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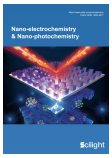

Review

Photo-Regulated Nanozymes for Sensing

Wenxuan Jiang [1], Yu Wu [1], Jingying Wang [1], Yuehe Lin [2,*] and Chengzhou Zhu [1,*]

[1] State Key Laboratory of Green Pesticide, International Joint Research Center for Intelligent Biosensing Technology and Health, College of Chemistry, Central China Normal University, Wuhan 430079, China
[2] School of Mechanical and Materials Engineering, Washington State University, Pullman, WA 99164, USA
* Correspondence: yuehe.lin@wsu.edu (Y.L.); czzhu@ccnu.edu.cn (C.Z.)

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Abstract: Advances in nanotechnology have facilitated the emergence of diverse nanozymes. Photo-regulated nanozymes represent a unique class of enzyme mimics with their activities being precisely modulated by irradiation. The distinct catalytic mechanisms of photo-regulated nanozymes enable their versatile applications across multiple fields, particularly in sensing. However, the low catalytic efficiency of most photo-regulated nanozymes limits their practical application. Designing advanced photo-regulated nanozymes is promising, yet achieving this remains a great challenge. In this review, the catalytic mechanisms of photo-regulated nanozymes are systematically introduced, and several effective strategies for the rational design of advanced photo-regulated nanozymes are also highlighted. Furthermore, we summarize the recent advances of photo-regulated nanozymes in sensing and discuss the potential challenges and the corresponding strategies in their development. It is believed that this review can revolutionize the design concepts of photo-regulated nanozymes and expand their prospects in sensing applications.

Keywords: photo-regulated nanozymes; biomimetic catalysis; sensing

1. Introduction

Nanozymes are a class of nanomaterials with enzyme-like activities [1,2]. As bio-inspired nanocatalysts, they can perform enzyme-like biocatalysis and follow fundamental enzyme kinetics, while the unique physicochemical properties endow them with novel capabilities that are absent in natural enzymes [3–5]. The rapid development of nanotechnology has promoted the emergence of novel nanozymes. As a typical representative among them, photo-regulated nanozymes can fully utilize the photoresponsive properties of nanocatalysts to rationally modulate their catalytic activities by light stimulation [6–8]. Compared with natural photo-regulated enzymes, several photo-regulated nanozymes exhibit similar catalytic mechanisms, including electron transfer and structural transformation, while also involving the generation of reactive intermediates [9–11]. Moreover, due to the unique properties, photo-regulated nanozymes also exhibit novel catalytic mechanisms such as photothermal effects, which are not observed in natural photo-regulated enzymes [12–15]. Photo-regulated nanozymes ingeniously integrate nanoscience, enzymology, and photochemistry, emerging as a robust new type of artificial enzyme.

Photo-regulated nanozyme catalytic systems utilize light energy to drive or enhance complex reactions. These systems exhibited multiple enzyme-like activities, including oxidase, peroxidase, superoxide dismutase, catalase, hydrolase, etc. [16–20]. Various biomimetic nanocatalysts, such as metal oxides, metal-organic frameworks, nitrogen-doped carbon materials, and noble metals [21–24], can serve as photo-regulated nanozymes and have been widely applied in the field of sensing. Despite the rapid development of photo-regulated nanozymes, the catalytic efficiency of most photo-regulated nanozymes is still lower than that of natural photo-regulated enzymes, hindering their practical applications. The rational design of advanced photo-regulated nanozymes with high activity to enhance their sensing performance remains a great challenge.

Herein, we deeply discuss the catalytic mechanisms of photo-regulated nanozymes and propose rational design strategies for advanced photo-regulated nanozymes based on their diverse catalytic mechanisms. Subsequently, the applications of photo-regulated nanozymes in sensing platforms are summarized, and personal perspectives on the challenges and limitations encountered during the development of photo-regulated nanozymes and the corresponding strategies are provided to promote the translation into practical applications. This review highlights effective strategies for the development of novel photo-regulated nanozymes and offers new insights into the design of next-generation photo-driven sensing platforms.

