

Recent advances in photoelectrochemistry-coupled dual-modal biosensors: From constructions to biosensing applications

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ABSTRACT

Precise and sensitive bioanalysis has been the major and urgent pursuit in pathologic diagnosis, food safety, environment monitoring, and drug evaluation. Photoelectrochemical (PEC) bioanalysis, as one of the most promising detection technologies, has rapidly expanded within the field of analysis. However, most of reported PEC analysis approaches still suffer from weak external anti-interference ability, high background, and the risk of false positive or negative errors due to their inherent single-signal readout. To overcome these shortcomings, new PEC-coupled dual-modal analysis approaches have been developed, where a dual-response signal can be derived through two completely different mechanisms and independent signal transduction pathways. This review introduces the basic principles of PEC biosensing and enumerates and classifies the substrate or probe selections, constructions, and applications of PEC-coupled dual-modal biosensors. Furthermore, the challenges and developmental prospects of PEC-coupled dual-mode sensing technologies are evaluated and discussed. We hope that this review will provide valuable insights into the latest advancements and practical applications of dual-mode PEC bioanalysis, which will be of great interest to those seeking to stay informed in this field.

KEYWORDS

photoelectrochemistry biosensor, electrochemistry, colorimetry, electrochemiluminescence, fluorescence, dual-mode detection

1 Introduction

In past decades, the dramatically increased requirements of biodetection drive to the development of a series of new analysis techniques. Specifically, there has been a significant surge in applying diverse amplification strategies into various detection techniques, such as electrochemistry (EC) [1], colorimetry [2], electrochemiluminescence (ECL) [3], fluorescence (FL) [4], and photoelectrochemistry (PEC) [5]. Among them, PEC analysis, which integrates the photovoltaic conversion process with sensor components, is a promising approach for investigating various biological interactions [6–9]. Essentially, similar to other developed analytical techniques such as ECL, the PEC technique can be seen as the next generation of EC methods [10, 11]. In PEC bioanalysis process, light is served as excitation source and the generated electrical signal is utilized as the detection readout. Benefiting from the two separate energy forms of excitation and detection, the PEC detection technology has higher sensitivity and reduced background compared with traditional EC and optical approaches [12, 13]. In addition, owing to the merits of simplicity, easy to operate, and miniaturization of the PEC devices, PEC assay technique has been quickly expanded within the field of analysis and applied for detecting wide-range objects, including metal ions [14], nucleic acids [15], proteins [16], and cancer cells [17].

Although significant progress has been achieved, most of reported PEC analysis approaches still suffer from weak external anti-interference ability, high background, and the risk of false

positive or negative errors due to their inherent single-mode readout [18, 19]. As described earlier, the detection mechanism of PEC technology is that the qualitative and quantitative analysis of targets is realized by monitoring the change of photocurrent intensity caused by certain biological interactions between identification components and their corresponding object analytes [20]. Due to the strong dependence on single-mode response of the PEC analysis, this determination is easily interfered by multiple factors, leading to abnormal fluctuations in photocurrent intensity. These distractions include different operators, nonstandard test processes, or diverse experimental environments, which may directly affect the accuracy of the result in some extent, especially for the detection of complex samples, such as blood or cell samples.

To solve the above-mentioned disadvantages for further improving the detection accuracy and confidence of the PEC analysis, two different schemes containing ratiometric assay and dual-modal detection have recently been proposed [9, 21]. For ratiometric assay, the wavelength-resolved or potential-resolved PEC ratiometric analysis, which employed one homemade electrode to produce two separated photocurrent signals, has been reported [14, 22]. However, for wavelength-resolved PEC sensing strategies, photoactive species are necessary, and the determination needs a continuous spectrum irradiation for the two photoactive substrates to generate two resolved photocurrents, which cannot be implemented in conventional PEC instruments

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[23]. As for potential-resolved PEC sensors, the requirement of two PEC active species with different photocurrent polarities to produce different PEC signals may barrier the generalized application of this type of PEC sensor [22]. In addition, signals crosstalk may still occur in PEC ratiometric assay under single-modal response when the distance between the two photocurrent signals is too close. In contrast to ratiometric assay, PEC-coupled dual-modal detection as another efficient method to reduce the external interference has been proposed recently, in which a dual-response signal can be derived through two totally different mechanisms and independent signal transduction pathways (light, electricity, and heat) [24, 25]. The combination of the PEC detection approach with another signal-transducing channel, such as EC [26], colorimetry [27], ECL [28], and FL [29], to construct dual-mode sensing platforms provides more flexible and optional tools for different samples. This approach not only empowers the inherent properties of each mode but also provides mutual authentication of detection results. Therefore, the PEC-coupled multi-mode sensing platforms have been the focus of investigations in analysis field, which can be endowed with more accurate results and fewer probabilities of false negative/positive assay than traditional single-signal assay strategies [30, 31]. Currently, the majority of reviews on PEC sensors either focus on a single type or class of photosensitive substrates and signal amplification strategies, or solely on the potential applications of PEC in different target analytes detection [32–34]. Up to now, there is limited systematic review published focusing on the construction and application of PEC-coupled dual-modal response sensing platform.

In this review, we summarized the recent progress in PEC-coupled dual-modal biosensors (Fig. 1). Firstly, the basic theory, properties, and advantages of the PEC biosensors were discussed. Next, we enumerated and classified the multimodal responsive matrixes or probes used to construct PEC-coupled dual-modal biosensing platform, followed by the recapitulation of different types of PEC-coupled dual-modal biodetection methods, including PEC-EC, PEC-colorimetry, PEC-ECL, and PEC-FL. Furthermore, the applications of these PEC-coupled dual-modal biosensors were exhibited, and the major challenges and future prospects were deliberated.

2 Basic principle of the PEC biosensor

So far, multiple configurations have been developed for PEC detection to satisfy different analytes of interest. In general, two vital elements are essential for PEC sensor: the photoactive substrates (transiting the light into electric signal) and the biological recognition components (converting the reaction signals into electrical signals under recognition process). In PEC sensing system, the design and fabrication of photoactive substrates with excellent photoelectric conversion efficacy and biocompatibility are necessary [35]. These photoactive species play a crucial role in the successful construction of the sensor, as they directly influence the amplitude of the photocurrent signals and ultimately determine the PEC sensitivity. Various photoactive materials have been designed and utilized for detecting target compounds across different fields, which are typically classified into various classes, including single semiconductor species [36], heterojunctions-based substrates [37], dyes-sensitized semiconductor [38], and metal matrix materials [39]. Under irradiation, these substrates can capture light photons and generate electron transitions, creating electron-hole pairs that provide the necessary energy for redox reactions. The electrode surfaces have then been immobilized with recognition elements. Once the recognition elements bind to their target analytes, a change in photocurrent occurs, enabling the quantification of the targets (Fig. 2(a)). Similar to numerous other biodetection approaches, the biological recognition components consisting of antibodies [40], polypeptides [41], nucleic acids [42], and molecularly imprinted polymers (MIPs) [43] are the key to realize the detection specificity of biosensors (Fig. 2(b)). Specifically, nucleic acid aptamers have been widely applied in constructing various types of PEC biosensors, benefiting from their high specificity, ease of synthesis, and reversibility. The PEC equipment consists of three parts: an excitation light source, a detection cell (containing electrolytes and three-electrode system), and a signal collecting device (such as electrochemical workstation) (Fig. 2(c)). The working electrode is first coated with various organic/inorganic photoactive species functioning as the photo-electric transducer to transition the light into electric signal, followed by the electrical output recorded by the electrochemical workstation. Owing to the direct photocurrent signal generated by photoactive materials, there is no requirement for the inclusion of

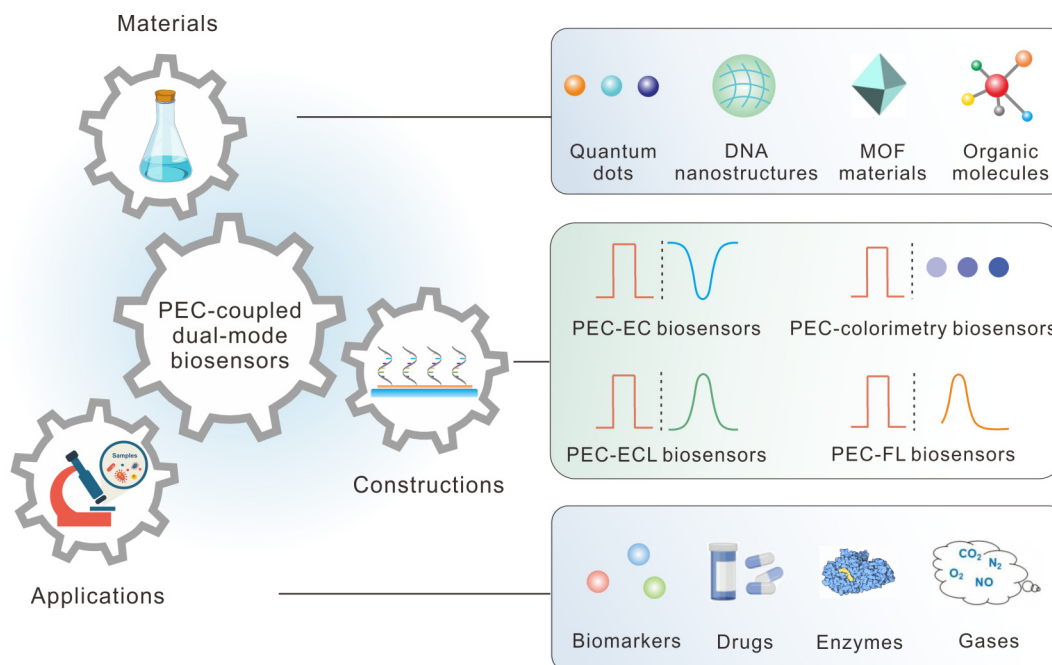


Figure 1 Schematic illustration of the materials, constructions, and applications of PEC-coupled dual-modal biosensors.

