDs in PEC immunoassays to introduce advances in QDs-based PEC immunoassays. Finally, challenges and future developmental trends are briefly discussed

Introduction

In recent decades, with increasing emphasis on health, safety, and the environment, the requirement for new detection techniques with high sensitivity and universality is strongly demanded. The integration of photoelectrochemical (PEC) techniques with bioanalysis has inaugurated an innovative methodology for the assay of trace amounts of biological targets, such as small molecules, macromolecules, viruses, bacteria, and even cells.[1] In particular, as a vigorous technique based on specific antigen–antibody recognition and photoelectric effects, PEC immunoassays, with completely different types of excitation source (light) and detection signal (electricity) and evolved from electrochemical bioanalysis, exhibit many intrinsic advantages, such as a fast response, a low background, and high sensitivity.[2] Additionally, compared with traditional methods, such as mass spectrometry (MS), surface plasma resonance (SPR), quartz crystal microbalance (QCM), and spectral analysis, their independence from sophisticated instrumentation and complex operations make PEC assay devices portable and easy to miniaturize.

Colloidal semiconductor nanocrystals that contain 100 to 10000 atoms with dimensions between about 1 and 10 nm, also referred as quantum dots (QDs), were discovered in 1983 and boomed in the fields of optics, electronics, and catalysis, which has opened a new nanotechnology age.[3] The unique physicochemical properties of QDs are amenable to versatile modulation of their composition, size, and surface modification at the nanoscale. Coupling of QDs with biomolecules provide elegant routes for various advanced biological applications.[4] For example, Willner et al. initially explored a QDs–biomolecule nanohybrid for PEC bioanalysis in 2001 and this pioneering work gave guidance for subsequent various QDs-based PEC bioanalysis.[5] Specifically, QDs-based PEC immunoassays have gained substantial attention and gradually evolved into a new and important branch of bioanalysis. To date, QDs-based species exhibit the most extensive and versatile utilization in PEC immunoassays. Enormous progress in sensing strategies and PEC detection devices has also been achieved in immunoassays. However, to the best of our knowledge, a special review of the advances in the use of QDs in PEC immunoassay, with a particular highlight of signal transduction formats, is absent.

Because PEC signal generation and transduction within the QDs system, and the merits of QDs in the PEC process, have been summarized in detail in a previous report,[6] we limit our domain here to an introduction of the basic concept and principle of QDs-based PEC immunoassays and cover a crucial aspect, that is, signaling strategies, to summarize recent progress in the various applications of QDs in PEC immunoassays. The aim of this review is to provide a comprehensive understanding of the fundamentals of and advances in QD-based PEC immunoassays to promote the exploration of novel and advanced PEC immunosensors.

Mechanism of QDs-based PEC immunoassays

General PEC properties of QDs

Due to their unique optical and electronic properties, QDs have been widely applied in the biosensing field. Generally, the desirable features of QDs can be summarized as two aspects. First, QDs have large freedom to tailor their optical and electronic characteristics because their bandgaps are intimately linked to the size and composition of the individual nanocrystal, according to the Brus equation:[7]

$$E_g \approx E_{bulk} + \frac{(\pi h)^2}{2R^2}\left(\frac{1}{m_e} + \frac{1}{m_h}\right),$$

in which E_g and E_{bulk} represent the bandgap energy of QDs and the bulk semiconductor, respectively; h is the Planck constant and R is the QDs radius; m_e and m_h are the effective mass of an electron and a hole. In a certain range associated with the Bohr exciton radius, QDs exhibit a bandgap energy change compared with that of the bulk material, in which the conduction-band (CB) edge and valence-band (VB) edge shift to more negative and positive potentials, respectively (Figure 1A). Additionally, the photon acquisition, multiple-exciton generation, and electron transfer abilities will be improved because the

