Application of Photocatalytic Nanomaterials in Photoelectrochemical Biosensors

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Abstract Recently, photoelectrochemical (PEC) biosensors are becoming the rising star in biosensing analysis because of their high potential to construct different biosensors with high sensitivity, selectivity, and low cost. It is well-known that semiconductor materials with intrinsic large band gaps limit their applications in the range of ultraviolet (UV) irradiation. Moreover, UV light is somewhat too energetic and has a destructive effect on biomolecules. By introducing metal nanoparticles, carbon-based nanomaterials, and even organic molecules into semiconductor materials, the light response window for these functionalized nanocomposites can be extended to the visible light region. In this review, we mainly discuss PEC biosensors' applications based on different state-of-the-art nanocomposites in three aspects, including the environmental field, food safety field, and medical field. The design principle and performance of PEC biosensors are systematically analysed. And we also briefly look forward to the development trend of this kind of PEC biosensors in the future.

1. Introduction
Biosensors, nowadays, have received a wide range of interests from various fields. It applies in the clinical diagnosis and is introduced in food or environmental hazards detection and analysis. The biosensor utilizes biological recognition molecules and transducers to identify a particular biomolecular interaction and analyse the target analyte's concentration. Due to their sensitivity, portability, and rapid response time, biosensor has become a significant role in clinical and non-clinical areas. Based on biorecognition's nature, the biosensor can be classified into two categories: biocatalytic and affinity-based device [1]. The affinity-based biosensors incorporate biological recognition molecules (i.e., aptamer or antibody) to precisely capture the target. The transducer is presented to translate biomolecular interaction into a readable signal, such as an optical or electrical signal. And thus, the transformation forms, including optical, acoustic, electronic, and photoelectrochemical mechanisms, have been used to develop different biosensors [2]. However, the developed biosensors suffer from some drawbacks, such as bad affordability or low S/N ratio. There is still a higher requirement for the development of supersensitive and highly selective biosensors.

The Photoelectrochemical (PEC) strategy can convert the chemical energy to potential energy under lighting conditions, which is more convenient and low-cost. Fujishima and Honda first used semiconducting nanomaterials (i.e., TiO₂) to construct a semiconductor electrode for electrochemical photolysis of water [3]. On this foundation, Fruk et al. synthesized Au/TiO₂ nanocomposite to enhance
nanomaterials' photocatalytic activity [4]. Such nanocomposites offer an excellent charge-transfer effect based on the electron storage ability of noble metals. And the fabrication of graphene-WO3-Au hybrid membranes also improves the photocatalytic activity in the biological detection of glucose level [5]. Both protocols take advantage of the noble metals' plasmonic characteristic to strengthen the catalytic abilities of semiconducting nanomaterials. Currently, research teams from all over the world are investigating the modifications of semiconducting nanomaterials to improve their photocatalytic efficiencies.

PEC biosensors based on functionalized semiconducting nanomaterials have received a broad range of interest. It could not only resolve environmental problems (i.e., photocatalytic degradation of pollutants), provide a renewable and sustainable energy source (i.e., production of H2, the energy source of hydrogen fuel cells or water splitting), but also applies in bioanalysis such as DNA analysis, cell-related detection, and enzymatic sensing [5]. Optical detection techniques such as fluorescence and chemiluminescence require cumbersome operation and technical imaging software compared to the PEC biosensing method [6]. To effectively utilize the PEC biosensor's photocurrent output, charge transfer should be taken place between the analyte, electrode, and the photocatalytic materials [7]. As a result, understanding the photoelectrochemical properties of photocatalytic materials is a fundamental part of PEC biosensors' application.

In this minireview, we first introduce the design mechanism of PEC biosensors. These biosensors' application performance is further systematically discussed within the environmental field, food safety field, and medical field. And the detection limit for different kinds of PEC biosensors is compared, as shown in Table 1.

| Application fields | Photocatalysts type | Analysis objects | Detection limit | Ref. |
|--------------------|---------------------|------------------|----------------|------|
| Environment        | CdS QDs             | CEA              | 0.72 ng/mL     | [11] |
|                    | CdS                 | MC-LR            | 0.021 μg/L     | [15] |
|                    | Ti-Fe-O nanotubes   | MC-LR            | 5 fM           | [16] |
| Food               | T(TA)2-TiO2         | OPs              | 5.6 × 10⁻¹³ g/mL | [19] |
|                    | CdS-MnO2            | OPs              | 0.017 ng/mL    | [20] |
|                    | NH2-MIL-125(Ti)/TiO2| Acetochlor       | 0.003 nM       | [22] |
|                    | ZnO-AuNPs-rGO       | Cd(II)           | 1.8×10⁻¹² mol/L | [23] |
|                    | BiOI-CdS            | Cu²⁺             | 0.02 μM        | [24] |
|                    | TiO2/BiOI/BiOBr     | SRT              | 0.04 nM        | [26] |
|                    | Bi4VO8Cl/N-GQDs     | OTC              | 0.03 nM        | [27] |
|                    | α-Fe2O3-NG-AuNRs    | E2               | 3.3×10⁻¹⁶ M    | [29] |
|                    | Mn²⁺-doped Zn(OH)₂V₂O₇| AFB1             | 0.3 pg/mL      | [32] |
|                    | ZnPe/TiO2 NRAs      | BPA              | 8.6 nM         | [33] |
| Medicine           | AuNPs/ZnSe QDs      | CEA              | 0.12 fg/mL     | [37] |
AuNPs-HCNT HER2 0.08 pg/mL [38]
Bi2S3 nanorods microRNA 3.5 fM [39]
ZnO/Ag2S AFP 8 pg/mL [41]
P-g-C3N4 PKA 0.077 U/mL [44]
AuNPs/MoSe2 Tau-381 protein 0.3 fM [47]
Co3O4-CNT-TiO2 Glucose 0.20 μM [49]
2D-FePS3 Glucose ~0.42 μM [51]
PbS/SiO2/AuNPs Glucose 0.46 μM [52]