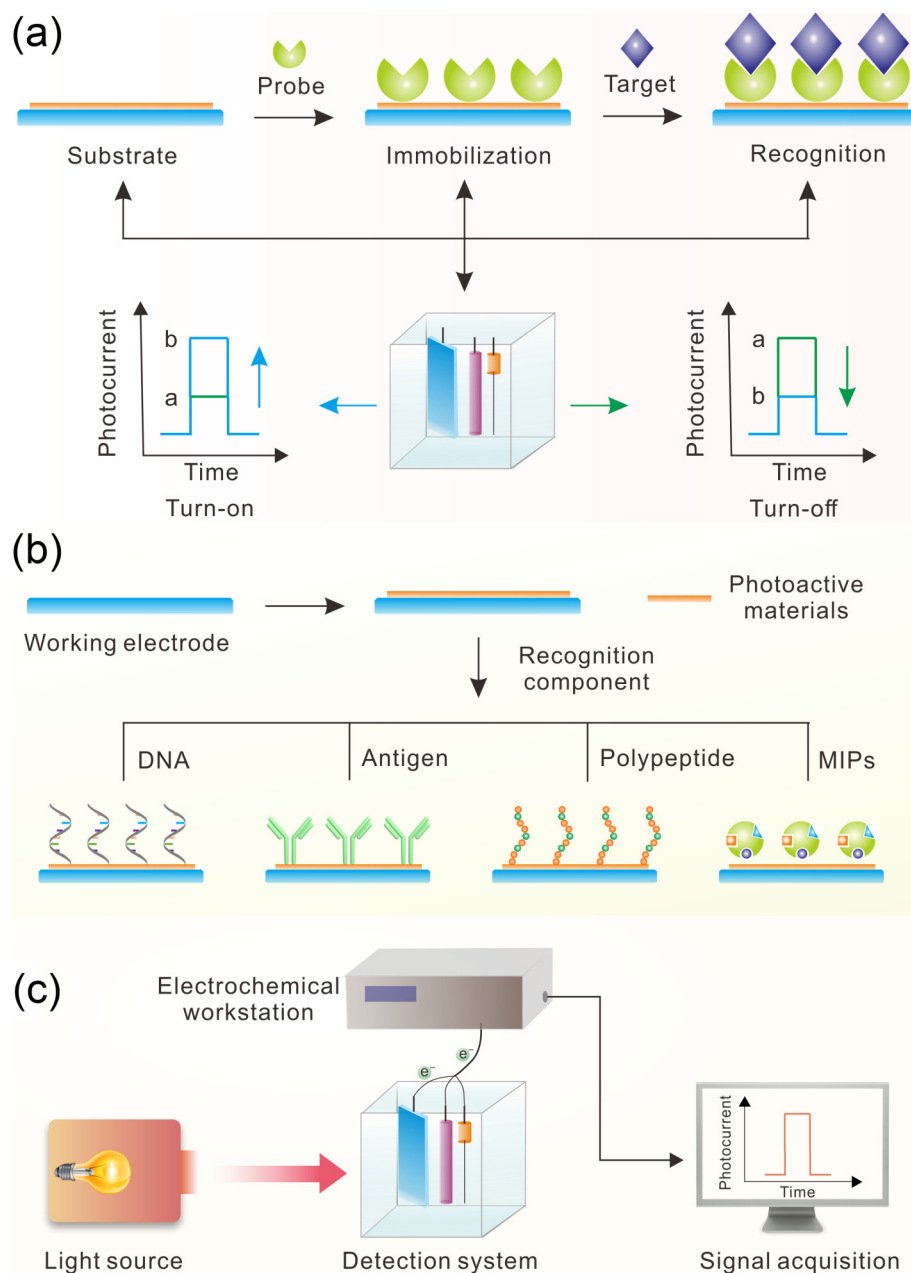


Figure 2 Schematic of (a) the general principle, (b) recognition elements, and (c) devices of PEC analysis.

additional signal transduction device. After further assembling the recognition elements on the walking electrode, the PEC detection is operated by monitoring the changes of photocurrent/voltage intensity before and after the interactions between recognition elements and corresponding objects through three electrodes system. This allows for the detection of biochemical information, such as analyte concentration, by observing changes in specific factors associated with the photoactive materials on or around the electrodes. When exposed to light, the transducer transforms the physical–chemical interactions between the biological recognition systems and photoactive materials into a current signal.

3 Multimodal responsive matrixes or probes used in PEC-coupled dual-modal biosensing platform

Multimodal responsive matrixes or probes which can respond to multiple stimuli and produce different output signals are essential components in PEC-coupled dual-modal biosensing system. With the advancement of nanotechnology, transducers such as

quantum dots (QDs) [44], DNA assembled nanostructures [45], metal-organic framework (MOF) materials [46], and multifunction organic small molecule probes [29] have exhibited significant potential in the development of dual-mode biosensors. These transducers have the capability to produce detectable signals by engaging in direct or indirect interactions with target analytes and receptors. For instance, QDs (including CdS, CdSe, and CdTe) have excellent FL properties and adjustable luminescence wavelength, making them ideal FL and ECL probes [47, 48]. By combining quantum dots with biomolecules (such as antibodies, DNA, or RNA), highly sensitive and selective detection of specific molecules can be achieved [49]. Meanwhile, QDs with high photoelectric conversion performance also play a crucial role in the development of PEC-coupled dual-modal biosensing platforms [50, 51]. DNA assembled nanomaterials have highly controllable structural characteristics and diverse functionalization potential [52, 53]. By introducing specific functional molecules such as fluorescent dyes and photoactive or electroactive molecules onto DNA nanostructures, specific FL, PEC, or electrochemistry functionalities can be imparted [54, 55]. Besides, MOF materials have the advantage of highly tunable pore

structures and surface functionalization capabilities, making them suitable as carriers or catalysts [39]. By introducing photosensitive or electroactive molecules into the pores of MOF materials and achieving specific interactions with target molecules through surface functionalization, the enhancement and amplification of PEC and EC signals can be realized, significantly improving the sensitivity and detection limit of dual-mode sensing [28, 56]. Moreover, some organic small molecule compounds and conjugated polymers with larger π -conjugated systems have significant potential applications in the fields of EC, PEC, and FL detection [4, 29, 57]. These materials possess high absorption coefficients, enabling them to effectively absorb light energy. Additionally, due to the flexibility of organic structures, their EC, PEC, and FL properties can be further optimized by adjusting the length of the conjugated system and introducing different functional groups, thereby enhancing their detection performance.

4 Construction of PEC-coupled dual-modal biosensors

4.1 PEC-EC dual-modal biosensors

EC sensors consist of an EC transducer that can convert the interaction between the target analyte and the sensing element into a detectable signal, which indicates the analyte concentration. In various fields such as clinical, industrial, environmental, and agricultural analysis, EC sensors play a crucial role and hold a significant position in the realm of biosensors, which is due to the high sensitivity, short detection time, and enable label-free detection, making point-of-care testing (POCT) feasible [58, 59]. Although significant advancements have been made in the past decade, the analytical performance of EC biosensors is still

influenced by matrix effects, even though they have been successfully tested in buffered solutions or diluted samples spiked with targets [60, 61]. Consequently, the accuracy of EC sensors continues to be the major challenge, particularly after repeated use and long-term storage [62].

The introduction of PEC sensing mode into EC analysis is an effective method to improve the accuracy and sensitivity of the sensors. In particular, the combination of PEC and EC can simplify the operation and reduce uncontrollable variability in different pathways. This is because it can be achieved using a single-probe electrode and a single instrument. For example, based on the “signal-off” strategy, a label-free PEC-EC dual-mode immunosensor was built by employing hetero-structured Au nanoparticles/CdS nanosheet as sensing substrate for ultrasensitive and accurate detection of human epididymis protein 4 (HE4) (Fig. 3(a)) [63]. The surface plasmon resonance (SPR) effects of Au nanoparticles provide the Au nanoparticles/CdS nanosheet heterostructures with remarkable enhancements in PEC and EC signals under light irradiation. While these enhancements gradually declined as the concentration of HE4 increased due to the steric barrier of the HE4. Similar, based on the high PEC and EC activity of $\text{BiOBr}_{0.8}\text{I}_{0.2}/\text{CoS}_x$ nanocomposite, a PEC and EC dual-mode sensing platform with highly sensitive and selective was fabricated for the detection of human epidermal growth factor receptor-2 (HER2) (Fig. 3(b)) [64]. Due to the formation of a heterojunction and the improved sensitization of CoS_x , the photocurrent of the composite showed a remarkable increase of 7.4 times compared with that of $\text{BiOBr}_{0.8}\text{I}_{0.2}$. In addition, PEC-EC dual-mode detection based on “signal-on” and photocurrent-polarity-switching strategy was also reported. For instance, a split-type PEC-EC dual-modal aptasensor was designed for ultrasensitively monitoring tumor necrosis factor- α by integrating

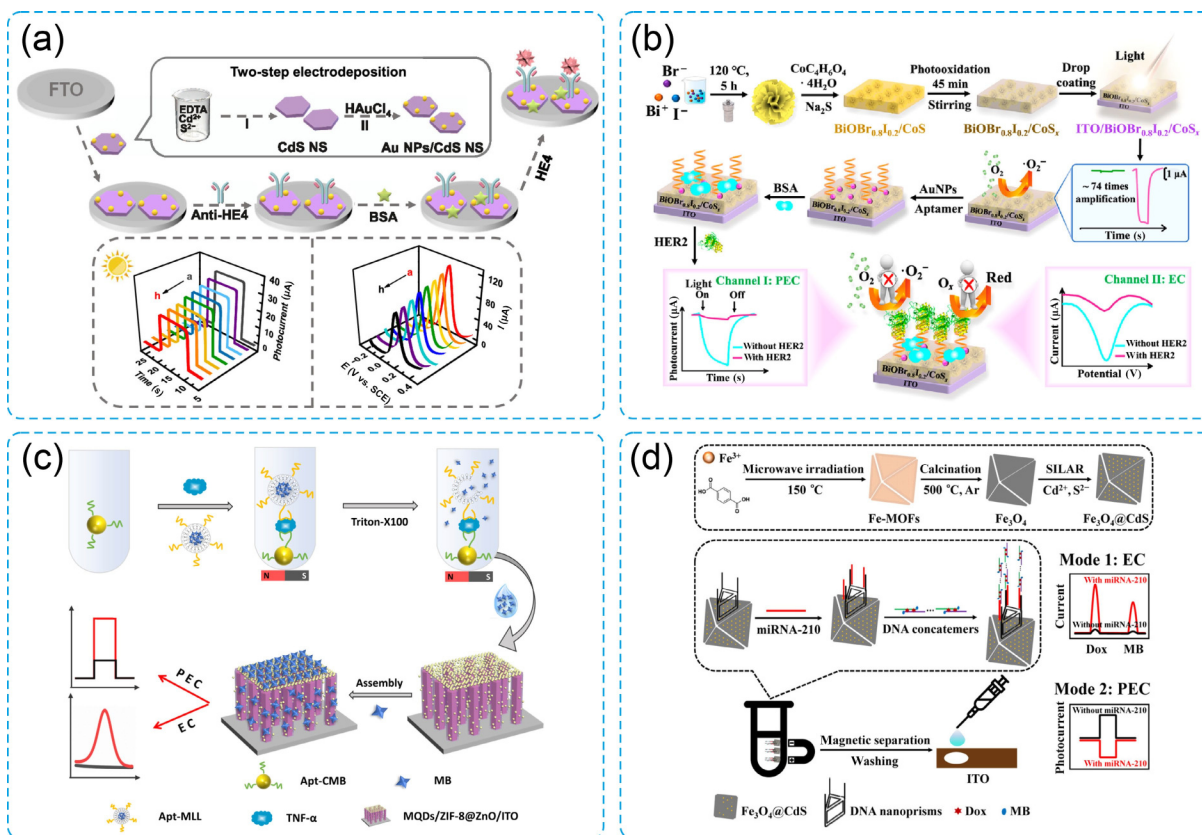


Figure 3 Schematic illustration of (a) the PEC-EC dual-mode sensor for HE4 detection based on Au nanoparticles/CdS nanosheet heterostructures. Reproduced with permission from Ref. [63], © American Chemical Society 2022. (b) The PEC-EC dual-mode sensing platform for HER2 analysis based on $\text{BiOBr}_{0.8}\text{I}_{0.2}/\text{CoS}_x$ p-n heterojunction. Reproduced with permission from Ref. [64], © American Chemical Society 2022. (c) The split-type PEC-EC dual-modal aptasensor for TNF- α tracking based on MQDs/ZIF-8@ZnO NR arrays. Reproduced with permission from Ref. [65], © American Chemical Society 2021. (d) The PEC-EC dual-mode biosensing platform for miRNA-210 evaluation based on $\text{Fe}_3\text{O}_4/\text{CdS}$ -DNA nanoprisms. Reproduced with permission from Ref. [66], © American Chemical Society 2021.