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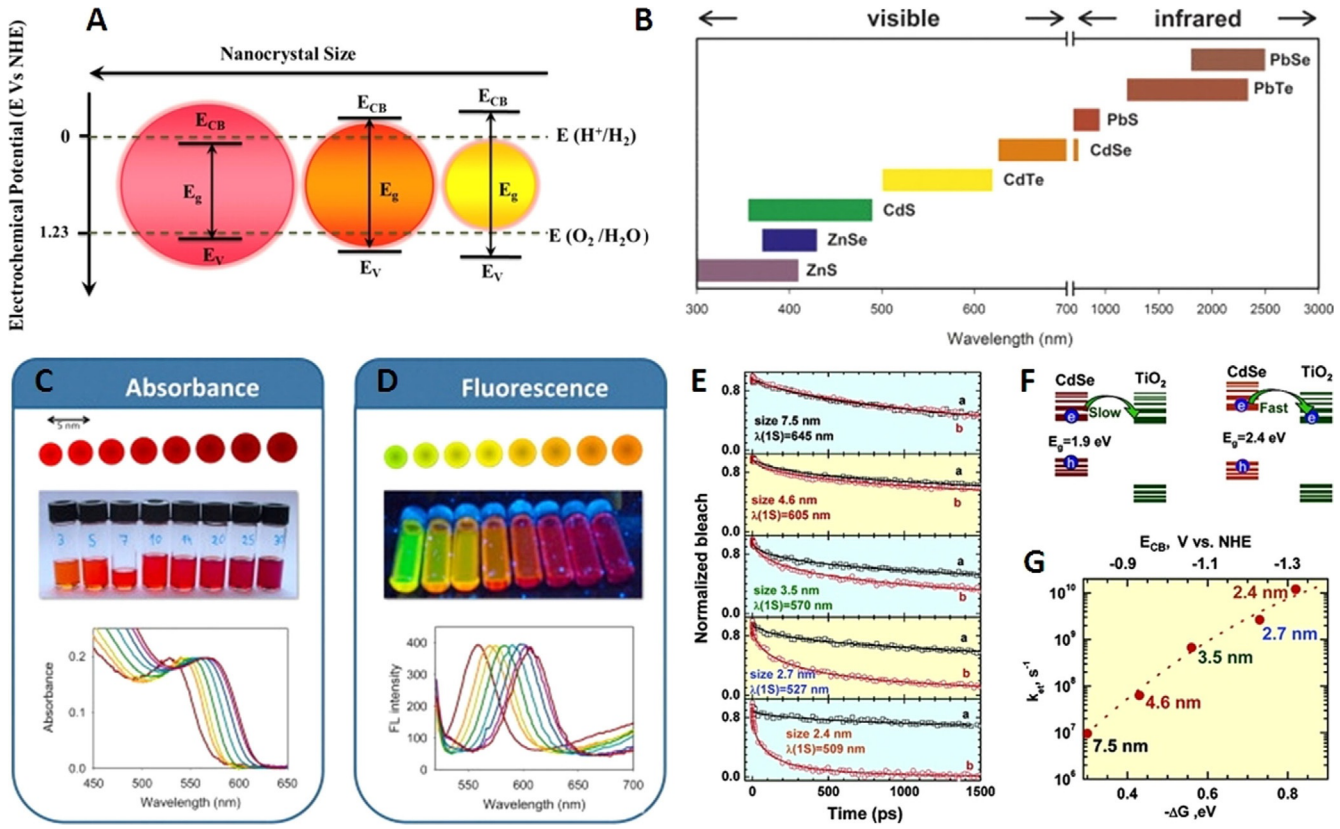

Figure 1. A) Quantum size effect in QDs.[6c] Reprinted with permission from Elsevier. B) Em wavelengths of QDs with various chemical compositions and C, D) the dependence of Abs and Em wavelengths on the size of CdSe QDs.[9] Reprinted with permission from Elsevier. E) The transient recovery of different-sized CdSe QDs a) without and b) with linked TiO_2 particles. F) Schematic illustration of electron transfer from CdSe QDs to TiO_2 and G) the relation between transfer rate and difference in their conduction bands.[11a] Reprinted with permission from the American Chemical Society.

energy level within the increased bandgap of QDs stimulated from the quantum confinement effect is discrete.[8] Their tailored properties are one of the most fascinating features of QDs in various fields. For example, the spectral range of absorption (Abs) and photoluminescence emission (Em) can be easily manipulated by the size and composition (Figure 1B–D), which is appropriate for biological probes.[9] One of the main purposes of QDs in PEC applications, such as PEC bioanalysis, photochemical water splitting, and solar cells, is to sensitize materials with large bandgaps (TiO_2, SnO_2, ZnO, or ZnS) to improve the efficiency of visible-light absorbance, charge separation, and charge transfer.[10] As a consequence of the narrowed size, the variation in free energy needed to migrate photoelectrons from excited QDs to the wide-bandgap semiconductor is reduced, whereas the thermodynamic driving force is enhanced, which significantly facilitates interfacial charge transfer.[6] Kuno et al. demonstrated that the driving force for electron migration originates from the energy difference between the CBs of the CdSe QDs and TiO_2 nanoparticles, and the transfer rate showed a dependence on size of the CdSe QDs (Figure 1E–G). As a result, the PEC response and incident photon to charge carrier efficiency (IPCE) could be modulated.[11] Second, QDs possess a high extinction coefficient and a large intrinsic dipole moment, which not only improve the light absorption but also accelerate the separation rate of photogener-

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ated charge carriers. Additionally, coupled with progressive surface engineering, QDs show excellent binding compatibility with biomolecules. Thus, regardless of whether they are used as a sensitizer for another wide-bandgap semiconductor or as a photoelectric material alone, QDs exhibit an excellent PEC response that offers unprecedented potential in PEC bioassays.

General principle of PEC immunoassays

Nowadays, lots of configurations for QDs-based PEC immunoassays have been proposed for different analytes. Ultimately, in one configuration or another, the general principles of assays are traced back to the transfer of biochemical information to a variety of specific factors on PEC-active species or their surrounding environment by a biological recognition system. Because a series of physical and chemical reactions would occur in the whole sensing system, the ingenious design of PEC systems and signaling strategies are the most significant features that define the overall performance of the PEC immunoassay. It is necessary to understand the basic instrumentation and the working principle fully. Given that recently developed methodologies are the current-mode PEC biosensors, other PEC biosensors reported earlier, such as light-addressable potentiometric sensor (LAPS), are not reviewed here. In general, a complete set of PEC immunoassay systems contains several indispensable components (Figure 2): biological species as target-recognition units (usually in intimate contact with the transducer), a light source, a PEC cell that contains a light-harvesting semiconductor working electrode (to generate the detection signal), a metal electrocatalytic counter electrode, a reference electrode, and a suitable electrolyte. The light absorbed by QDs with energy that exceeds their bandgap will effectively excite electrons transition from the VB to the CB. The photogenerated charge carriers migrate to the QDs surface and then to the electrode to generate a photocurrent or to the electrolyte solution to perform redox reactions. As soon as the electron–hole pairs form, a portion of carriers inevitably recombine with different ways. The magnitude, shape, and direction of the output photocurrent are affected by the contest between charge excitation, transfer, and recombination. Reasonable engineering of these processes by means of biological events