2. Mechanism of PEC biosensors
A typical PEC biosensor takes advantage of the photocatalytic effect of the radiation-absorbing semiconductor particles (SC), as shown in Figure 1. The general mechanism of such a process is as follows: (1) The SC absorbs the radiation energy (hv) to produce electrons-holes (e⁻/h⁺) pair. (2) While the positive hole (h⁺) leaves in the valence band (VB), the photoexcited charge carrier (e⁻) is promoted to a conducting band (CB), and a series of reactions take place individually [8]. For example, escaping from recombination, the electron migrates to the SC surface to cause a reduction reaction, and the positive hole can further oxidize biochemical molecules.

3. Application of PEC biosensors in environmental field
In the past century, the planet has suffered from great environmental pollution and climate changes due to urbanization and industrialization. The environmental issue needs to be addressed as soon as possible. Any discussion on environmental problems would turn into renewable energy sources. The use of photocatalyst has been demonstrated as one of the "green" strategies to address the environmental pollution problems [9]. It could be used in energy conversion to offer renewable solar energy sources [10]. The applications evolve water splitting, photocatalytic degradation, transformation CO into hydrocarbon fuels. In this part, we discuss the application of nanomaterials-based PEC biosensors in environmental fields, such as solar energy design, water splitting, and environmental hazards detection.

3.1. CEA detection
A group of researchers designed a PEC biosensor by in situ generations of CdS quantum dots (QDs) on graphene oxide (GO) [11]. As shown in Figure 2, GO was introduced onto the indium tin oxide (ITO) electrode's surface. And then, carcinoembryonic antigen (CEA) is coupled to the horseradish...
peroxidase-labeled antibody (HRP-Ab) through the immune recognition process. Then the H₂O₂ and Na₂S₂O₃ were introduced and reacted to generate H₂S and form CdS QDs. The photoexcited CdS QDs could generate photocurrent and be used as a readout signal. By analyzing the change of photocurrent, the specific interaction between the CEA and HRP-Ab could be detected. The detection limit for detection of CEA using a designed PEC biosensor was 0.72 ng mL⁻¹. This application could be used for solar cell design, water splitting, and so on.

Figure 2. Schematic illustration of the ITO electrode in PEC biosensor.

3.2. Water splitting
The photoelectrochemical biosensor water splitting using semiconductor nanomaterials as photocatalysts to produce hydrogen and oxygen has attracted lots of interest. Among several kinds of materials to be photocatalysts, the bismuth ferrite has got most of the scientists' interest. Mukherjee et al. design a PEC biosensor for water splitting with the help of reduced graphene oxide-supported bismuth ferrite (RGO-BFO) nanocomposite electrocatalyst [12]. In this work, BFO nanomaterials are distributed to the RGO sheet to enhance BFO's water splitting particle application. Reducing exfoliated graphene oxide in the presence of BFO nanocomposite generates RGO-BFO nanocomposite, which band gap of RGO-BFO much smaller than the BFO. This is in favor of the generation of excitation of lower energy. The catalytic activity of the RGO-BFO leads to rapid passing through the interface charge transport layer and hinders the photogenerated electron-hole pairs. Thus, the RGO-BFO composite performance shows photocurrent density at 10.2 mA·cm⁻² and solar hydrogen efficiency at 3.3%.

Another researcher’s team used photocatalytic reduction of graphene oxide (GO) to reduced graphene oxide (rGO) with BiVO₄ in BVO/GO to design a simple PEC method, which enhances the efficiency of the water-splitting process and photocatalytic degradation [13]. By using as-prepared BVO/rGO nanocomposites, the charge transfer resistance was decreased, carrier concentration was increased, and photocarrier lifetime for BVO electrode was extended. Therefore, this research enhances the efficiency of photocatalytic degradation and increases water splitting performance of the PEC method.

3.3. MC-LR detection
PEC biosensors are also utilized to detect toxic substances in a freshwater sample [14]. This could help scientists or government staff evaluate water safety for residents to use and keep water quality. Tian and his colleagues developed a photoelectrochemical immunnoassay to determine the amount of microcystin-LR (MC-LR) in the water using Cds-graphene composite [15]. The prepared Cds-graphene composite on fluorine-doped tin oxide glass showed excellent PEC properties. Using this point, they designed a label-free and efficient PEC biosensor to detect MC-LR with a detection limit of 0.021 μg L⁻¹.