disulfide quantum dots (MQDs)/zeolitic imidazolate framework-8 (ZIF-8)@ZnO nanorod (NR) arrays with a methylene blue (MB)-liposome-mediated amplification strategy (Fig. 3(c)) [65]. In this system, the MB served as a versatile signal indicator, while the MB-encapsulated liposome functioned as a dual-mode signal indicator carrier. Later on, a photocurrent-polarity-switching PEC and magnetic-assisted EC dual-mode biosensing platform was developed for the sensitive and selective detection of miRNA-210 (Fig. 3(d)) [66]. Fe-based MOF (Fe-MOF)-derived porous magnetic Fe_3O_4 octahedra were used for biological recognition and separation in a homogeneous system. Subsequently, a self-assembled DNA nanoprism with three thiols/hanging arms, capable of efficiently capturing miRNA-210, was immobilized on the Fe_3O_4 @CdS octahedra via the Cd-S bond. In the presence of miRNA-210, double-stranded DNA concatemers formed, which consisted of hybridized MB-labeled single-stranded DNAs (AP1 and AP2) and intercalated adriamycin (Dox) into their grooves. MB and Dox acted as redox probes in the EC mode and cooperatively switched the photocurrent polarity of the Fe_3O_4 @CdS octahedra in PEC analysis.

4.2 PEC-colorimetry dual-modal biosensors

Colorimetry sensors utilize color change assay to achieve qualitative and quantitative monitoring of objects. This color change can be observed directly with the naked eye or through a smartphone color readout device. Colorimetry sensors have gained significant attention due to their quick response and low cost, and they do not require sophisticated instruments or professional operators [67, 68]. Consequently, colorimetric assays

based on natural or nanozymes provide a reliable biocatalytic potential for point-of-care diagnosis and cost-effective daily applications [69]. Although colorimetric analysis has many advantages, it also faces shortcomings. First, colorimetric analysis based on visual observation may introduce subjective errors [70]. Second, the dynamic range of colorimetric analysis is usually limited by the linear range of the detector. If the concentration of target substance exceeds the linear range of the detector, accurate measurement may not be possible [71]. Third, the sensitivity of colorimetric analysis is often influenced by factors such as the concentration of target substance, sample color, and background interference [72]. In some cases, the concentration of the target substance may be too low to be accurately detected.

Combining the colorimetry with PEC analysis technology to enhance the accuracy and reliability of assay has received wide attention. For instance, a PEC-colorimetry multimodal sensing platform was developed for the detection of carcinoembryonic antigen (CEA) using a three-dimensional (3D) hollow HCdS@Au nanosphere (Fig. 4(a)) [73]. Dual-aptamer recognition was utilized to form a sandwich structure on magnetic beads in the presence of the target CEA. Rolling circle amplification (RCA) was then initiated to bind CuO-DNA probes, which, upon stimulation with ascorbic acid, release Cu^{2+} ions. These ions interacted with yellow HCdS@Au on the electrode, resulting in the production of dark CuS through ion exchange. Consequently, as the CEA level increases, the photocurrent weakened, and the color of the electrode interface changed from yellow to dark, enabling PEC and colorimetric detection of CEA. Subsequently, a tailored dual-modal split-type PEC immunosensor with complementary

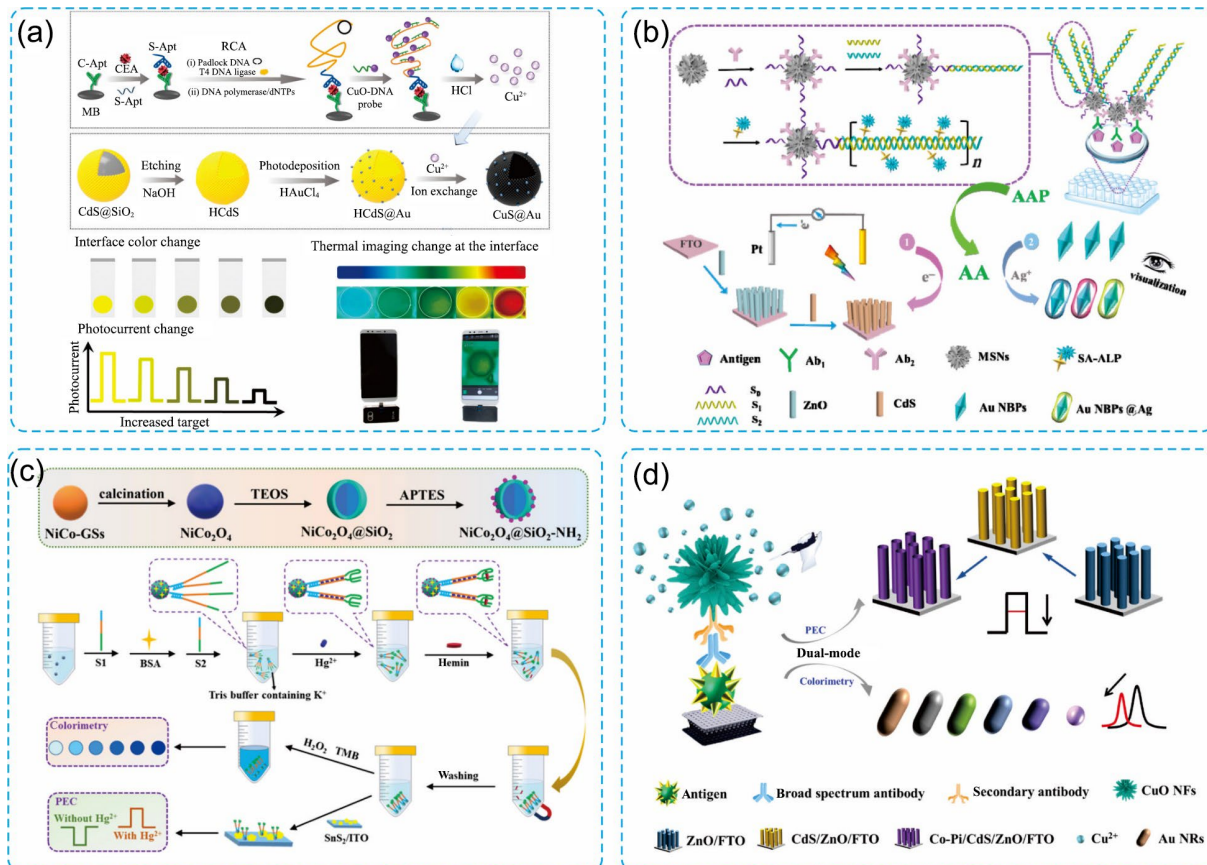


Figure 4 Schematic diagram of (a) the biometric PEC-colorimetry biosensor for CEA detection based on 3D hollow HCdS@Au nanosphere coupled with RCA and target-induced ion exchange reaction. Reproduced with permission from Ref. [73], © American Chemical Society 2022. (b) The PEC-colorimetry dual-modal split-type immunosensor for MC-LR analysis based on CdS/ZnO HNRs and $\text{Au nanobipyramids@Ag}$. Reproduced with permission from Ref. [74], © American Chemical Society 2018. (c) The PEC-colorimetry dual-mode sensing of Hg^{2+} based on $\text{NiCo}_2\text{O}_4@SiO_2-NH_2$ sphere. Reproduced with permission from Ref. [75], © American Chemical Society 2022. (d) The PEC-colorimetry dual-mode immunosensor for simultaneous monitoring of OTA, OTB, and OTC based on Co-Pi sensitized CdS/ZnO NTs and CuO NFs . Reproduced with permission from Ref. [76], © Elsevier B.V. 2020.

colorimetric detection was developed for the detection of microcystin-LR (MC-LR) in water (Fig. 4(b)) [74]. The design involved the direct growth of CdS/ZnO hollow nanorod arrays (HNRS) with excellent photoelectric properties on F-doped SnO₂ (FTO) as the photoelectrode. The immune reaction was conducted in a microplate, and the hybridization chain reaction (HCR) triggered the formation of an enzymatic concatemer on mesoporous silica nanospheres (MSNs) to achieve signal amplification. The enzymatic hydrolysate, ascorbic acid (AA), acted as an electron donor, capturing the holes generated from CdS/ZnO-HNRS, resulting in a “signal-on” PEC detection. Furthermore, AA induced *in situ* silver (Ag) metallization on Au nanobipyramids (NBPs), forming Au NBPs@Ag, which led to vivid color variations and a blue shift of the localized surface plasmon resonance (LSPR) band. Recently, the development of a PEC-colorimetry dual-mode sensing platform for Hg²⁺ assay was achieved based on 3,3',5,5'-tetramethylbenzidine (TMB) and split G-quadruplex-hemin complex in a magnetic NiCo₂O₄@SiO₂-NH₂ sphere (Fig. 4(c)) [75]. Initially, the amino-labelled single-stranded DNA1 (S1) was immobilized onto NiCo₂O₄@SiO₂-NH₂ and partially hybridized with another single-stranded DNA2 (S2). Upon the presence of Hg²⁺, the formation of thymine-Hg²⁺-thymine base pairs between S1 and S2 occurred, leading to the generation of the split G-quadruplex in the presence of K⁺. Subsequently, the addition of hemin resulted in the formation of the split G-quadruplex-hemin complex, which effectively catalyzed the H₂O₂-mediated oxidation of TMB. Consequently, the color and absorbance intensity of the TMB solution were altered, enabling visual and colorimetric detection of Hg²⁺. In addition, a novel PEC-colorimetry dual-mode immunosensor was designed for the simultaneous detection of ochratoxin A (OTA), ochratoxin B (OTB), and ochratoxin C (OTC). In this system, broad-spectrum antibodies were utilized as recognition elements, cobalt phosphate (Co-Pi) sensitized CdS/ZnO nanotubes (NTs) arrays were used as photoactive materials, and bifunctional copper oxide

nanoflowers (CuO NFs) were employed as dual-signal probes. In the PEC mode, Cu²⁺ released by CuO NFs replaced Cd²⁺ in the photoactive material, creating a new band gap that accelerated electron-hole recombination, leading to changes in the PEC current. In the colorimetric mode, Cu²⁺ facilitated the etching of Au NRs, resulting in multiple color changes and shifts in the LSPR of Au NRs.