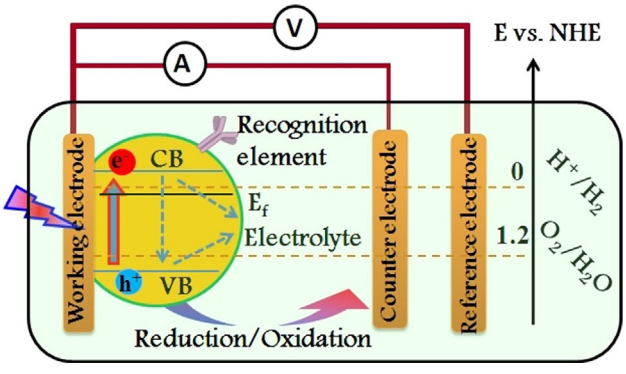

Figure 2. Schematic diagram of a typical PEC process in a QDs-based PEC immunoassay.

allows the photoelectrical signal to be scaled as a function of the target concentration. Consequently, various analytes, such as natural toxins, disease biomarkers, and cells, become detectable even in complicated samples.

Signaling strategies in QD-based PEC immunoassays

As the most extensive photoactive materials in PEC immunoassays, QDs can not only immobilize on the electrode to generate photocurrent, but can also be functionalized as signal tags conjugated with biomolecules. A considerable number of QDs-based PEC detection protocols with various signaling strategies have been studied.[12] These protocols can be categorized differently under different criteria, and each type covers the special function and scope of the strategies and shows its particularity. To understand and broadly catch most protocols with primary instances, this review expounds the signaling strategies for QDs-based PEC immunoassays from two perspectives: the influence of biological recognition events on the electrolyte solution composition and photoelectric matrices.

On electrolyte solution composition

Similar to photocatalytic water splitting, the ultrahigh reactivity of photoelectrons and holes can effectively react with chemical and biological molecules (e.g., enzymatic hydrolysate). Under light irradiation, the photoelectric conversion efficiency of QDs in the PEC system is heavily affected by the components of the electrolyte. The concentration of dissolved oxygen (O_2), ascorbic acid (AA), hydrogen peroxide (H_2O_2), glucose, or other biomolecules often have an obvious effect on the photocurrent because they act as donors or acceptors of charge carriers, and these species are also the reactants or products of common enzyme catalysis. Thus, the PEC response could be sensitively changed by the generation of donor or acceptor species from biological events. Enzymes, such as glucose oxidase (GOx), alkaline phosphatase (ALP), horseradish peroxidase (HRP), glucose dehydrogenase (GDH), acetylcholine esterase (AChE), fructose dehydrogenase (FDH), alcohol dehydrogenase (ADH), DNAzyme, and mimic enzymes, are often used as mediators to trigger the signal chain for PEC immunosensing systems.[13] Ge et al. proposed a facile dual-signal amplification PEC immunosensor for carcinoembryonic antigen (CEA) and α-fetoprotein (AFP) detection, in which CdS QDs-sensitized ZnO nanorods with improved photoelectric conversion efficiency were used as the photoactive matrix (Figure 3A). Then the H_2O_2 generated by the signal tags of GOx-functionalized nanoporous silver could scavenge the photogenerated holes, which amplified the photocurrent.[14] To improve the detection efficiency and accuracy, simultaneous detection by multiplexed biomarker proteins is significant. By using specific enzyme tags, Zhao and co-workers proposed a PEC immunosensor for the simultaneous assay of dual cardiac markers by using a CdS QDs-functionalized TiO_2 nanotubes electrode.[15] In a conventional PEC bioassay, the biorecognition event that occurs directly on the photoelectric materials and the intrinsic strong