There also are several researchers that utilize different nanomaterials to analyze the concentration of MC-LR. Another PEC biosensor was invented using rGO/Ti-Fe-O nanocomposite [16]. The Ti-Fe-O nanotubes were synthesized on Ti-Fe alloy through the electrochemical anodic oxidation method. The
rGO was used to immobilize MC-LR aptamers and amplify the detection signal. Therefore, when MC-LR exists in this system, the corresponding aptamer for MC-LR on the electrode surface could recognize the MC-LR molecules. With this PEC biosensor, the detection limit for MC-LR was 5 fM.

4. Application of PEC biosensors in the food safety field

Food safety detection methods with high sensitivity and selectivity become a more and more crucial task to enhancing general public health. PEC biosensors are eye-catching due to their advantages in both electrochemical and optical analysis [17]. To improve PEC biosensors' performance, many research teams investigate synthesizing new heterocomposite photocatalytic nanomaterials and design various PEC biosensors. We, herein, will discuss the up-to-date applications of PEC biosensors in pesticides detection, heavy metals detection, antibiotics detection, estrogens detection, mycotoxins detection, and bisphenol A (BPA) detection.

4.1. Pesticides detection

Pesticides are a type of chemical material that is applied purposely for pest elimination [18]. Wu et al. designed a PEC assay method for the detection of organophosphorus pesticides (OPs) by using di-branched di-anchoring triphenylamine dye (T(TA)2) functionalized TiO2 nanoparticles [19]. Figure 3 shows the structure of the fluorine-doped tin oxide (FTO) electrode. TiO2 nanocomposites show excellent photo-to-electron transferability, owing to their extensive π-conjugated system, more photoelectron injection paths, and unique non-planar structure. Under optimal conditions, the detection limit is 5.6 × 10−13 g/mL.

Later, Zhu et al. have developed another OPs PEC detector using CdS-MnO2 nanocomposites as photocatalysts [20]. In this study, the use of the as-prepared CdS-MnO2 nanocomposites efficiently reduced background current during the experiment and greatly enhanced the present method's sensitivity. A low detection limit of 0.017 ng/mL is obtained. As an important herbicide, acetochlor is widely used in agricultural applications. However, the overuse of such pesticides could be a potential factor in causing cancers [21]. Jin et al. developed a visible-light-activated PEC biosensor to detect the acetochlor concentration in agricultural goods using the GOx/CS/NH2-MIL-125(Ti)/TiO2 nanocomposite [22]. Such nanocomposite under light irradiation generates a stable photocurrent and thus produces an ultra-low detection limit, 0.003 nM.

4.2. Heavy metals detection

Industrial production-induced heavy metal pollution is becoming an urgent issue for public health. Sun's team constructed a PEC aptasensor for Cd (II) detection by using ZnO and reduced graphene oxide (ZnO-rGO) nanocomposite [23]. With the help of localized surface plasmon resonance (LSPR) and
excellent conductivity of AuNPs, the photocurrent signal of the proposed PEC aptasensor is increased. The detection limit for Cd (II) determination is 1.8×10^{-12} mol/L, and such PEC biosensor produced reliable results in real water samples.

Zeng et al. developed another heavy metal PEC biosensor to detect Cu^{2+} using Z-scheme bismuth oxyiodide functionalized CdS (BiOI-CdS) nanocomposite as a photocatalyst [24]. Both PEC performance and photocatalytic activity are higher than pure CdS and BiOI itself. The detection limit of such a PEC biosensing method is 0.02 μM using the increased photocurrent intensity.

4.3. Antibiotics detection
Streptomycin (SRT) is a widely used antibiotic for bacterial infections, vegetable diseases treatment, and animal feed additives [25]. However, SRT abuses can also cause several problems, such as drug residues in agricultural environments and photodermatitis of the human body. Tan et al. designed a PEC aptasensor using TiO₂/BiOI/BiOBr as photoactive material for sensitive and specific SRT detection [26]. With TiO₂/BiOI/BiOBr, the prepared PEC aptasensor exhibits excellent photocurrent response. Thus, the detection limit of this aptasensor is 0.04 nM.

As another commonly used antibiotic in animal husbandry, oxytetracycline (OTC) protects vegetables from various bacteria. However, the overuse of it also causes allergic effects and antibiotic resistance. Looking for a solution, Wang et al. developed a new PEC aptasensor for OTC detection using Bi₄VO₈Cl/nitrogen-doped graphene quantum dots (Bi₄VO₈Cl/N-GQDs) nanohybrids as photocatalysts [27]. Because of the narrow band gap of Bi₄VO₈Cl, and the good electrical conductivity, compatibility, and photochemical properties of N-GQDs, the nanohybrids show high photocurrent intensity and high stability as compare to pure Bi₄VO₈Cl. The detection ranges from 0.1 to 150 nM with a detection limit of 0.03 nM.