4.3 PEC-ECL dual-modal biosensors

ECL is a process of converting electrical energy into light emission through electric-to-photo conversion [47]. It utilizes an electrical potential as an excitation source to trigger a substance near the electrode to enter an excited state, leading to the emission of light. This conversion of the electrical signal into a light signal serves as a detection signal, which can be considered as the reverse process of PEC detection. The integration of PEC and ECL dual-signal detection enables the exploitation of the unique benefits offered by both methods [77]. This flexibility allows for the selection of different detection modes based on specific requirements, facilitating the achievement of multi-method detection for individual samples. As a result, the accuracy and reliability of the detection process can be significantly enhanced, leading to more robust and trustworthy results.

QDs possess remarkable ECL and PEC properties as well as good biocompatibility and excellent controllability, making them highly promising for the development of PEC and ECL dual-signal sensing platforms [78]. As an example, a versatile PEC-ECL dual-mode biosensor based on 3D CdSe QDs-DNA nanonetwork-SnO₂ nanoflower and DNA walker amplification strategy for HIV assay was developed (Fig. 5(a)) [45]. This system utilized a 3D CdSe QDs-DNA nanonetwork to sensitize a mesoporous SnO₂ PEC substrate. The QDs-DNA nanonetwork acted as multifunctional probes for both PEC and ECL signals. Furthermore, a target-triggered biped DNA walker-cascade amplification technique was employed to generate a large amount

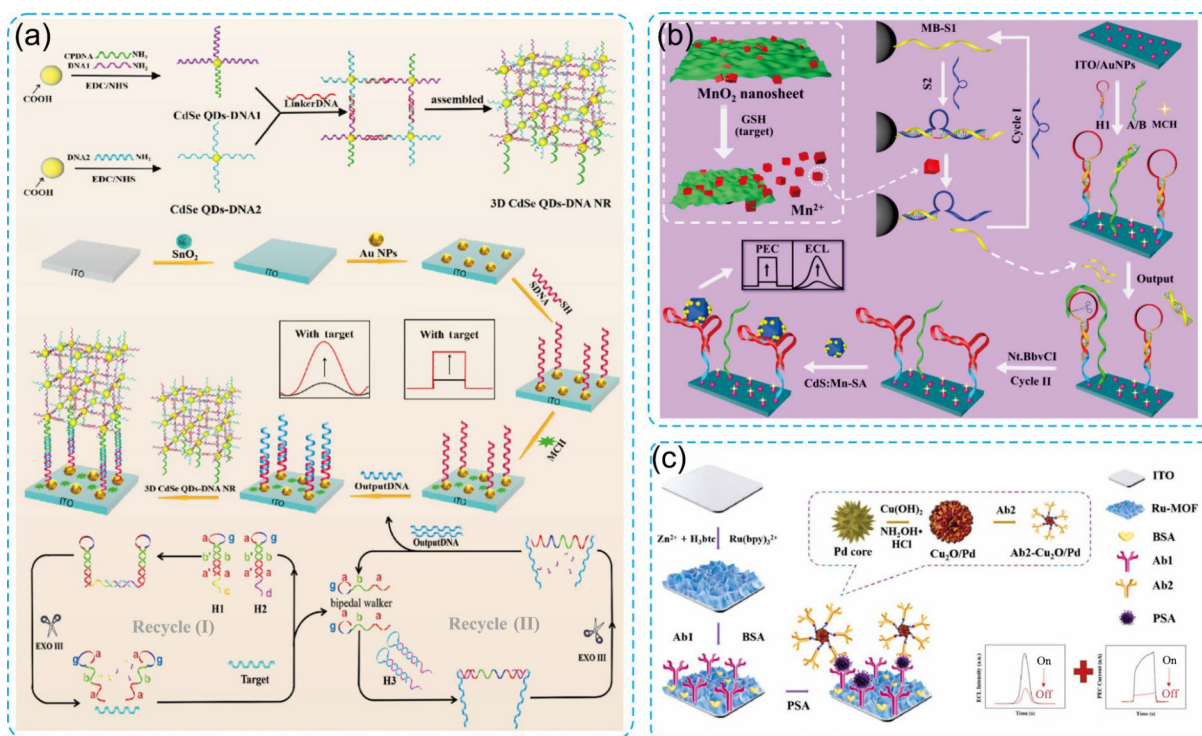


Figure 5 Schematic images of (a) the PEC-ECL dual-mode biosensing platform for HIV detection based on 3D CdSe QDs-DNA nanonetwork SnO₂ nanoflower coupled with DNA walker multiple amplification. Reproduced with permission from Ref. [45], © Elsevier B.V. 2021. (b) The PEC-ECL “signal on” biosensing platform for GSH assay based on Mn²⁺-powered DNAzyme amplification strategy combined with DNA-walker triggered allosteric conversion. Reproduced with permission from Ref. [79], © American Chemical Society 2019. (c) The PEC-ECL dual-signal immunosensor for PSA analysis based on Ru-MOF composite material and Pd/Cu₂O nanoparticles. Reproduced with permission from Ref. [28], © Elsevier B.V. 2023.

of output DNA. This DNA was then used to link numerous 3D CdSe QDs-DNA nanonetwork probes to the electrode, resulting in greatly amplified signals for the sensitive detection of HIV. Utilizing a Mn^{2+} -powered DNAzyme amplification strategy, in combination with DNA-walker-triggered allosteric conversion, a sensitive PEC-ECL dual-mode assay for the detection of glutathione (GSH) was developed (Fig. 5(b)) [79]. The assay began by reducing MnO_2 nanosheets to Mn^{2+} through the presence of GSH. The Mn^{2+} ions then acted as a substitute target, initiating DNAzyme-assisted cleavage-cycling amplification to generate numerous DNA output molecule. Simultaneously, a DNA molecular machine, consisting of hairpin DNA as a track and an arm as a walker, was introduced to bridge signal probes for versatile biosensing. The presence of DNA output activated the swing arm, causing it to hybridize with the hairpin DNA and be cleaved by Nt.BbvCI enzyme. This cleavage initiated autonomous walking of the arm, leading to the formation of a large number of streptavidin aptamers. Subsequently, CdS:Mn-SA tags, serving as versatile signal probes, were linked to the electrode through specific SA-aptamer binding. This configuration generated highly enhanced ECL and PEC signals, enabling the sensitive detection of the target. Based on strong ECL signals and good PEC property of the $Ru(bpy)_3^{3+}/MOF$ (Ru-MOF) composite material, a PEC-ECL dual-mode immunosensor for the detection of prostate-specific antigen (PSA) was developed (Fig. 5(c)) [28]. To achieve optimal quenching of ECL and PEC intensities, a quencher consisting of Cu_2O -coated Pd shell-core nanoparticles (Pd/ Cu_2O) was introduced into the system. A signal-reduced sandwich immunosensing structure was constructed with the primary antibody Ab_1 connected to the Ru/MOF modified electrode, the PSA analyte, and the secondary antibody Ab_2 loaded with Pd/ Cu_2O quencher. The excellent dual signals generated by the

Ru/MOF were effectively quenched by the presence of the Pd/ Cu_2O quencher.

4.4 PEC-FL dual-modal biosensors

FL analysis technique is an analytical method based on the luminescent properties of substances. It utilizes the FL signal emitted by substances when they are excited by light to obtain information about the sample [80]. Since the intensity of the FL signal is related to the concentration of the target molecules in the sample, a standard curve can be established, or the linear relationship between FL intensity and concentration can be used to achieve quantitative detection of the target molecules. FL analysis method has the characteristics of high sensitivity, strong specificity, and wide linear range [81, 82]. It is also a non-destructive detection method. However, FL analysis is very sensitive to other fluorescent substances or luminescent substances present in the sample, which may cause interference and misjudgment of the signal [83]. Additionally, during FL detection, the excitation light may interfere with the emitted light. This interference arises from directing excitation of the emitted fluorophore by the excitation light, scattering of the excitation light leading to background noise, and autofluorescence from the sample itself [84]. These interferences can affect the accuracy and sensitivity of FL detection.

PEC-FL dual-mode detection provides a feasible approach to address the above issues. By complementing and comparing the two detection modes, it can effectively improve the detection accuracy and reliability. Utilizing a layer-by-layer modified indium-tin oxide (ITO)/Au/BiOI electrode as the matrix and $NaYF_4:Yb^{3+}$, $Tm^{3+}@NaGdF_4:Yb^{3+}$ core/shell upconversion nanoparticles (UCNPs) as the signal labels, a sensing platform for the high-precision assay of PSA was developed (Fig. 6(a)) [85]. The

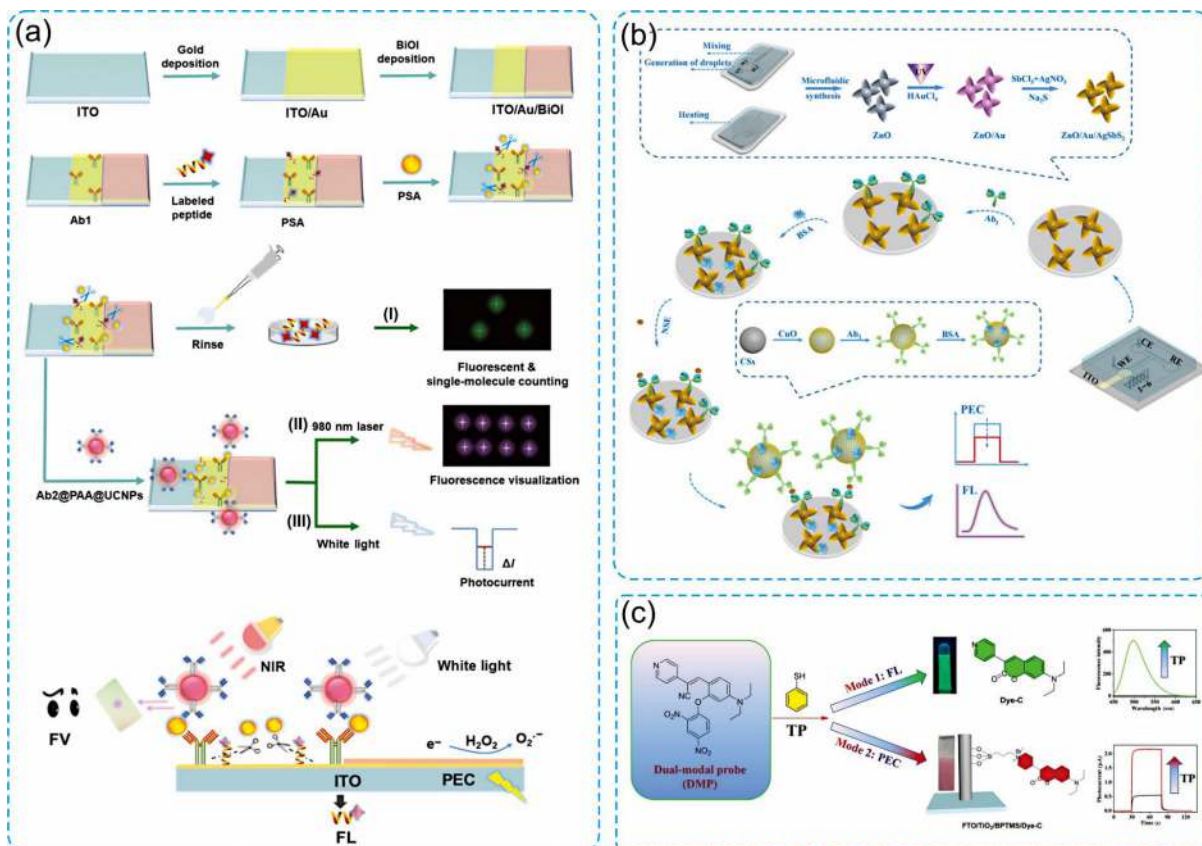


Figure 6 Schematic illustration of (a) the PEC-FL multi-signal readout sensing platform for PSA monitoring based on BiOI electrodeposited ITO/Au electrode and $NaYF_4:Yb^{3+}$, $Tm^{3+}@NaGdF_4:Yb^{3+}$ core/shell UCNPs. Reproduced with permission from Ref. [85], © Elsevier B.V. 2022. (b) The PEC-FL dual-mode microfluidic sensing platform for NSE detection based on $ZnO/Au/AgSbS_2$ hybrids and CuO nanozymes. Reproduced with permission from Ref. [86], © American Chemical Society 2022. (c) The PEC-FL dual-modal sensor for TP assay based on a single chemodosimetric probe. Reproduced with permission from Ref. [29], © Elsevier B.V. 2022.