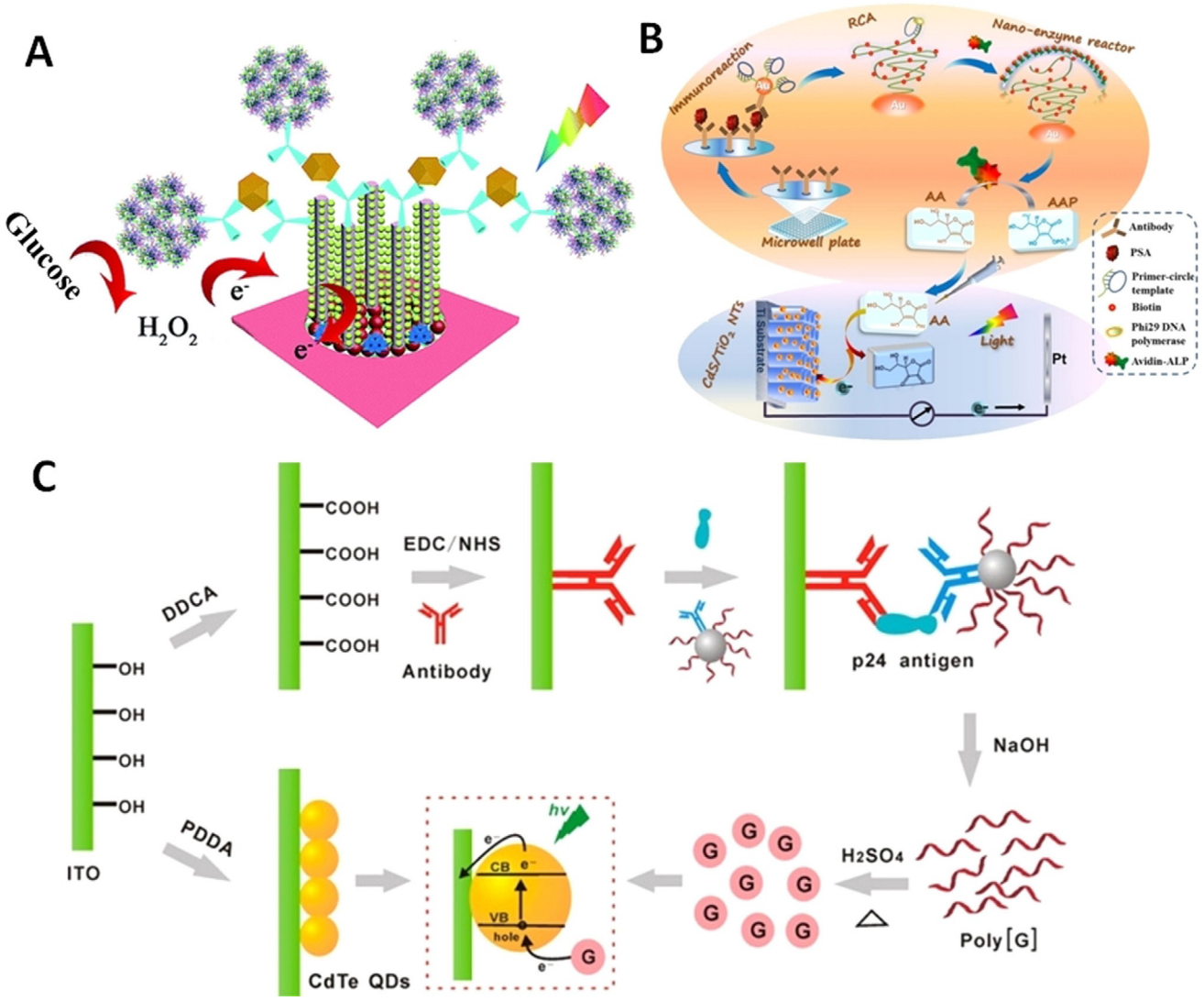

Figure 3. Schematic illustrations of PEC immunoassays based on the effect of biological events on the electrolyte. A) GOx-catalyzed signal amplification for a CdS QDs/ZnO nanorods based immunosensor.[14] Modified with permission from Elsevier. B) RCA reaction coupling ALP-catalyzed signal amplification of the split-type PEC immunoassay.[17] Reprinted with permission from the American Chemical Society. C) CdTe QDs-based PEC immunoassay with a poly[G]/S-NPs biological label.[16b] Reprinted with permission from the American Chemical Society.

oxidization of holes within the photoelectric materials inevitably impact each other.[16] Faced with this problem, our group proposed a split-type high-throughput immunoassay based on target-induced nanoenzyme-reactor-mediated hole trapping, as shown schematically in Figure 3B. AA, the enzymatic hydrolysate of ascorbic acid 2-phosphate (AAP), amplified the photocurrent of the CdS QD-modified TiO_2 nanotube array.[17]

Although enzyme-based signal amplification is the current mainstream strategy for immunoassays, enzyme-labeled probes are often inferior in stability and highly sensitive to multiple factors (pH, temperature, and solvent) in application. In addition to generation and consumption that alters the composition of electrolyte, the newly developed target-induced or -introduced release system has become another efficient signaling strategy. A typical example is the electroactive purine used for QDs-based PEC immunosensing. As shown in Figure 3C, by using CdTe QDs as an eminent photoactive material, Xu et al. developed a PEC immunoassay for HIV-1 capsid protein with poly(guanine)-functionalized Si nanoparticles as the biological label. The free nucleobases released from dipurinization of the introduced DNA were oxidized by the CdTe QDs and permitted a sensitive assay of the HIV-1 capsid protein.[16b] Obviously, compared with the formats of enzymatic labels, these labels not only exhibit advantages in cost and preparation, but also possess enhanced stability. In addition to purine, the PEC oxidation of other molecules, such as hemin and glucose, are also suitable for PEC immunoassay based on the above principles.[18]

On QDs-based photoelectric matrices

Because the photocurrent is generated from photoelectric matrices, the use of specific biological events to impact the photoelectric matrices directly is also a prevailing path for signal-

ing. In QDs-based PEC immunoassays, the photoelectric matrices are usually affected by photon absorbance, electron transfer, and photophysical/chemical properties of QDs.

Due to the large volume and natural insulation of most biomacromolecules and enzyme products, the presence of these molecules in the electrode interfacial region can result in significant steric hindrance. The formation of antibody–antigen, aptamer–target, and biotin–avidin complexes are the most common formats to produce steric hindrance, which is a simple but effect strategy to manipulate photoelectrical signals. The popular label-free QD PEC immunosensors usually rely on the hindrance effect. Typically, by using CdS QDs–Fe_3O_4 magnetic nanocomposites as photoactive materials, Wei et al. proposed a simple label-free PEC platform for the sensitive detection of aflatoxin B_1 (AFB_1). The formation of the immunocomplex increased steric hindrance, which blocked the diffusion of the sacrificial electron donor (H_2O_2) to the electrode and suppressed the scavenging of photogenerated holes.[19] As the first developed PEC biosensing strategy, label-free PEC protocols are relatively simple and universal for the detection of various analytes. Furthermore, label-free PEC protocols are quicker and cheaper than the conventional sandwich enzyme immunoassay technique. However, the analytical performance hardly suits the critical demands because of the limited analyte loading and inability to amplify the signal. Later, the improved steric hindrance effects were not only implemented with bioaffinity binding, but also employed catalytic amplification. For example, use of HRP or peroxidase mimetic catalytic oxidation of 4-chloro-1-naphthol (4-CN) in the presence of H_2O_2 to produce the insoluble and insulating benzo-4-chlorohexadienone is a typical strategy. This product not only exhibits obstruction to photon absorbance, but also isolates the photoactive species from electron donors and acceptors in the electrolyte solution. Zhang et al. used CdSe QDs/graphene to construct a PEC immunosensor in which the goat *anti*-mouse IgM and HRP-functionalized graphene oxide (GO) conjugate (GO-Ab_2-HRP) was used to amplify the signal.[20] Recently, our group proposed a "signal-off" PEC immunosensor that used Mn-doped CdS QDs-functionalized g-C_3N_4 nanosheets (Mn:CdS QDs/g-C_3N_4) as the enhanced photoactive material and combined DNAzyme-mediated catalytic precipitation signal amplification.[21] As shown in Figure 4A, numerous DNAzyme concatamers were formed after the initiator DNA label on the AuNPs triggered the hybridization chain reaction, which catalyzed 4-CN with a peroxidase-like activity to generate an insulating precipitate on the electrode surface and decrease the photocurrent.