2. Catalytic Mechanism and Design Strategies of Photo-Regulated Nanozymes

As advanced mimics of natural enzymes, the development and design of nanozymes are often guided by the catalytic mechanisms of natural enzymes. Photo-regulated enzymes are a class of efficient catalysts found in nature that can directly harness light energy to drive specific chemical reactions. Currently, only three types of natural photo-regulated enzymes have been discovered, including DNA photolyase [25–28], fatty acid oxidoreductase [29–32], and fatty acid photodecarboxylase [33–36]. The key catalytic mechanism of them involves triggering electron excitation and structural changes through light absorption, thereby activating their catalytic activity [37,38]. Specifically, photosensitive cofactors within enzymes such as flavin adenine dinucleotide and nicotinamide adenine dinucleotide phosphate can absorb light at specific wavelengths and transition from the ground state to an excited state. This process is also accompanied by structural transformation in the enzyme. Subsequently, the electron transfers to the substrate and generates free radicals or high-energy intermediates, which significantly reduce the activation energy of the target chemical reaction, enabling it to proceed rapidly under mild conditions. After the reaction is completed, the enzyme returns from the excited state to the ground state, completing the catalytic cycle. Inspired by this mechanism, a variety of photo-regulated nanozymes have emerged in succession. Notably, the photo-regulated nanozymes also possess the unique physicochemical properties of nanomaterials, which endow them with novel catalytic mechanisms. In this section, we unveil the catalytic mechanisms in depth, expecting to guide the precision design of advanced photo-regulated nanozymes.

2.1. Electron Transfer

The electron transfer mechanism of photo-regulated nanozymes is one of the most efficient mechanisms, which exhibits the closest resemblance to the catalytic processes of natural photo-regulated enzymes. As shown in Figure 1A, when irradiated by the light with a specific wavelength, the nanozyme or photosensitive unit on the nanozyme absorbs photons to produce high-energy electrons, which can transition from the ground state to an excited state. The excited electrons can be further injected into the active site by chemical bonds. Following the adsorption of the substrate onto the catalytic site, the high-energy electrons are transferred to the substrate, accompanied by the generation of reactive radicals or other high-energy intermediates. This direct electron transfer process exhibits an exceptionally high quantum conversion efficiency, thereby enhancing the catalytic efficacy of substrate transformation [14].

Inspired by the catalytic mechanism of natural photo-regulated enzymes, the introduction of photosensitizers onto nanozymes promises to mimic the role of cofactors. One example utilized the adsorptive property of polydopamine (PDA) to assemble the photosensitizer IR820 with mesoporous ceria ($mCeO_2$), resulting in the synthesis of the IR/P@Ce nanozyme. Under near-infrared (NIR) light irradiation, photo-generated electrons from IR820 were capable of transferring to $mCeO_2$ via PDA. This phenomenon facilitated the reduction of Ce^{4+} to Ce^{3+}, thereby enhancing the peroxidase-like activity of IR/P@Ce nanozyme with a maximum rate (V_{max}) of 1.67×10^{-7} M s^{-1} and Michaelis constant (K_m) of 6.67 mM. This result demonstrates that the electron transfer under irradiation can significantly enhance catalytic activity, achieving photoregulation [39]. However, given that the majority of photosensitizers are organic compounds that face challenges in binding to nanozymes, the further exploration of alternative photosensitizers is an effective method. A strategy anchoring Ru sites onto the bipyridine ligands of UiO-67 was developed to mimic the structure of the photosensitizer tris(bipyridine)ruthenium(II) (Figure 1B). *In situ* experiments demonstrated that the photoelectrons transfer from ligand to Ru sites, following the electron transfer process analogous to that in natural enzymes. The atomically dispersed Ru sites served as highly active catalytic sites, enhancing the photoelectric conversion efficiency and reducing the energy change to 0.33 eV for the formation of Ru = O intermediates. Based on the phenomenon of electron transfer under irradiation, it results in a 7.0-fold enhancement in peroxidase-like activity [40].

2.2. Photothermal Effect

The utilization of light energy extends beyond chemical transformation to include its conversion into thermal energy, a process known as the photothermal effect. Due to nanometer confinement and localized surface plasmon resonance, nanocatalysts such as noble metal nanoparticles exhibit remarkable photothermal conversion performance. The photothermal effect primarily enhances the catalytic activity of nanozymes through two pathways, including the rise of local temperature and the transfer of hot electrons, which can also work synergistically. Specifically, when exposed to light of specific wavelengths (especially NIR light), electrons within the nanozyme transition from the ground state to an excited state. These high-energy hot electrons rapidly return to the stable ground state through collisions and vibrations. During this process, energy is converted into thermal lattice vibrations by non-radiative relaxation, macroscopically manifested as localized temperature increase. Furthermore, hot electrons can also be injected into the active sites of the nanozyme, further accelerating substrate catalysis, which is similar to the mechanism of electron transfer (Figure 1C) [41,42].