platform offered a triple-qualitative readout (smartphone-based naked-eye, PEC, and FL) and a double-quantitative readout (PEC and FL). In the PEC mode, the sensing was achieved based on the PSA bio-recognition events, while the FL sensing was enabled by the specific enzymatic activity of PSA for a 5-carboxyfluorescein (FAM) labeled helix peptide. Furthermore, under the excitation of a 980 nm near-infrared (NIR) laser, the signal antibody@UCNPs bioconjugates emitted visible light for smartphone-based naked-eye readout. The accuracy of PSA serodiagnosis was significantly improved compared with the single-signal method. Later on, a PEC-FL microfluidic biosensor was developed for accurate determination of neuron specific enolase (NSE) using CuO nanozymes as a multifunctional signal label and ZnO/Au/AgSbS₂ composites as a photoactive matrix (Fig. 6(b)) [86]. The photocurrent of ZnO NFs decorated with Au and AgSbS₂ nanoparticles was significantly enhanced due to the LSPR effect of Au and the matching band structure between ZnO and AgSbS₂. To achieve a “signal-off” state in PEC, a strategy involving the catalytic oxidation of AA by CuO nanozymes was proposed. CuO nanoparticles grown on conductive carbon spheres (CuO@CSs) were used as secondary antibody labels and efficiently catalyzed the oxidation of AA. This resulted in the quenching of PEC signals. Subsequently, the dehydroascorbic acid produced reacted with o-phenylenediamine to generate a strong FL signal. Furthermore, a dual-modal probe (DMP) capable of simultaneously detecting thiophenol (TP) through FL and PEC methods was developed by incorporating the TP recognition group, dinitrophenyl (DNP), into a coumarin dye precursor molecule (Fig. 6(c)) [29]. In an aqueous solution, the DMP

specifically reacts with TP, removing the DNP group and undergoing intramolecular cyclization to produce a highly fluorescent coumarin dye. When covalently attached to a TiO₂ substrate, the DMP also exhibits a structural response to TP, resulting in enhanced photoelectric effects. Consequently, the DMP enables both “off-on” FL and photocurrent signals upon TP detection. Moreover, the DMP enables FL imaging of TP in living cells and PEC detection in real water samples.

4.5 Others PEC-coupled dual-modal biosensors

In addition, there have been reports on the coupling of PEC method with other detection strategies. As an illustration, a dual-mode sensing platform combining PEC and quartz crystal microbalance (QCM) techniques for the assay of protein tyrosine phosphatase 1B (PTP1B) activity was developed (Fig. 7(a)) [87]. The platform utilized hollow CuO and TiO₂ polyhedra as the active components. First, PTP1B-specific phosphopeptide (P-peptide) was immobilized onto an ITO electrode decorated with hollow CuO polyhedra. Then, hollow TiO₂ polyhedra were introduced to the sensing platform through specific interaction with the phosphate groups of P-peptide. The matched energy levels of CuO and TiO₂ facilitated the generation of a large cathodic photocurrent upon visible light irradiation. In the presence of PTP1B, it specifically recognized and dephosphorylated the P-peptide, leading to the detachment of TiO₂ polyhedra from the electrode and a subsequent decrease in photocurrent. Additionally, the detached hollow TiO₂ polyhedra were quantitatively detected using a QCM electrode. After that, a PEC-gasochromic dual-readout immunosensing platform for

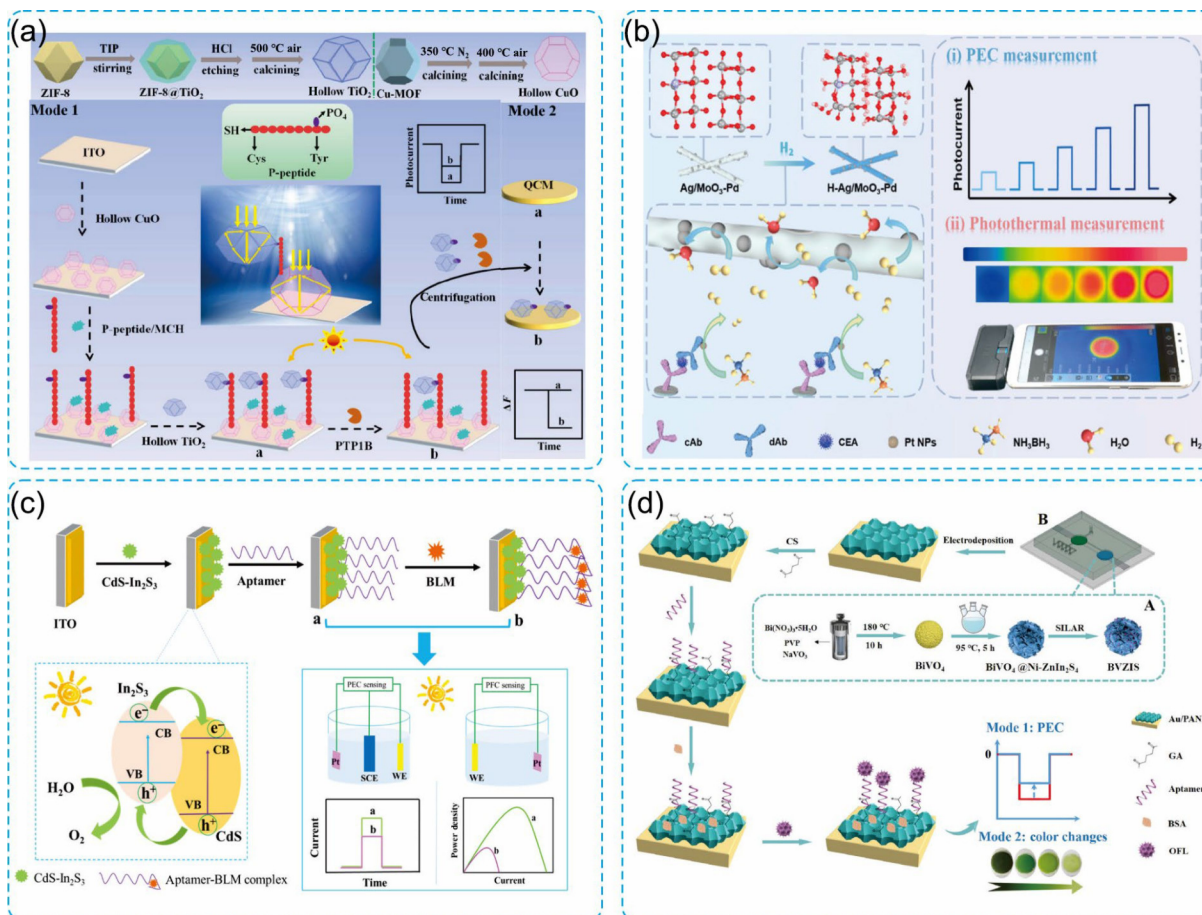


Figure 7 Schematic demonstration of (a) the PEC-QCM dual-mode sensing platform for PTP1B assay based on hollow CuO and TiO₂ polyhedra. Reproduced with permission from Ref. [87], © Elsevier B.V. 2021. (b) The PEC-photothermal dual-mode detection of CEA based on Ag/MoO₃-Pd. Reproduced with permission from Ref. [88], © Elsevier B.V. 2023. (c) The PEC-PEC dual-mode aptasensing platforms for BLM analysis based on CdS-In₂S₃ heterojunction. Reproduced with permission from Ref. [89], © Elsevier B.V. 2019. (d) The self-powered PEC-electrochromic visualization dual-mode aptasensor for OFL monitoring based on BVZIS heterojunction. Reproduced with permission from Ref. [90], © American Chemical Society 2022.

accurate and sensitive detection of CEA was constructed based on Ag-doped/Pd nanoparticles loaded MoO_3 nanorods (Ag/ MoO_3 -Pd). This platform enabled dual-readout through photocurrent and temperature signals (Fig. 7(b)) [88]. The presence of the CEA analyte triggered a sandwich-type immunoreaction, along with the introduction of Pt nanoparticles labeled on the detection antibody. Subsequently, NH_3BH_3 was added to produce hydrogen (H_2), which acted as a bridge between the sensing interface and the biological assembly platform. The interaction between H_2 and Ag/ MoO_3 -Pd significantly enhanced the PEC performance and photothermal conversion capability of the system. Recently, a PEC-photofuel cell (PFC) dual-mode visible light-induced biosensor was fabricated for highly sensitive and selective detection of bleomycin (BLM) based on a CdS- In_2S_3 heterojunction with enhanced PEC performance (Fig. 7(c)) [89]. The CdS- In_2S_3 composite demonstrated improved absorption in the visible region and effectively suppressed the recombination of electron-hole pairs in the heterojunction. Additionally, the CdS- In_2S_3 photoanode was employed to construct a PFC. The PFC operated by harnessing the oxidation of water on the CdS- In_2S_3 photoanode under visible light illumination and the reduction of oxygen on a Pt cathode, resulting in the generation of electricity. When the BLM aptamer was modified on CdS- In_2S_3 substrate, a PEC-PFC aptasensor displaying a declined photocurrent and output power response to BLM was developed. Additionally, a dual-mode microfluidic analytical device for ultrasensitive

detection of ofloxacin (OFL) was constructed by integrating self-powered PEC sensing with electrochromic visualization analysis (Fig. 7(d)) [90]. To facilitate steady electron provision, an advanced dual direct Z-scheme $\text{BiVO}_4/\text{Ni-ZnIn}_2\text{S}_4/\text{Bi}_2\text{S}_3$ (BVZIS) heterojunction was synthesized as the photoanode matrix. For immobilizing aptamers and enabling visual readout, an electrochromic material, polyaniline-modified Au (Au/PANI), was electrodeposited on the photocathode. Au/PANI, with excellent conductivity, received electrons from the photoanode without the need for an external energy supply. The PANI underwent rapid reduction upon receiving the electrons, causing a noticeable color change from blue to green. As the concentration of OFL increased, steric hindrance increased, leading to a significant decline in the PEC signal and the RGB green value.