QDs are usually first confined to the electrode surface by some affinity to generate or enhance the photoelectric signal. In contrast, the introduction or generation of QDs on the elec-

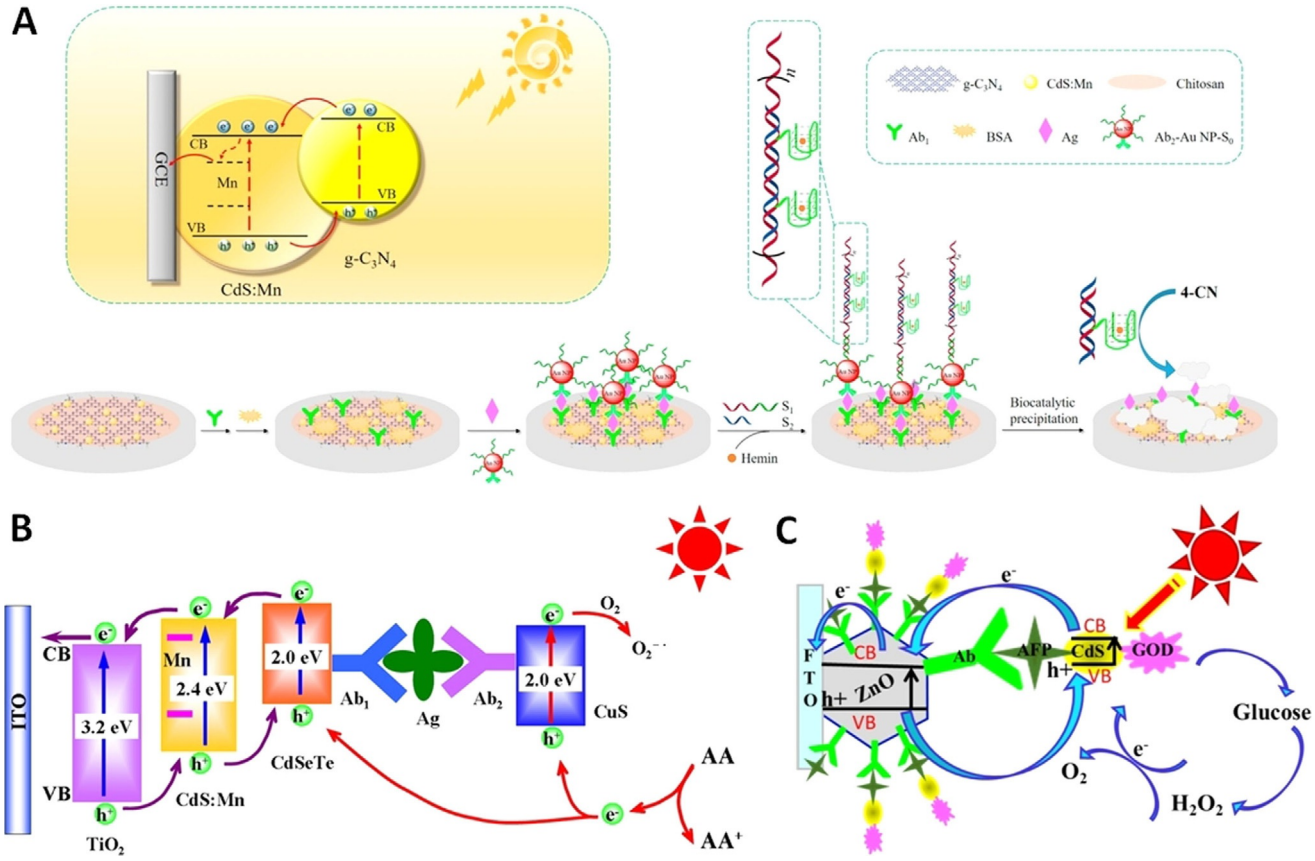

Figure 4. Schematic illustrations of PEC immunoassays based on the effect of biological events on photoelectric matrices. A) Mechanism of photocurrent generation and the immunosensing process.[21] Reprinted with permission from Elsevier. B) CuS QDs tag based PEC immunosensing platform.[23] Reprinted with permission from the American Chemical Society. C) ZnO-based PEC immunoassay with signal amplification by CdS QDs and GOx.[24] Modified with permission from Elsevier.