To enhance photothermal conversion efficiency, the primary consideration should be given to using the plasmonic resonance effects of noble metals such as Au, Ag, and Pd to enhance the catalytic activity. Our group synthesized gold nanoparticle-loaded UiO-66 (UiO-66/Au NPs), which possesses a 4.03-fold photoenhanced hydrolase-like activity with a V_{max} of 14.7 × 10^{-8} M s^{-1}. Under irradiation, the Au NPs simultaneously generate localized heating and facilitate electron transfer (Figure 1D). This synergistic effect of UiO-66 and Au NPs also significantly improves the substrate affinity with a K_m of 1.24 × 10^{-3} M, resulting in a remarkable 17.8-fold enhancement in the catalysis of organophosphorus substrates [43]. For semiconductor nanozymes, regulating the bandgap structure can induce a redshift in the absorption edge, thereby expanding the wavelength range of absorbed light. Wang and coworkers constructed a heterojunction by integrating Co_3O_4 with carbon nanodots. The resultant CD@Co_3O_4 heterojunctions possess a photothermal conversion efficiency of 62.1%, which is higher than the CDs (51.1%) and Co_3O_4 (46.8%). Compared to the control group, the CD@Co_3O_4 exhibited a temperature increase of ~43 °C within 1 min under irradiation, demonstrating outstanding photothermal performance and leading to a 1.85-fold enhancement of peroxidase-like activity with 4.8 × 10^{-7} M s^{-1} and a 1.51-fold enhancement of glutathione peroxidase-like activity [44].