4.4. Estrogens detection
Estrogen, as one type of hormone-disrupting chemicals, widely exists in environmental media and food. It largely disrupts the hormone balance in human bodies, thus interfering with various physiological body functions and increasing breast cancer risk [28]. Wang et al. developed a PEC aptasensor for ultrasensitive detection of 17β-estradiol (E2) using a ternary hybrid as a photoelectrochemical catalyst [29]. As a new photoactive material, the as-prepared ternary hybrid was synthesized by utilizing gold nanorods to modify hematite/N-doped graphene films (α-Fe₂O₃-NG). In this work, gold nanorods with excellent LSPR properties were used to promote the separation of e⁻/h⁺ pairs to improve PEC biosensor's biosensing performance. Under optimal conditions, the detection limit is 3.3×10^{-16} M, and the present PEC aptasensor was also used to detect the E2 in milk powder. Ding et al. also constructed a sensitive electrochemical enzyme biosensor for E2 detection based on electropolymerized L-lysine modified critic acid@graphene nanocomposites (Lac/PLL/CA-GR) [30]. By introducing an electron-transfer mediator, the detection limit for E2 detection is up to 1.3×10^{-13} M. This biosensor was also applied in human urine for real sample detections.

4.5. Mycotoxins detection
Mycotoxins are secondary metabolites produced by organisms like fungus and exist in many agricultural products, such as corn, bean, and peanut. Research has shown that mycotoxins are carcinogenic and teratogenic. Thus, they are considered more threatening than pesticides [31]. In Tang's research, Mn²⁺-doped Zn₃(OH)₂V₂O₇·2H₂O nanobelts were constructed and used to develop a PEC immunoassay for detection of aflatoxin B1 (AFB1) in foodstuff [32]. The Mn²⁺-doped Zn₃(OH)₂V₂O₇·2H₂O nanobelts showed excellent photocatalytic response ability under UV light due to its wide band gap. After doping Mn²⁺, the absorption range of radiation was improved so that the nanobelts provided good detection performance under visible light. The experiment results showed a linear range from 0.5 pg/mL to 10 ng/mL with a detection limit of 0.3 pg/mL.
4.6. BPA detection

Bisphenol A (BPA) is commonly used as a monomer compound to produce BPA-based plastics, such as polycarbonate. As an environmental endocrine disruptor, BPA widely exists in plastic food containers, such as water bottles and food packaging bags. Dong et al. developed a PEC sensor for BPA detection in food and plastic products [33]. As shown in Figure 4, they constructed a zinc phthalocyanine/TiO$_2$ nanorod arrays-modified FTO electrode (ZnPc/TiO$_2$ NRAs/FTO). The one-dimensional TiO$_2$ NRAs have excellent photon-to-electron transferability under UV radiation. The ZnPc modification extends the detection wavelength range successfully to the visible light range. As a result, the biosensor demonstrated an excellent linear detection range from 0.047 to 52.1 μM with a low detection limit of 8.6 nM.

![Figure 4. Schematic representation of the construction of ZnPc-modified FTO electrode.](image)

5. Application of PEC biosensors in the Medical field

5.1. Cancer detection

The discovery has recognized the close relationship between the abnormal concentration of particular proteins and cancer development [34]. These proteins were considered cancer biomarkers in the past decade, which could offer essential and important hints for cancer diagnosis. The PEC biosensor shows great performance in detecting biomarkers with a low detection limit [35]. For example, Ge et al. designed an innovative, general, and immobilized free PEC biosensor to detect cancer biomarkers [36]. Gao et al. designed a PEC biosensor using ZnSe QDs as photoactive materials for ultrasensitive detection of cancer biomarkers, carcinoembryonic antigen (CEA) [37]. Compare to other types of photoactive materials, ZnSe QDs have low toxicity, good water stability, good photostability, and so on. By incorporating multiple enzyme-free amplification strategies with 3D DNA nanosphere, the fabricated PEC biosensor has a low detection limit and a broad detection range.

As for the detection of breast cancer biomarkers, Luo et al. developed a PEC biosensor that utilized hexagonal carbon nitride tubes (HCNT) as photocatalysts to detect the human epidermal growth factor receptor 2 (HER2) [38]. In this study, Au nanoparticles (AuNPs) deposited on the surface of the HCNT were used to increase photocurrent efficiency. A kind of phosphate precipitate would form upon the interaction of HER2 molecules and HER2 aptamers. That precipitate adheres to the surface of HCNT, preventing electron transfer. And finally, the photocurrent intensity from the PEC biosensor was decreased. Based on such a reaction mechanism, this newly designed PEC biosensor for HER2 detection shows a low detection limit at 0.08 pg/mL.
Increasing research have shown that microRNA is directly related to colorectal cancer, lung cancer, diabetes, and rheumatoid arthritis. As a result, it is vital to develop a PEC biosensor to quickly detect microRNA in clinical diagnosis. The study utilizes the excellent low band gap, high absorption of Bi$_2$S$_3$ nanorods to act as photocatalytic material to design a PEC biosensor for microRNA detection with a detection limit of 3.5 fM [39]. The two-dimensional materials-transition metal carbides (MXenes) have become a new research field and are widely applied in several fields, such as batteries, thermoacoustic devices, and photo-degeneration. Ti$_3$C$_2$ has become a popular research topic and plays an indispensable role in research with its excellent properties. Liu et al. developed a PEC biosensor using Ti$_3$C$_2$: CdS nanocomposite as a photocatalyst to detect microRNA159c with a detection limit of ~33 fmol/L [40].