trode surface by biological events is also a feasible path. For the introduction of QDs to a PEC system, the QDs are generally functionalized as signal tags conjugated with biomolecules.[22] For example, because of the suitable matching energy between CdTe, CdS QDs, and TiO_2, the introduce of a CdSe QDs–antigen bioconjugate and the subsequent formation of a TiO_2/CdS/CdSe dual co-sensitized structure improved the photocurrent greatly by suppressing charge recombination. Zhu et al. used CuS QDs-conjugated signal antibodies as a signal amplification element to absorb photons competitively, consume electron donors, and hinder electron transfer, and thus an ultrasensitive "signal-off" PEC immunosensing platform was proposed (Figure 4B).[23] The different biomolecules loaded on QDs and acting as a signal element could achieve multiple amplification. Liu et al. reported a competitive immunosensor for sensitive AFP detection (Figure 4C), in which CdS QDs loaded with AFP and GOx were immobilized on the ZnO surface through an immunoreaction to improve its photoabsorption and charge separation.[24] Furthermore, H_2O_2 generated by the GOx catalysis of glucose scavenged the holes at the CdS QDs and further improved the photocurrent. These dual effects dramatically improved the sensitivity. By adopting a similar principle of CdTe QDs sensitization on TiO_2/CdS and cleverly designing immune recognition and DNA hybridization, Ju et al. proposed the first PEC proximity assay (PECPA) method for protein detection, as shown in Figure 5A.[25]

For the in situ generation of QDs strategy, one of the merits in immunoassays is a low background and high sensitivity. Zeng et al. proposed the in situ production of CdS QDs on GO for a PEC immunoassay of CEA, as depicted in Figure 5B.[26] The reaction of H_2O_2 and $Na_2S_2O_3$ was catalyzed by labeled HRP and produced H_2S, which subsequently reacted with the Cd^{2+} in the electrode. The photocurrent intensity of the generated CdS QDs is associated with the target concentration. Dai et al. generated CdS QDs on multifunctional TiO_2 mesocrystals based on a similar enzymatic reaction for the PEC immunosensing of AFP.[27] Additionally, Pavlov et al. used the catalytic hydrolysis of ALP to sodium thiophosphate to generate CdS QDs in the presence of Cd^{2+} and then applied it to PEC immunosensing by measuring the photocurrent of CdS.[28] Obviously, this type of signaling strategy usually constructs a "turn-on" QDs-based immunosensor. The opposite design, which harnesses biological events to cause damage to QDs, is a convenient option because the QDs possess high activity, particularly under light excitation. As shown in Figure 6A, Ju et al. developed a "signal-off" PEC immunoassay through tag-induced exciton trapping by using a CuO NPs-conjugated secondary antibody.[29] The dissolved Cu^{2+} from CuO NPs reacted with CdTe QDs under light irradiation, which produced trapping sites on the QD surfaces and reduced the photocurrent. Based on the ion-exchange reaction between Ag^+ and CdTe QDs-mediated hole trapping, we exploited a competitive-type immunosensor for AFB_1 detection.[30] Additionally, the in situ-generated enzymatic hydrolysates that react directly with the QDs and then trigger the PEC signal also have been exploited. The composite material of carbon quantum dots (CQDs)-functionalized MnO_2 nanosheets (MnO_2-CQDs) exhibits enhanced PEC activity because

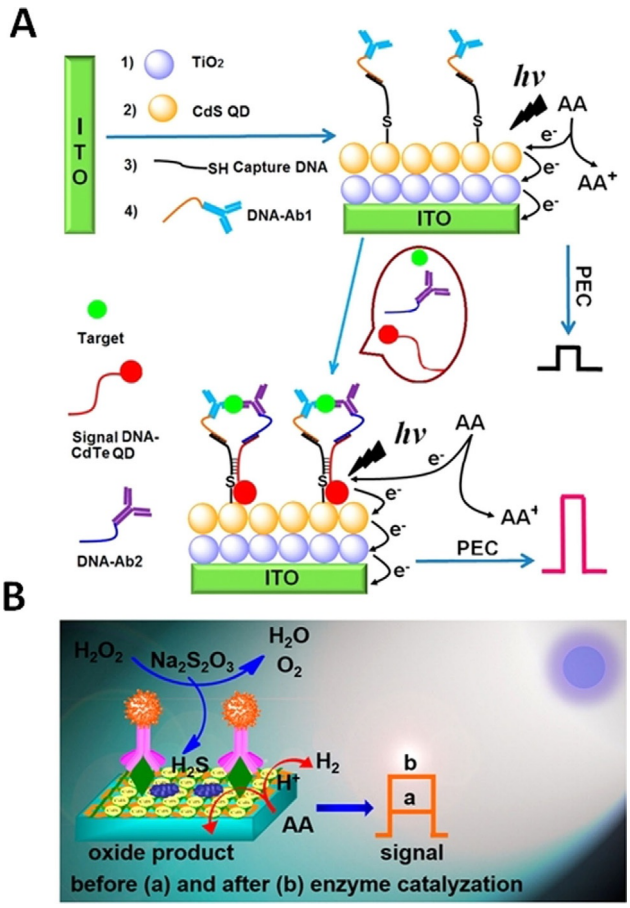

Figure 5. A) Preparation and mechanism of the PEC proximity assay.[25] B) Enzyme-catalyzed in situ generation of CdS QDs for a PEC immunoassay.[26] Reprinted with permission from the American Chemical Society.

the CQDs with excellent conductivity essentially enhance the charge separation. By using MnO_2-CQDs as photoelectric matrix, our group designed a novel PEC immunosensor for AFB_1 assay based on the enzymolysis product (H_2O_2) decomposition of MnO_2 nanosheets.[31] As demonstrated in Figure 6B, the labeled GOx oxidized the glucose molecules to generate H_2O_2, which dissociated the CQDs from the electrode by reducing/etching MnO_2 nanosheets. The photocurrent varied obviously with the concentration of AFB_1, with a detection limit of 2.1 pg mL^{-1}.