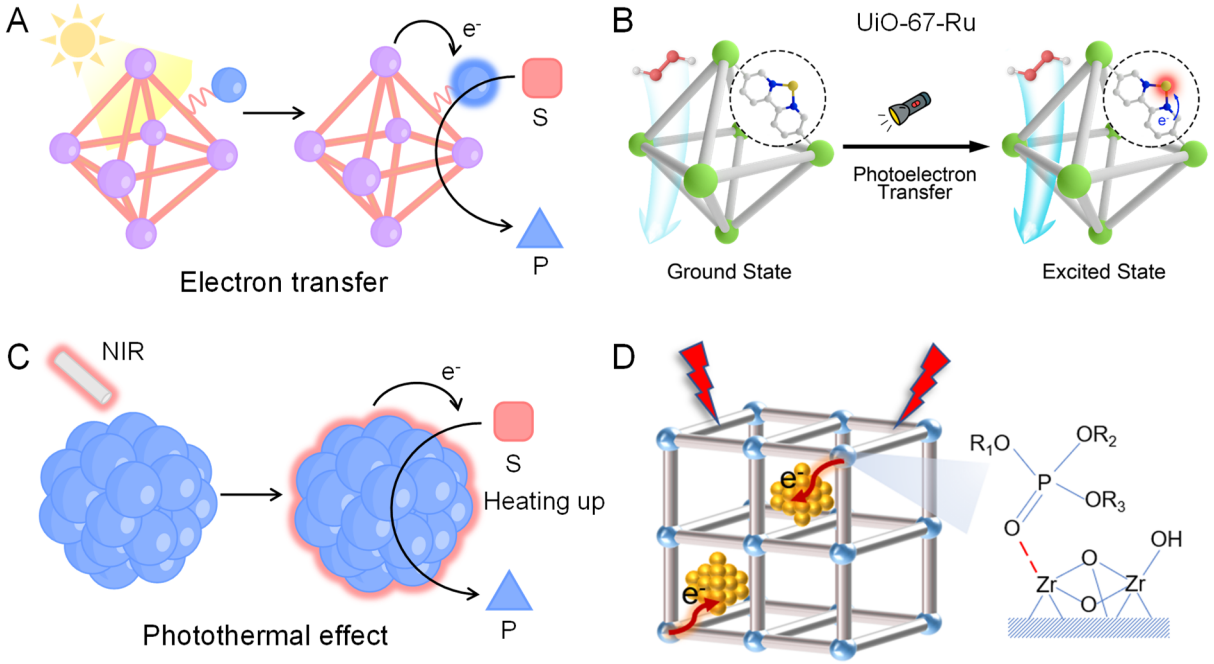

Figure 1. (**A**) Schematic illustration of the electron transfer mechanism of photo-regulated nanozymes. (**B**) Schematic illustration of the electron transfer mechanism of UiO-67-Ru [40]. Copyright 2023, National Academy of Sciences. (**C**) Schematic illustration of the photothermal effect mechanism of photo-regulated nanozymes. (**D**) Schematic illustration of the photothermal effect mechanism of UiO-66/Au NPs [43]. Copyright 2025, Wiley.

2.3. Structural Transformation

During the catalytic processing of substrates by natural photo-regulated enzymes, photosensitive cofactors not only engage in electron transfer with the substrate but also undergo structural transformation. Inspired by this phenomenon, structural transformation mechanisms have been proposed for photo-regulated nanozymes. For

nanozymes containing photosensitive units, the steric hindrance effect of these photosensitive units can impede substrate access to the active sites, resulting in catalyst deactivation. Upon absorption of photons at specific wavelengths, reversible structural changes occur in either the photosensitive units themselves or their surface functional groups. This transformation eliminates the steric hindrance effect, thereby activating the catalytic function. When the light source is turned off, the structure of the photosensitive units reverts to its original state [10]. Furthermore, nanozymes can also undergo structural transformation relying on their inherent photoresponsive properties. Under irradiation, reversible or irreversible changes take place in the structure or surface groups of nanozymes. This phenomenon alters the microenvironment of the active centers in nanozymes, which can regulate their catalytic activity (Figure 2A) [45].