Alpha fetal protein (AFP) could be used as another cancer biomarker in diagnosing liver cancer. Jiang et al. developed a PEC biosensor based on Ag$_2$S nanoparticles (NPs)-modified ZnO inverse opals structure electrodes to detect AFP [41]. The used ZnO/Ag$_2$S composite extended their light adsorption to a long wavelength and was helpful to accelerate electron transfer. In this case, the fabricated PEC biosensor shows a low detection limit at 8 pg/mL.

5.2. Protein detection

Some diseases have increased during these years, for example, diabetes, Alzheimer's, and Parkinson's. This kind of disease is caused by incorrect protein folding rather than bacteria or virus [42]. One of the main groups of protein is a protein kinase. The kinase is essential cellular signaling, in which mutation could lead to diabetes, endocrine activity, and immunodeficiencies [43]. Therefore, it is better to detect proteins earlier for disease diagnosis and treatment.

Graphite-like carbon nitride has received interest from researchers due to its mental-free, high stability under visible light, unique bandgap structure. Moreover, this material is mental free, which is environmentally friendly. Li et al. designed a novel PEC biosensor based on phosphorylated graphite-like carbon nitride (P-g-C$_3$N$_4$) to detect kinase activity [44]. The results show that the prepared PEC biosensor is highly sensitive to the protein kinase A (PKA) and owns the detection limit of 0.077 U/mL by optimizing the experimental conditions.

Another group of researchers, Ma et al., created a PEC biosensor that provides a feasible way to probe DNA-protein interactions [45]. They constructed a CdS QDs-modified ITO electrode to develop such a PEC biosensor, as shown in Figure 5. CdS QDs were utilized as photocatalyst materials, and they are modified on the ITO electrode surface. This is used to prepare a visible light-driven PEC platform and subsequently anchor single-stranded DNA. This PEC biosensor is more economical than other methodology, and also shows good selectivity and a wide detection range.

![Figure 5. Schematic representation of the designed CdS QDs-modified ITO electrode.](image)
Alzheimer's disease becomes one of the most serious health problems among elderly populations [46]. The significant step for diagnosis of Alzheimer's disease is to precisely detect the tau protein. Hun et al. devised a PEC biosensor to detect the Tau-381 protein with AuNPs/MoSe2 nanosheets modified electrode [47]. MoSe2 was chosen as a semiconductor because of its narrow band gap between 1.7~1.9 eV. It could also increase photocurrent response since it could transfer electrons efficiently. Thus, the created PEC biosensor displays a high-selectivity and low detection limit of 0.3 fM.

5.3. Glucose detection

Due to the simple structures, high affordability, and specificity characteristics of biosensors, they are widely used in medical applications such as glucose detection [48]. Özacar and Çakıroğlu constructed a PEC biosensor based on supercapacitor carbon nanotubes (CNT)-Co3O4 nanocomposite for detection of glucose [49]. The Co3O4-CNT-anatase TiO2 semiconductor hybrid hybrids could increase visible light adsorption and strengthen the generated photocurrent. The result yielded a good linear detection range of 0-4 mM with a detection limit of 0.20 μM. Another research developed an ultrasensitive PEC biosensor for glucose detection using nitrogen-doped carbon sheets (NDC) wrapped titanium dioxide nanoparticles (TiO2 NPs) [50]. Due to the high conductivity of NDC, the hybrids demonstrate good charge transferability. The detector showed a detection range from 0.05 to 10 μM with a low detection limit of 13 nM.

Zhang et al. used the novel two-dimensional metal phosphorus trichalcogenide nanomaterials (2D-MPX3) to design a PEC biosensor for glucose detection [51]. The 2D-FePS3 nanosheets were composed in this biosensor design by applying a facile salt-templated strategy (Figure 6). The prepared FePS3 nanosheets displayed excellent optical properties with a narrow band gap, which allowed sensitive detection of glucose concentration under visible light radiation. The result showed a linear interrelation between the photocurrent and the logarithm of glucose concentration with a detection limit of ~0.42 μM.

![Figure 6. Schematic representation of the preparation of 2D-FePS3 nanosheets.](image)

Using AuNPs as a mimic enzyme of glucose oxidase, Di et al. constructed a PEC glucose sensor based on ITO/PbS/SiO2/AuNPs nanostructure [52]. In this study, the nanocomposites were firstly structured with several layers of PbS quantum dots on top of the ITO electrode surface. Then, the SiO2 nanospheres were placed between the PbS and AuNPs layers to reduce the base current, resulting in an enhanced detection limit. For the result, the linear detection range of glucose concentration was from 1.0 μM to 1.0 mM. And the limit of detection was 0.46 μM. Another PEC glucose biosensor was constructed by Neri et al. based on CuO-TiO2 heterojunctions to detect glucose in alkaline media [53].
Amin et al. also developed a nonenzymatic PEC glucose sensor [54]. In this work, they chose nickel nanotube networks (Ni-NTNWs) loaded with NiNiell cobalt layered double hydroxide (NiCo-LDH) nanosheets as photocatalytic materials. The nanohybrids have a unique advantage in conductivity due to the special structure property. Thus, the work demonstrated a wide linear response range, and the detection limit was 0.20 μM.