In addition, some noble-metal NPs have a wide absorption spectrum and a high extinction coefficient, and easily overlap with the emission of QDs. In such cases, exciton states in the QDs under light irradiation could be efficiently tuned through energy transfer under the effect of local electric fields that result from the plasma resonance of these noble-metal NPs at very short ranges, which changes the photocurrent of the QDs (Figure 7A).[13d,32] Biological events could serve as a facile mediator to control the interparticle distances between noble-metal NPs and QDs to manipulate the photoelectric signal. Xu et al. pioneered the energy transfer between CdS QDs and Au NPs as a powerful signaling format to exploit an advanced energy-transfer-based PEC bioanalysis protocol.[32a] Damping of the photoresponse by the energy transfer between CdS QDs and

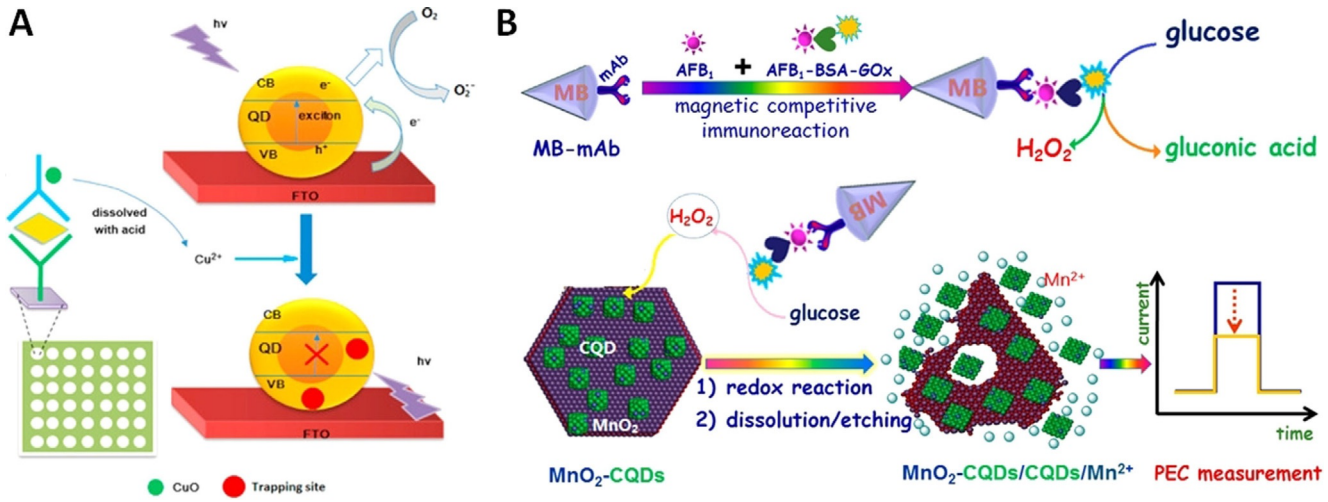

Figure 6. Schematic illustration of a PEC immunosensing platform. A) Cu^{2+}-ion-induced exciton trapping on CdTe.[29] Reprinted with permission from Elsevier. B) H_2O_2 etching of MnO_2 nanosheets.[31] Reprinted with permission from the American Chemical Society.