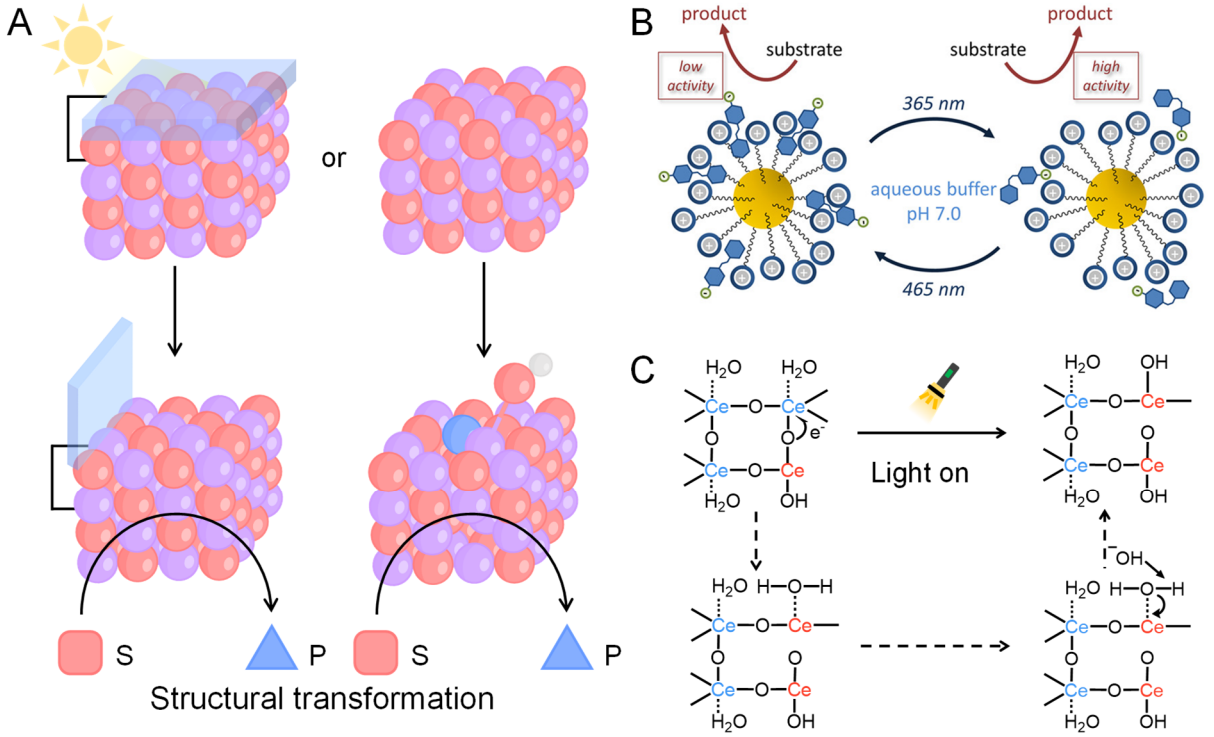

Figure 2. (**A**) Schematic illustration of the structural transformation mechanism of photo-regulated nanozymes. (**B**) Schematic illustration of the structural transformation mechanism of Au NPs with azobenzene [46]. Copyright 2017, American Chemical Society. (**C**) Schematic illustration of the structural transformation mechanism of GB-CeO_2 [18]. Copyright 2024, American Chemical Society.

Achieving switchable enzyme-like activity relies critically on the selection and integration of appropriate photosensitive units into the nanozyme. Small molecules such as azobenzene and spiropyran are widely employed as photosensitive units in photo-regulated nanozymes, which can be easily chemically modified onto the surface of nanozymes. An early example of this strategy involved modifying azobenzene onto Au NPs to achieve photo-regulated hydrolytic catalysis of the substrate 2-hydroxypropyl-4-nitrophenylphosphate. Under dark conditions, azobenzene adopts the trans-configuration and binds to the surface of Au NPs, thereby blocking substrate access to the active sites. Upon irradiation with 365 nm light, azobenzene underwent isomerization to the cis-form. The cis-configured azobenzene desorbed from the Au NPs, exposing the catalytic sites. Subsequently, azobenzene reverted to its initial structure under irradiation with light at a wavelength of 465 nm. By switching between different light sources, the Au NPs-azobenzene catalyst was endowed with reversible on-off hydrolytic catalytic activity (Figure 2B) [46]. Besides modifying photosensitive units, regulating the photoresponsive property of nanozymes can also accelerate their structural transformation. One way involves the modulation of the crystalline phase structure of CeO_2 nanozymes by grain boundary engineering (GB-CeO_2). The presence of abundant grain boundaries enhanced the photoresponsive property of GB-CeO_2 under irradiation, accelerating the transfer of electrons. *In situ* experiments demonstrated that Ce^{4+} sites can transform into Ce-OH sites under irradiation, accompanied by the formation of abundant oxygen vacancies on the surface (Figure 2C). After testing under irradiation, GB-CeO_2 nanozymes exhibit a V_{max} of 90.37 μM min^{-1}, indicating that their phosphatase-like activity was 114.39 times higher than that of CeO_2 without irradiation (0.79 μM min^{-1}). This phenomenon demonstrates that the photo-induced structural transformation provides a feasible approach for enhancing catalytic activity [18].

3. Application in Sensing

Taking advantage of the unique catalytic functions and controllable catalytic activities, photo-regulated nanozymes have been extensively employed to construct stable and efficient sensors, demonstrating favorable sensing performance. In this section, recent advances in sensing applications of photo-regulated nanozymes are summarized, which focus specifically on their roles in sensing platforms.

3.1. Signal Amplification

Under irradiation, photo-regulated nanozymes typically exhibit significantly enhanced catalytic activity, which plays the role of signal amplification in sensing processes and further improves the detection sensitivity. Based on this, various sensing platforms have been developed. The direct detection strategy for the target has emerged as a preferred sensing mode owing to its operational simplicity and rapid response characteristics (Figure 3A). For example, a $Co_3V_2O_8$–TiO_2 composite with a Type-II heterojunction architecture was successfully synthesized through *in situ* growth of $Co_3V_2O_8$ on TiO_2 templates. Under irradiation, this heterostructure demonstrated efficient catalytic generation of reactive oxygen species from H_2O_2. When 3,3′,5,5′-tetramethylbenzidine (TMB) was introduced as the chromogenic substrate, it underwent rapid oxidation and resulted in distinct colorimetric changes (Figure 3B). The designed sensor exhibited a linear detection range of 10–80 μM with a calculated limit of detection of 1.98 μM [47]. However, this strategy requires the substrate to possess redox properties, which limits its application in detecting biomacromolecules such as nucleic acids and proteins, making it difficult to utilize in the field of sensing.