6. Conclusions
To conclude, as can be seen from this review, PEC biosensors have become an emerging method to detect different analyte types. In these several years, more and more PEC biosensors have developed and been utilized in various fields. It could use in agriculture and food to detect toxic materials, which help to provide healthier food. It could also play a fundamental role in the environment. Apart from these applications, one of the most significant applications is in the medical field. It could detect glucose and several proteins, which could be an indicator for disease diagnosis. A better and systematic understanding of the PEC method's basic principles will help develop next-generation PEC biosensors. PEC biosensors' research is still in the start-up stage, so researchers face some critical opportunities and challenges for developing perfect PEC biosensors in a wider range of fields.

Reference
[1] Zhao, W.-W., Xu, J.-J., & Chen, H.-Y. (2015). Photoelectrochemical bioanalysis: the state of the art [10.1039/C4CS00228H]. *Chemical Society Reviews, 44*(3), 729-741.
[2] Victorious, A., Saha, S., Pandey, R., Didar, T. F., & Soleymani, L. (2019). Affinity-Based Detection of Biomolecules Using Photo-Electrochemical Readout. *Frontiers in Chemistry, 7.*
[3] Fujishima, A., & Honda, K. (1972). Electrochemical Photolysis of Water at a Semiconductor Electrode. *Nature, 238*(5358), 37-38.
[4] Miljevic, M., Geiseler, B., Bergfeldt, T., Bockstaller, P., & Fruk, L. (2014). Nanocomposites: Enhanced Photocatalytic Activity of Au/TiO2Nanocomposite Prepared Using Bifunctional Bridging Linker (Adv. Funct. Mater. 7/2014). *Advanced Functional Materials, 24*(7), 1028-.
[5] Devadoss, A., Sudhagar, P., Das, S., Lee, S. Y., Terashima, C., Nakata, K., Fujishima, A., Choi, W., Kang, Y. S., & Paik, U. (2014). Synergistic Metal–Metal Oxide Nanoparticles Supported Electrocatalytic Graphene for Improved Photoelectrochemical Glucose Oxidation. *ACS Applied Materials & Interfaces, 6*(7), 4864-4871.
[6] Zhang, X., Guo, Y., Liu, M., & Zhang, S. (2013). Photoelectrochemically active species and photoelectrochemical biosensors. *RSC Adv., 3*(9), 2846-2857.
[7] Ikram, S., Singh, P., & Abdullah, M. (2016). Role of Nanomaterials and their Applications as Photo-catalyst and Senors: A Review. *nanoresearch and applications, 2.*
[8] Zhang, L., Mohamed, H. H., Dillert, R., & Bahmann, D. (2012). Kinetics and mechanisms of charge transfer processes in photocatalytic systems: A review. *Journal of Photochemistry and Photobiology C: Photochemistry Reviews, 13*(4), 263-276.
[9] Jiaguo Yu, P. Z., Huogen Yu, Christos Trapalis. (2012). Environmental Photocatalysis. *International Journal of Photoenergy, 2012, 4.*
[10] Wang, W., Wong, P. K., Pillai, S. C., Ming, T., & Dunlop, P. S. M. (2016). Photocatalysis in Environment, Energy, and Sustainability. *International Journal of Photoenergy, 2016, 1-2.*
[11] Zeng, X., Tu, W., Li, J., Bao, J., & Dai, Z. (2014). Photoelectrochemical Biosensor Using Enzyme-Catalyzed in Situ Propagation of CdS Quantum Dots on Graphene Oxide. *ACS Applied Materials & Interfaces, 6*(18), 16197-16203.
[12] Mukherjee, A., Chakraborty, S., Kumari, N., Su, W.-N., & Basu, S. (2018). Visible-Light-Mediated Electrocatalytic Activity in Reduced Graphene Oxide-Supported Bismuth Ferrite. *ACS Omega, 3*(6), 5946-5957.
[13] Soltani, T., Tayyebi, A., & Lee, B.-K. (2018). Enhanced Photoelectrochemical (PEC) and Photocatalytic Properties of Visible-Light Reduced Graphene-Oxide/Bismuth Vanadate. *Applied Surface Science, 448.*
[14] Pang, P., Lai, Y., Zhang, Y., Wang, H., Conlan, X. A., Barrow, C. J., & Yang, W. (2020). Recent Advancement of Biosensor Technology for the Detection of Microcystin-LR. *Bulletin of the Chemical Society of Japan*, 93(5), 637-646.

[15] Tian, J., Zhao, H., Zhao, H., & Quan, X. (2012). Photoelectrochemical immunoassay for microcystin-LR based on a fluorine-doped tin oxide glass electrode modified with a CdS-graphene composite. *Microchimica Acta, 179*(1), 163-170.

[16] Lu, H., Wang, G., Dai, R., Ding, X., Liu, M., Sun, H., Sun, C., & Zhao, G. (2019). Visible-light-driven photoelectrochemical aptasensor based on reduced graphene oxide/Ti–Fe–O nanotube arrays for highly sensitive and selective determination of microcystin-LR. *Electrochimica Acta, 324*, 134820.