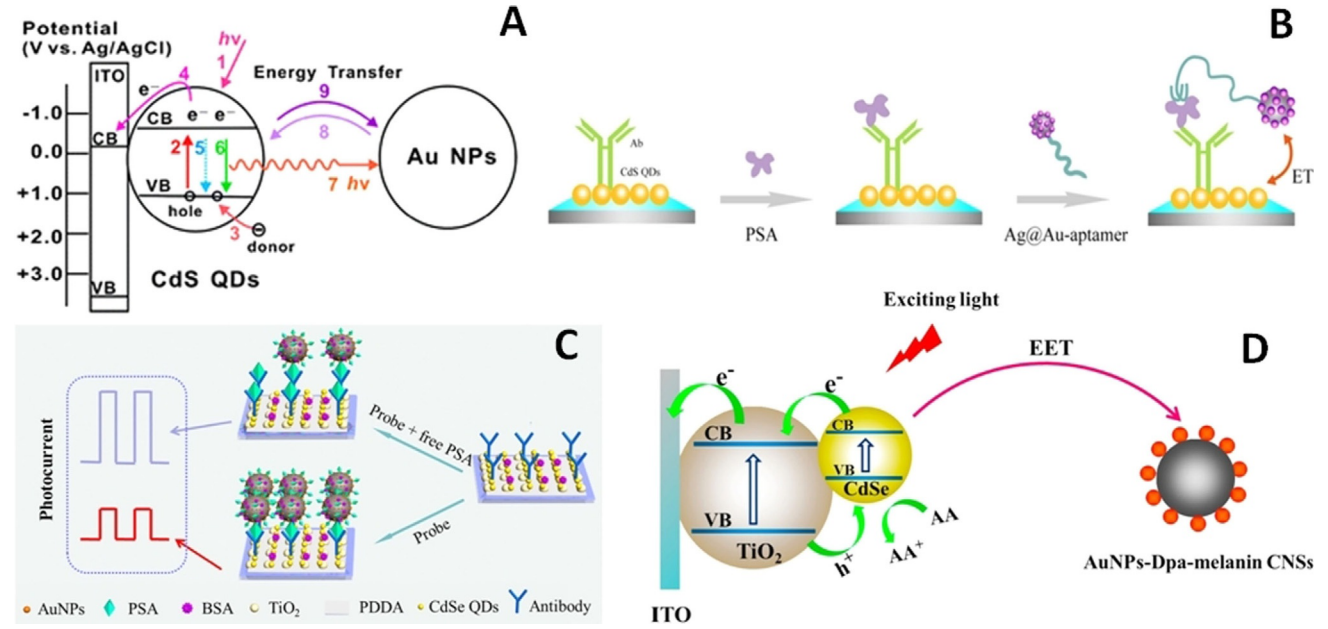

Figure 7. A) Interaction between excited CdS QDs and AuNPs.[32a] Reproduced with permission from the Royal Society of Chemistry. B)–C) Different immunosensing formats based on the energy-transfer effect.[34,35] D) The PEC mechanism of C). B)–D) modified with permission from Elsevier.

Ag NPs and Ag@Au nanostructures was also demonstrated.[33] Recently, they used Ag@Au core–satellite nanoassemblies functionalized with DNA as signal probes and CdS QDs as a PEC matrix to develop a novel energy-transfer-based PEC immunosensor (Figure 7B).[34] At the same time, Dong et al. designed a competitive PEC immunosensor for PSA assays based on the synergistic quenching effect of the steric hindrance and energy transfer, as shown in Figure 7C–D.[35]

Other new signaling strategies

With the rise of renewable energy conversion technologies, biofuel cells (BFCs), hybrid systems that combine electrochemical energy conversion with biocatalysis, have spurred enormous interest in biosensing. In particular, with the application of QDs-based high-performance materials, the poor detection performance of conventional BFCs based sensors is improving.[36] By coupling the dual conversion processes of light energy and chemical energy, Yu et al. proposed a novel and portable BFCs-based sensing platform for sensitive PSA assays with CdS QDs-sensitized TiO_2 nanorods as the photoanode.[37] Bilirubin oxidase (BOD), which acted as the biocatalyst, changed over the target concentration and subsequently resulted in a variety of output signals.

The essential physical light source in traditional PEC immunoassays no doubt complicates the detection devices and analysis process to a certain extent. Thus, the search for a suitable substitute for a physical light source is significant. Ju et al.

constructed a universal luminol-H_2O_2-HRP-*p*-iodophenol chemiluminescence (CL) system to excite an RGO-CdS QDs-based PEC immunoassay platform. The photocurrent of the CdS QDs remarkably relied on the amount of labeled luminol and HRP, which was associated with the target concentration. This work opened up a novel and convenient CL-excitation-based PEC platform for immunoassays.[38] Subsequently, combined with paper-based devices, microfluidics techniques, and digital multimeters (DMM), the development of various self-illuminated and portable PEC immunoassay platforms has attracted great interest.[39] For example, Yu et al. first incorporated a CL source and microfluidic paper-based analytical device (μ-PADs) to design a novel PEC immunosensor for point-of-care testing with a DMM readout.[40]

Conclusions and Perspectives

This review focused on the recent progress in the application of QDs in PEC immunoassays and describes the basic principles, the acting roles of QDs, signaling strategies, and novel PEC platforms in immunoassays. Tremendous achievements have been made in QD-based PEC immunoassays, however, some important issues are still waiting to be solved. First, only minor amounts of QD materials have been developed in current formats and most of them are toxic (Cd chalcogenide QDs), particularly those that contain heavy metals. Although C-based QDs are considered to be nontoxic and biocompatible substitutions for traditional QDs, the quantum yields/photoelectric conversion efficiency of C-based QDs are much lower than semiconductor QDs. Exploiting novel photoactive QD species with unique properties has the benefit of meeting diverse demands and provides more options for next-generation PEC immunosensors. Second, although some signaling strategies have been employed in QDs-based PEC immunoassays, their exploration is still in the initial stages. Third, the poor stability and reproducibility of the current PEC immunoassays are hardly comparable to those of commercial enzyme-linked immunoassays (ELISAs), which greatly limits their applications. In particular, the immobilization of biological molecules should be carefully controlled because nonspecific events on the sensing interface are an important cause of low reproducibility.[1] A great deal of effort should be devoted to overcome this problem. Finally, simultaneous multicomponent analysis and high-throughput immunoassays are particularly valuable for diagnostic screening.[41] However, related reports are rare.

Fortunately, along with the constant developments in science and technology, there are also great opportunities and bright prospects for the development of advances in PEC immunosensors and related devices based on QDs. By drawing on the progress and accomplishment of material science, many functionalized and nontoxic nanomaterials with high PEC activity and stability could be employed in PEC immunoassays. Moreover, by incorporating a recognition unit (nanobodies, protein receptors, or peptide aptamers) into the multifunctional nanomaterials with excellent biocompatibility may open paths into new areas for PEC immunoassays.[2a,42] By taking full advantage of novel manufacturing technologies, such as 3D printing and microelectromechanical systems, miniaturization and even ultrafine integrated processes and batch manufacturing with negligible differences can be implemented easily. Devices produced with different analytical formats can not only improve the reproducibility and stability, but also easily achieve portable and real-time monitoring. Furthermore, the incorporation of automatic technology into microarray platforms will hopefully solve the problems of achieving accurate and high-throughput assay for large quantities of complex samples.

Acknowledgements

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Keywords: immunoassays · photoelectrochemistry · quantum dots · sensors · signal transduction

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