5 The applications of PEC-coupled dual-modal sensing platform

5.1 Detection of disease related biomarkers

The PEC-coupled dual-mode sensing strategy has remarkable applications in disease prevention and diagnosis [91, 92]. By integrating different sensing modes, it can enhance the accuracy and reliability of early disease detection and diagnosis, providing strong support for disease prevention and treatment. Recently, a dual readout detecting platform was constructed for PSA assay by

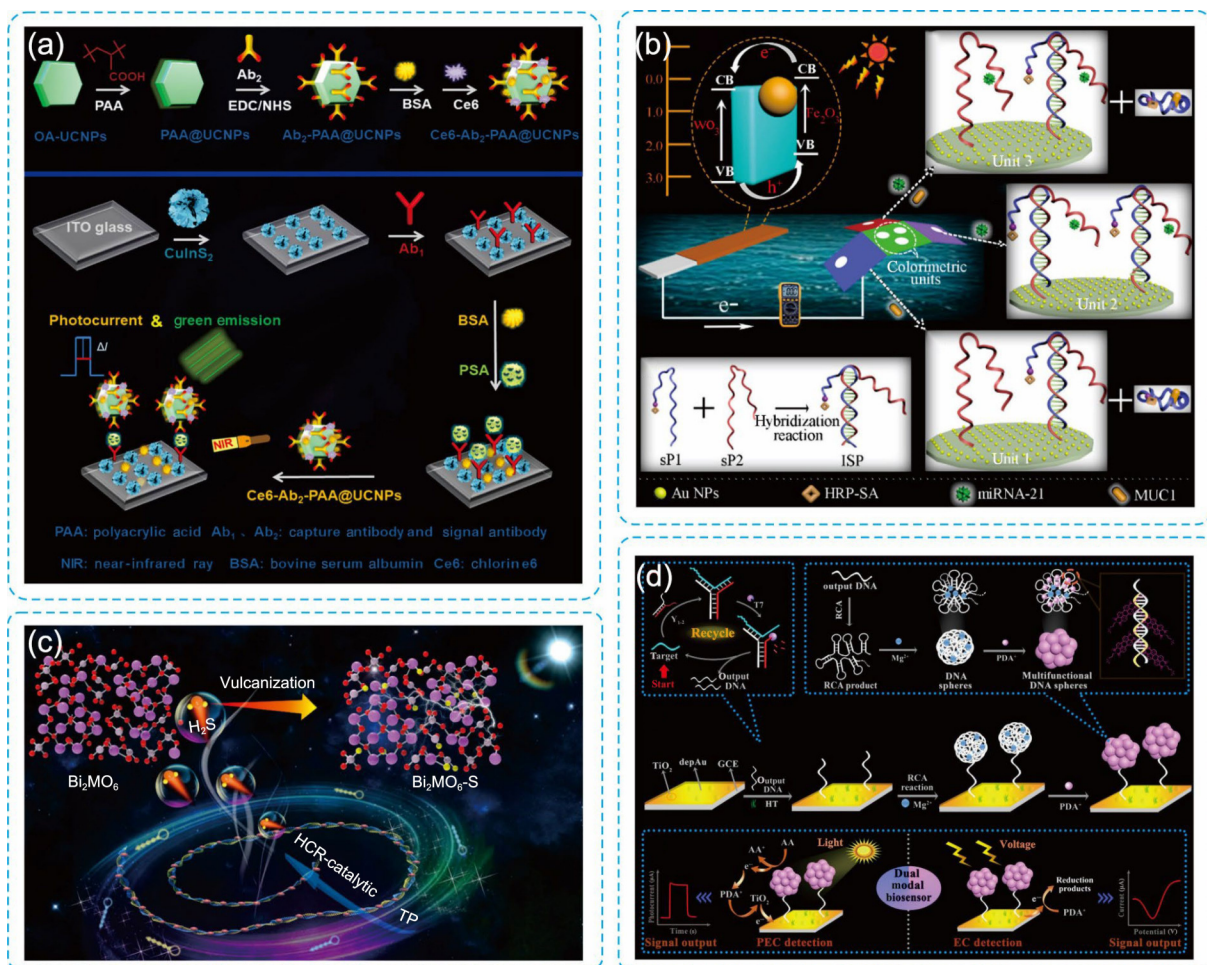


Figure 8 Schematic pictures of (a) the PEC-NIR-induced FV dual readout sensing platform for PSA analysis based on Ce6-Ab₂-PAA@UCNP bioconjugates and CuInS₂ matrix. Reproduced with permission from Ref. [93], © American Chemical Society 2021. (b) The PEC-colorimetry dual-mode aptasensor for the assaying of MUC1 and miRNA-21 based on WO₃/Fe₂O₃ heterojunction. Reproduced with permission from Ref. [94], © American Chemical Society 2021. (c) The magnetic-assisted PEC-colorimetry dual-modal sensing platform for PSA detection based on BMO matrix and aptamer-guided HCR. Reproduced with permission from Ref. [27], © American Chemical Society 2022. (d) The PEC-EC dual-mode sensing platform for miRNA-141 detection based on cationic PDA⁺-decorated versatile DNA spheres. Reproduced with permission from Ref. [95], © American Chemical Society 2020.

combining PEC method with NIR-induced fluorescence visualization (FV) (Fig. 8(a)) [93]. In this system, CuInS₂ microflowers served as the matrix to provide background photocurrent, while chlorin e6 (Ce6) was conjugated to antibody-modified UCNP to act as a signal label for PEC sensing and naked-eye readout. Unlike traditional PEC immunosensors, the dual-mode sensing platform, when illuminated by NIR light, allowed for both quick qualitative analysis and quantitative analysis. Later on, a PEC-colorimetry dual-mode aptasensor was developed for the assaying of mucin 1 (MUC1) and microRNA 21 (miRNA-21) (Fig. 8(b)) [94]. To facilitate the photocurrent signal, the WO₃/Fe₂O₃ heterojunction was synthesized as the photoactive material. For visual colorimetric assay, gold nanoparticles (AuNPs) were used to modify the paper-based working units, and integrated signal probe (ISP) composed of signal probe 1 (sP1) and signal probe 2 (sP2) was introduced. In the presence of MUC1 protein, both sP1 and the target on the working unit were released into the corresponding colorimetric unit due to DNA specific recognition. The horseradish peroxidase-streptavidin (HRP-SA) carried by free sP1 could oxidize TMB, resulting in the formation of a blue-colored oxidized TMB (oxTMB) in the presence of hydrogen peroxide (H₂O₂). This process ultimately generated a higher photocurrent signal. Additionally, miRNA-21 was modified on another working unit by binding with sP2. This modification led to changes in the current signal, allowing for real-time detection of analytes with the aid of a digital multimeter. Similarly, a magnetic-assisted PEC-colorimetry dual-modal sensing platform for PSA detection was established (Fig. 8(c)) [27]. This platform utilized Bi₂MoO₆ (BMO) nanosheets as the matrix and then employed the aptamer-guided HCR in conjunction with the hydrolysate-induced vulcanization reaction of BMO nanosheets. When PSA was introduced, the target analyte interacted with the aptamer, leading to the release of trigger DNA (tDNA). This tDNA then was hybridized with anchor DNA (aDNA) that was conjugated to magnetic beads. The released tDNA initiated a target-assisted HCR in the presence of two alternating hairpin sequences (Bio-H1 and Bio-H2), resulting in the formation of nicked long double-stranded DNA on the surface of the MBs. Numerous alkaline phosphatase (ALP) enzymes can then assemble with the MBs through the biotin-avidin reaction. This assembly triggered the hydrolysis of sodium thiophosphate (TP) to produce hydrogen sulfide (H₂S). The generated H₂S reacts

with BMO to form vulcanized BMO (BMO-S), leading to a significant enhancement in PEC performance under visible light. After that, a PEC-EC dual-mode sensing platform based on cationic N,N-bis(2-(trimethylammoniumiodide)propylene)-perylene-3,4,9,10-tetracarboxydiimide (PDA⁺)-decorated versatile DNA spheres was prepared for miRNA-141 detection (Fig. 8(d)) [95]. Through the utilization of a target-related ternary “Y” structure cleavage cycling reaction, the target DNA was transformed into a large quantity of output DNA that is firmly attached to a TiO₂ substrate. This process subsequently initiated the RCA reaction. In the presence of magnesium ions and PDA⁺, the long DNA tailed of the RCA product was condensed to form multifunctional DNA spheres. These DNA spheres were in close proximity to the TiO₂ substrate, creating an effective PDA⁺-TiO₂ sensitization structure that facilitated fast electron transfer and resulted in a significantly enhanced PEC signal when assisted by AA. Additionally, the cationic PDA⁺ contributed to favorable redox activity and can be loaded onto the DNA spheres, producing a distinct and well-defined cathodic peak for conducting EC biodetection on the same sensing platform.

5.2 Analysis of drugs

The PEC-coupled dual-mode sensors have also been employed for the analysis of certain antibiotics and anti-inflammatory drugs. As an illustration, a PEC “signal-on” and an EC “signal-off” dual-detection model were established for streptomycin ratiometric detection (Fig. 9(a)) [96]. In this work, CdTe QDs and a methylene blue-labeled aptamer (MB-Apt) were applied to generate PEC and EC signals. The conformational change induced by the target causes MB-Apt to move away from the electrode, resulting in a decrease in the EC signal. Simultaneously, the reduced steric hindrance facilitated the restoration of the PEC signal from the CdTe QDs. Consequently, this PEC-EC strategy enabled the simultaneous achievement of a PEC “signal-on” and an EC “signal-off” state. Furthermore, it allowed for quantitative analysis of the target by measuring the ratio of current intensities. In addition, the sensing capabilities of four different aptamers (A22, A34, A42, and A45) targeting patulin (PAT) using EC and PEC methods were investigated (Fig. 9(b)) [97]. The combined influence of steric hindrance and electron transfer distance had a substantial impact on the EC and PEC responses of PAT when using aptasensors fabricated with A22, A34, A42, or A45.