[17] Ge, L., Liu, Q., Hao, N., & Kun, W. (2019). Recent developments of photoelectrochemical biosensors for food analysis [10.1039/C9TB01644A]. *Journal of Materials Chemistry B, 7*(46), 7283-7300.

[18] Huang, J., Hu, R., Pray, C., Qiao, F., & Rozelle, S. (2003). Biotechnology as an alternative to chemical pesticides: a case study of Bt cotton in China. *Agricultural Economics, 29*(1), 55-67.

[19] Song, J., Wu, S., Xing, P., Zhao, Y., & Yuan, J. (2018). Di-branched triphenylamine dye sensitized TiO2 nanocomposites with good photo-stability for sensitive photoelectrochemical detection of organophosphate pesticides. *Analytica Chimica Acta, 1001*, 24-31.

[20] Qin, Y., Wu, Y., Chen, G., Jiao, L., Hu, L., Gu, W., & Zhu, C. (2020). Dissociable photoelectrode materials boost ultrasensitive photoelectrochemical detection of organophosphorus pesticides. *Analytica Chimica Acta, 1130*, 100-106.

[21] Deryabina, M. A., Yakovleva, Y. N., Popova, V. A., & Eremin, S. A. (2005). Determination of the herbicide acetochlor by fluorescence polarization immunoassay. *Journal of Analytical Chemistry, 60*(1), 80-85.

[22] Jin, D., Gong, A., & Zhou, H. (2017). Visible-light-activated photoelectrochemical biosensor for the detection of the pesticide acetochlor in vegetables and fruit based on its inhibition of glucose oxidase [10.1039/C7RA00164A]. *RSC Advances, 7*(28), 17489-17496.

[23] Niu, Y., Luo, G., Zhang, Y., Wu, X., Li, G., & Sun, W. (2020). ZnO-reduced graphene oxide composite based photoelectrochemical aptasensor for sensitive Cd(II) detection with methylene blue as sensitizer. *Analytica Chimica Acta, 1118*, 1-8.

[24] Wang, H., Ye, H., Zhang, B., Zhao, F., & Zeng, B. (2017). Electrostatic interaction mechanism based synthesis of a Z-scheme BiOI–CdS photocatalyst for selective and sensitive detection of Cu2+ [10.1039/C7TA02691A]. *Journal of Materials Chemistry A, 5*(21), 10599-10608.

[25] You, F., Wei, J., Cheng, Y., Wen, Z., Ding, C., Guo, Y., & Wang, K. (2020). A novel electrochemical enzyme biosensor for detection of streptomycin based on a TiO2/BiOI/BiOBr heterostructure. *Analytica Chimica Acta, 1115*, 33-40.

[26] Lu, X., Sun, J., Sun, X. (2020). Recent advances in biosensors for the detection of oxytetracycline in the environment and food. *TRAC Trends in Analytical Chemistry, 127*, 115882.

[27] Du, X., Dai, L., Jiang, D., Li, H., Hao, N., You, T., Mao, H., & Wang, K. (2017). Gold nanorods plasmon-enhanced photoelectrochemical aptasensing based on hematite/N-doped graphene films for ultrasensitive analysis of 17β-estradiol. *Biosensors and Bioelectronics, 91*, 706-713.

[28] Wang, A., Ding, Y., Li, L., Duan, D., Mei, Q., Zhuang, Q., Cui, S., & He, X. (2019). A novel electrochemical enzyme biosensor for detection of 17β-estradiol by mediated electron-transfer system. *Talanta, 192*, 478-485.
[31] Zhou, Q., & Tang, D. (2020). Recent advances in photoelectrochemical biosensors for analysis of mycotoxins in food. TrAC Trends in Analytical Chemistry, 124, 115814.

[32] Lin, Y., Zhou, Q., & Tang, D. (2017). Dopamine-Loaded Liposomes for in-Situ Amplified Photoelectrochemical Immunoassay of AFB1 to Enhance Photocurrent of Mn2+-Doped Zn3(OH)2V2O7 Nanobelts. Analytical Chemistry, 89(21), 11803-11810.

[33] Fan, Z., Fan, L., Shuang, S., & Dong, C. (2018). Highly sensitive photoelectrochemical sensing of bisphenol A based on zinc phthalocyanine/TiO2 nanorod arrays. Talanta, 189, 16-23.

[34] Wu, J., Fu, Z., Yan, F., & Ju, H. (2007). Biomedical and clinical applications of immunoassays and immunsensors for tumor markers. TrAC Trends in Analytical Chemistry, 26(7), 679-688.

[35] Liu, R., Ye, X., & Cui, T. (2020). Recent Progress of Biomarker Detection Sensors. Research (Wash D C), 2020, 7940937.

[36] Ge, L., Wang, W., Hou, T., & Li, F. (2016). A versatile immobilization-free photoelectrochemical biosensor for ultrasensitive detection of cancer biomarker based on enzyme-free cascaded quadratic amplification strategy. Biosensors and Bioelectronics, 77, 220-226.