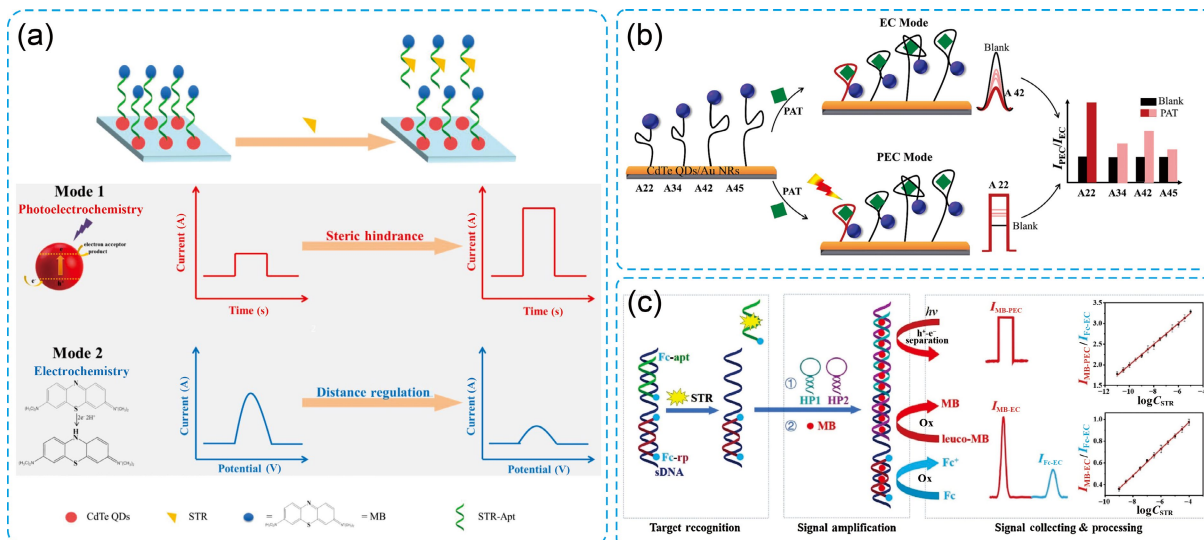


Figure 9 Schematic diagrams of (a) the PEC “signal-on” and an EC “signal-off” dual-detecting of streptomycin based on CdTe QDs and MB-Apt. Reproduced with permission from Ref. [96], © Shen, X. L. et al. 2019. (b) The PEC-EC dual-mode sensing of PAT based on gold nanorod-sensitized CdTe quantum dots (CdTe QDs/Au NRs) and four different aptamers. Reproduced with permission from Ref. [97], © Elsevier Ltd. 2023. (c) The PEC-EC dual-ratiometric aptasensor for the assay of STR based on MB. Reproduced with permission from Ref. [98], © Elsevier B.V. 2021.

Surprisingly, despite A42 exhibiting the highest affinity for PAT, A22 emerged as the optimal aptamer for aptasensing. This suggested that factors other than affinity, such as the aforementioned synergistic effect, played a critical role in determining the sensing behavior of PAT. Besides, a dual-ratiometric aptasensor for the detection of streptomycin (STR) by combining PEC and EC assays was proposed (Fig. 9(c)) [98]. The key feature of this method was the utilization of MB as a bifunctional probe, enabling the simultaneous generation of photocurrent (IMB-PEC) and redox current (IMB-EC). By acting as a bridge, MB facilitated the coupling of PEC and EC assays, resulting in a dual-mode sensing platform (PEC-EC). To establish a reference signal, the redox current of ferrocene (IFc-EC) was incorporated into the system. The specific recognition of STR triggered the stripping of the Fc-tagged aptamer, initiating an HCR that led to the formation of a DNA duplex capable of absorbing MB.

5.3 Assay of enzyme activities

The application of dual-mode detection in enzymatic activity analysis can provide more comprehensive, accurate, and reliable results, contributing to a deeper understanding of enzyme functionality and the mechanisms of biochemical reactions. For example, a PEC-QCM dual-mode biosensor was exploited for the analysis of PTP1B activity by utilizing bifunctional magnetic $\text{Fe}_3\text{O}_4@\text{Cu}_2\text{O}@\text{TiO}_2$ nanosphere-mediated PEC photocurrent polarity switching and QCM signal amplification (Fig. 10(a)) [99]. The PTP1B-specific P-peptide was first immobilized onto the QCM. The $\text{Fe}_3\text{O}_4@\text{Cu}_2\text{O}@\text{TiO}_2$ nanosphere was then linked to the P-peptide and incubated with PTP1B. The P-peptide underwent dephosphorylation, leading to the release of $\text{Fe}_3\text{O}_4@\text{Cu}_2\text{O}@\text{TiO}_2$ nanospheres from the chip surface. The magnetic separation technology was employed to quickly separate these released magnetic nanospheres (labeled as R- $\text{Fe}_3\text{O}_4@\text{Cu}_2\text{O}@\text{TiO}_2$) and attached them to the $\text{Bi}_2\text{S}_3/\text{MITO}$ electrode through

magnetic force. This attachment induced a photocurrent polarity switch from anodic current (at the $\text{Bi}_2\text{S}_3/\text{MITO}$ electrode) to cathodic current (at the $\text{R-Fe}_3\text{O}_4@\text{Cu}_2\text{O}@\text{TiO}_2/\text{Bi}_2\text{S}_3/\text{MITO}$ electrode). Additionally, the non-dephosphorylated P-peptide-linked $\text{Fe}_3\text{O}_4@\text{Cu}_2\text{O}@\text{TiO}_2$ nanospheres acted as nanozymes with horseradish peroxidase activity. They catalyzed the formation of precipitation on the surface of the Au chip, resulting in a frequency change of the QCM. Furthermore, a PEC-EC dual-mode sensing platform was developed to detect polynucleotide kinase (PNK) activity by utilizing a $\text{BiOBr}_{0.8}\text{I}_{0.2}/\text{CuSCN}$ as multifunctional matrix (Fig. 10(b)) [100]. The nanocomposite was loaded with Au nanoparticles, which were used to immobilize the capture probe P1. The signal probe P2 was labeled with glucose oxidase modified AuNPs ($\text{GOx}@\text{AuNPs}$ -P2). When P1 and P2 precisely hybridized, a double-stranded DNA (ds-DNA)-contained composite was formed on the ITO electrode. This composite can be phosphorylated in the presence of PNK and selectively cleaved by λ -exonuclease, causing it to detach from the electrode surface. The uncut ds-DNA, along with $\text{GOx}@\text{AuNPs}$ -P2, catalyzed glucose to generate H_2O_2 . Under the catalysis of peroxidase-like $\text{BiOBr}_{0.8}\text{I}_{0.2}/\text{CuSCN}$, 4-chlorohexadione precipitation was produced, leading to the amplification of both PEC and EC signals. In addition, a self-regulated dual-modal PEC-EC bioassay based on AuPtPd nanosphere was developed for urease activity (Fig. 10(c)) [101]. The AuPtPd nanospheres worked synergistically to catalyze the oxidation of 4-chloro-1-naphthol, resulting in the production of benzo-4-chlorohexadienone precipitation on the surface of photoactive materials. This led to a decrease in photocurrent and an increase in charge-transfer resistance.

5.4 Monitoring of gases

PEC-coupled dual-mode detection provides more accurate and reliable results in gas detection. For instance, the excessive usage and burning of fossil fuels have led to severe pollution caused by H_2S , which necessitates urgent supervision. A renewable tungsten

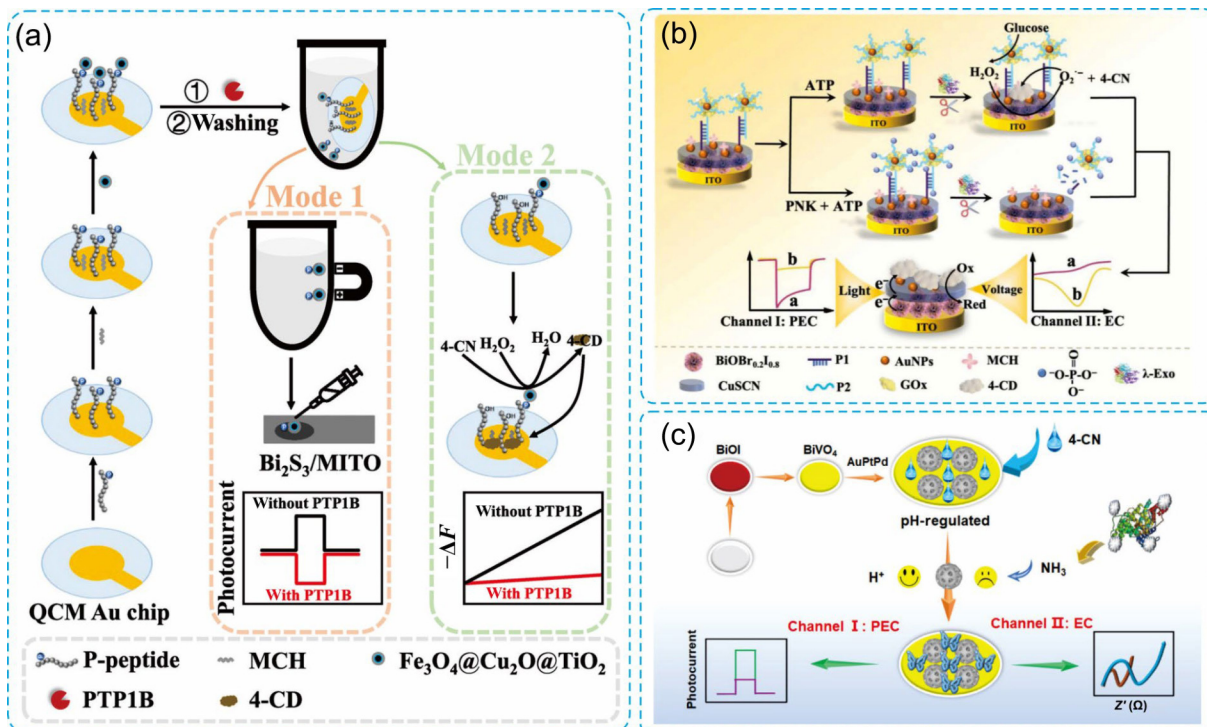


Figure 10 Schematic illustrations of (a) the PEC-QCM dual-mode biosensor for PTP1B activity monitoring based on $\text{Fe}_3\text{O}_4@\text{Cu}_2\text{O}@\text{TiO}_2$ nanosphere. Reproduced with permission from Ref. [99], © American Chemical Society 2022. (b) The PEC-EC dual-mode sensing platform for PNK activity assay based on $\text{BiOBr}_{0.8}\text{I}_{0.2}/\text{CuSCN}$ multifunctional matrix. Reproduced with permission from Ref. [100], © Elsevier B.V. 2023. (c) The PEC-EC dual-modal bioassay for urease activity analysis based on mesoporous trimetallic AuPtPd nanosphere. Reproduced with permission from Ref. [101], © American Chemical Society 2021.

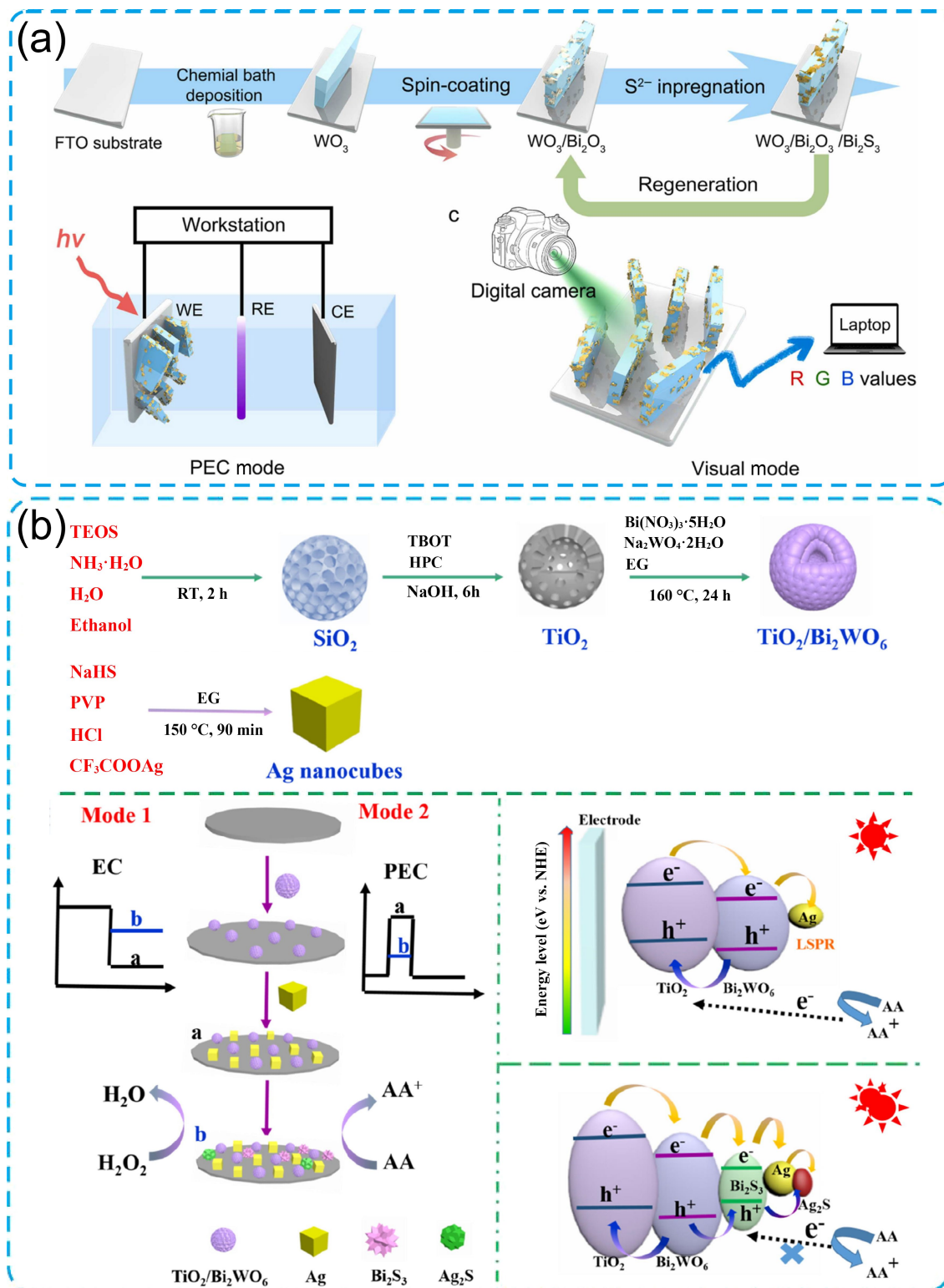


Figure 11 Schematic pictures of (a) the PEC and visual dual-mode detection of harmful H_2S base on $\text{WO}_3/\text{Bi}_2\text{O}_3$ heterojunction. Reproduced with permission from Ref. [102], © Elsevier B.V. 2022. (b) The PEC-EC dual-mode sensing platform for H_2S assay based on $\text{TiO}_2/\text{Bi}_2\text{WO}_6/\text{Ag}$ heterojunction. Reproduced with permission from Ref. [103], © Elsevier Inc. 2020.

trioxide/bismuth oxide ($\text{WO}_3/\text{Bi}_2\text{O}_3$) heterojunction was synthesized, which enabled dual-mode PEC and visual detection of harmful H_2S (Fig. 11(a)) [102]. The spontaneous ion-exchange reaction triggered a partial transformation of Bi_2O_3 to Bi_2S_3 , enabling a “signal-on” PEC detection strategy. Additionally, the noticeable color change from light cyan to khaki enabled visual determination, particularly under high concentrations of H_2S . The detection process can be easily repeated through a simple regeneration treatment, making it a user-friendly approach for controlled monitoring of H_2S . Subsequently, a dual-mode sensing

platform that enabled highly selective detection of H_2S was fabricated based on PEC and EC signal responses of the $\text{TiO}_2/\text{Bi}_2\text{WO}_6/\text{Ag}$ heterojunction (Fig. 11(b)) [103]. The $\text{TiO}_2/\text{Bi}_2\text{WO}_6/\text{Ag}$ heterojunction demonstrated excellent catalytic performance in the reduction of H_2O_2 , making it an effective probe for H_2S detection. By employing an amperometric $i-t$ method, this heterojunction produced a remarkable EC response. Additionally, this hybrid heterojunction featured a favorable energy-band configuration, serving as a photoelectric beacon. Notably, when exposed to sulfide ions, the functionalized

Table 1 Some representative applications of PEC-coupled dual-mode biosensors

Method	Matrix or probe	Target	Linear range	Detection limit (LOD)	Ref.
PEC-FV	CuInS ₂ microflowers Ce ₆ -Ab ₂ -PAA@UCNP	PSA	0.0001–50 ng/mL (PEC) 0.001–10 ng/mL (FV)	0.03 pg/mL (PEC)	[93]
PEC-colorimetry	WO ₃ /Fe ₂ O ₃ heterojunction	MUC1 miRNA-21	0.01–100,000 pg/mL (PEC) 0.1 pM–10 nM (PEC)	3.4 fg/mL (PEC) 36 fM (PEC)	[94]
PEC-colorimetry	Bi ₂ MoO ₆ nanosheets	PSA	0.005–100 ng/mL (PEC)	5 pg/mL (PEC) 0.1 ng/mL (colorimetry)	[27]
PEC-EC	PDA ⁺ -decorated DNA spheres	miRNA-141	0.1–0.001 fM (PEC) 0.001–500 pM (EC)	0.037 fM (PEC) 0.67 fM (EC)	[95]
PEC-EC	CdTe QDs MB-Apt	streptomycin	0.1–1.0 μM (PEC) 0.03–10 μM (EC)	0.03 μM (PEC) 0.01 μM (EC)	[96]
PEC-EC	CdTe QDs/Au NRs	PAT	0.1–100 pg/mL (PEC) 0.0005–10 ng/mL (EC)	39 fg/mL (PEC) 25 fg/mL (EC)	[97]
PEC-EC	MB	STR	0.01–10,000 nM (IMB-EC/IFc-EC) 1–100,000 nM (IMB-PEC/IFc-EC)	0.01 nM (IMB-EC/IFc-EC)	[98]
PEC-QCM	Fe ₃ O ₄ @Cu ₂ O@TiO ₂ nanosphere	PTP1B	0.04–10,000 pM (PEC) 0.01–10,000 pM (QCM)	0.014 pM (PEC) 0.003 pM (QCM)	[99]
PEC-EC	BiOBr _{0.8} I _{0.2} /CuSCN	PNK	0.0005–10 U/mL (PEC) 0.005–15 U/mL (EC)	0.0588 mU/mL (PEC) 0.621 mU/mL (EC)	[100]
PEC-EC	AuPtPd nanosphere	urease	10–750 mU/mL (PEC) 10–750 mU/mL (EC)	8.4 mU/mL (PEC) 6.6 mU/mL (EC)	[101]
PEC-visual	WO ₃ /Bi ₂ O ₃ heterojunction	H ₂ S	0.1–500 μM (PEC) 0.05–5 mM (visual)	ca. 38 nM (PEC) ca. 1.24 μM (visual)	[102]
PEC-EC	TiO ₂ /Bi ₂ WO ₆ /Ag heterojunction	H ₂ S	0.5–300 μM (PEC) 0.5–300 μM (EC)	0.06 μM (PEC) 0.08 μM (EC)	[103]

electrodes generated Bi₂S₃ and Ag₂S nanoparticles, leading to a proportional decrease in EC and PEC responses. This decrease can be attributed to the poor catalytic properties of Bi₂S₃ and Ag₂S, as well as the recombination of photoexcited electron–hole pairs.

6 Conclusions and perspectives

In spite of the significant progress achieved in PEC detection, it still faces several challenges, such as weak external anti-interference ability, high background, and the risk of false positive or negative errors in complex samples detection. To enhance accuracy and reliability, the integration of PEC detection with other complementary methods is a promising approach. By combining different detection techniques, researchers can leverage the strengths of each method and overcome their individual limitations. This review discusses the latest developments in this intriguing and cutting-edge subject, including designs, fabrications, and applications (Table 1) of various PEC-coupled dual-modal sensing strategies.

In our opinion, one of the most popular research directions is the integration of PEC with the colorimetry for bioassays. Natural or nanozymes used in colorimetry are often relatively independent of PEC methods and do not cause interference. Additionally, the color change can be directly observed visually, making it ideal for assisting other detection schemes. Although the PEC-FL mode is not as common as the PEC-colorimetry mode, it has gained popularity in recent years as a tool for detecting cancer-related biomarkers. Furthermore, the PEC-ECL dual-mode detection has emerged as a novel subject of study, with numerous researchers experimenting with different approaches. In comparison to the aforementioned PEC-coupled dual-mode detection methods, the PEC-EC detection strategies have been widely reported due to their ability to be achieved using a single-probe electrode and a single instrument. Moreover, an increasing number of other detection modes coupled with PEC have been reported, such as PEC-PFC, PEC-photothermal, and PEC-electrochromic visualization. Among these, the PEC-electrochromic visualization mode may become the next hotspot of research, as it can not only

be applied for the diagnosis of traditional objects, but also have the potential for monitoring body fluids in wearable devices, demonstrating its enormous potential for development.

Currently, the PEC-coupled dual-modal sensing strategies are in their early stages, and there are several trends that require further investigation: (i) Exploitation of novel multi-stimulus response materials. One approach being pursued is the design and synthesis of hybrid materials that combine different components with complementary properties. Another strategy involves the development of smart nanomaterials that can switch between different states or properties in response to specific stimuli. (ii) Avoid or reduce the influence of structural or property changes in a material caused by one energy source on the accuracy of another detection method. One approach is to develop materials that are resistant to the unwanted effects induced by one energy source. Another strategy involves optimizing the experimental conditions and parameters, including the intensity, duration, and wavelength of the excitation energy, to minimize the undesired effects. (iii) Simplify the analysis process and reduce the detection time and cost. At present, ongoing research and advancements in technology are aimed at addressing these limitations. As an illustration, the development of miniaturized and integrated detection systems can simplify the setup and reduce costs. Additionally, the use of advanced data analysis algorithms and automation can streamline the detection process and reduce the time required for analysis.

In the future, ongoing efforts to develop materials, optimize experimental conditions, and streamline the detection process can help overcome these limitations and expand the applications of dual-mode detection in various fields, including biomedical diagnostics, environmental monitoring, and materials research. With increasing interest and continuous efforts from the scientific and business communities, it is anticipated that the existing limitations associated with PEC-coupled dual-mode detection will be addressed in the near future.



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