[37] Gao, X., Niu, S., Ge, J., Luan, Q., & Jie, G. (2020). 3D DNA nanosphere-based photoelectrochemical biosensor combined with multiple enzyme-free amplification for ultrasensitive detection of cancer biomarkers. Biosensors and Bioelectronics, 147, 111778.

[38] Luo, J., Liang, D., Qiu, X., & Yang, M. (2019). Photoelectrochemical detection of breast cancer biomarker based on hexagonal carbon nitride tubes. Analytical and Bioanalytical Chemistry, 411(26), 6889-6897.

[39] Wang, M., Yang, Z., Guo, Y., Wang, X., Yin, H., & Ai, S. (2015). Visible-light induced photoelectrochemical biosensor for the detection of microRNA based on Bi2S3 nanorods and streptavidin on an ITO electrode. Microchimica Acta, 182(1), 241-248.

[40] Liu, S.-T., Liu, X.-F., Chen, J.-S., Mao, C.-j., & Jin, B.-K. (2020). Highly sensitive photoelectrochemical biosensor for microRNA159c detection based on a Ti3C2:CDs nanocomposite of breast cancer. Biosensors and Bioelectronics, 165, 112416.

[41] Jiang, Y., Liu, D., Yang, Y., Xu, R., Zhang, T., Sheng, K., & Song, H. (2016). Photoelectrochemical detection of alpha-fetoprotein based on ZnO inverse opals structure electrodes modified by Ag2S nanoparticles. Scientific Reports, 6(1), 38400.

[42] Reynaud, E. (2010). Protein misfolding and degenerative diseases. Nature Education, 3(9), 28.

[43] Stenberg, K. A. E., Riikonen, P. T., & Vihinen, M. (1999). KinMutBase, a database of human disease-causing protein kinase mutations. Nucleic Acids Research, 27(1), 362-364.

[44] Li, X., Zhou, Y., Xu, Y., Xu, H., Wang, M., Yin, H., & Ai, S. (2016). A novel photoelectrochemical biosensor for protein kinase activity assay based on phosphorylated graphite-like carbon nitride. Analytica Chimica Acta, 934, 36-43.

[45] Ma, Z.-Y., Ruan, Y.-F., Zhang, N., Zhao, W.-W., Xu, J.-J., & Chen, H.-Y. (2015). A new visible-light-driven photoelectrochemical biosensor for probing DNA–protein interactions [10.1039/C5CC01832C]. Chemical Communications, 51(39), 8381-8384.

[46] Žolarová, M., García-Sierra, F., Bartos, A., Ricjny, J., & Ripova, D. (2012). Structure and pathology of tau protein in Alzheimer disease. Int J Alzheimers Dis, 2012, 731526.

[47] Hun, X., & Kong, X. (2021). An enzyme linked aptamer photoelectrochemical biosensor for Tau-381 protein using AuNPs/MoS2 as sensing material. Journal of Pharmaceutical and Biomedical Analysis, 192, 113666.

[48] Wen, Y. X., Liu, S. G., Tao, B. X., Luo, H. Q., & Li, N. B. (2020). A signal-off photocathode biosensor based on a novel metal-organic polymer for the detection of glucose. Sensors and Actuators B: Chemical, 304, 127279.

[49] Çakıroğlu, B., & Özacar, M. (2018). A self-powered photoelectrochemical glucose biosensor based on supercapacitor Co3O4-CNT hybrid on TiO2. Biosensors and Bioelectronics, 119, 34-41.

[50] Atchudan, R., Muthuchamy, N., Edison, T., Perumal, S., Vinodh, R., Park, K. H., & Lee, Y. R. (2019). An ultrasensitive photoelectrochemical biosensor for glucose based on bio-derived nitrogen-doped carbon sheets wrapped titanium dioxide nanoparticles. Biosens Bioelectron, 126, 160-169.
[51] Huang, H., Shang, M., Zou, Y., Song, W., & Zhang, Y. (2019). Iron phosphorus trichalcogenide ultrathin nanosheets: enhanced photoelectrochemical activity under visible-light irradiation [10.1039/C9NR07300K]. *Nanoscale*, 11(44), 21188-21195.

[52] Cao, L., Wang, P., Chen, L., Wu, Y., & Di, J. (2019). A photoelectrochemical glucose sensor based on gold nanoparticles as a mimic enzyme of glucose oxidase [10.1039/C9RA02088H]. *RSC Advances*, 9(27), 15307-15313.

[53] Tobaldi, D. M., Espro, C., Leonardi, S. G., Lajaunie, L., Seabra, M. P., Calvino, J. J., Marini, S., Labrincha, J. A., & Neri, G. (2020). Photo-electrochemical properties of CuO–TiO2 heterojunctions for glucose sensing [10.1039/D0TC01975E]. *Journal of Materials Chemistry C*, 8(28), 9529-9539.

[54] Amin, K. M., Muench, F., Kunz, U., & Ensinger, W. (2021). 3D NiCo-Layered double Hydroxide@Ni nanotube networks as integrated free-standing electrodes for nonenzymatic glucose sensing. *Journal of Colloid and Interface Science*, 591, 384-395.