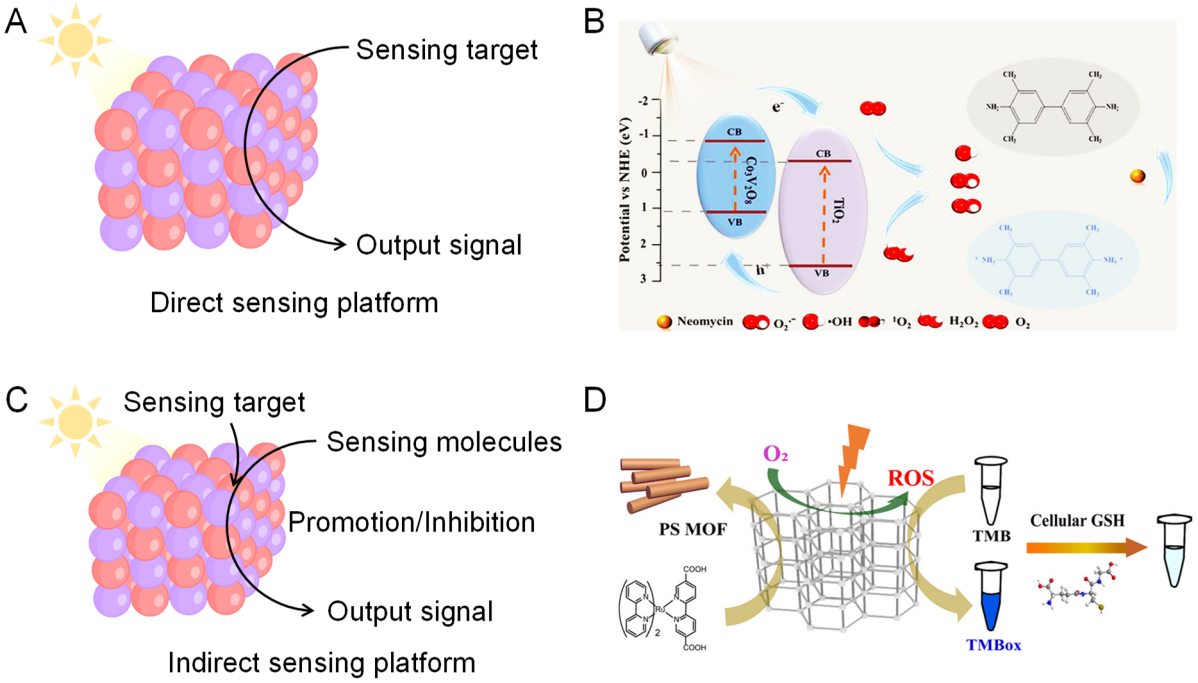

Figure 3. (**A**) Schematic illustration of the direct sensing platforms constructed by photo-regulated nanozymes. (**B**) Schematic illustration of the direct sensing platforms constructed by $Co_3V_2O_8$–TiO_2 for H_2O_2 [47]. Copyright 2025, American Chemical Society. (**C**) Schematic illustration of the indirect sensing platforms constructed by photo-regulated nanozymes. (**D**) Schematic illustration of the indirect sensing platforms constructed by PSMOF for GSH [48]. Copyright 2019, American Chemical Society.

Another common sensing strategy is indirect detection, which operates on the principle of inhibiting or promoting signal output upon the introduction of the targets (Figure 3C). Liu et al. synthesized a photosensitive MOF (PSMOF) by incorporating a $Ru(bpy)_3^{2+}$ derivative and biphenyl-dicarboxylic acid through a mixed-ligand strategy. The resulting PSMOF enabled the reversible switching of oxidase-like activity under irradiation. By utilizing the competitive interaction between the chromogenic substrate TMB and glutathione (GSH), an inhibitory sensing platform was designed for the indirect detection of GSH (Figure 3D). This sensor offered the advantages of excellent selectivity and high sensitivity, with a detection limit for GSH of 0.68 μM [48]. Although indirect sensing strategies have broadened the detection scope of substrates, their drawback of poor substrate selectivity makes them difficult to apply in complex samples containing multiple interfering molecules.

Multi-enzyme cascade sensing platforms, capable of detecting complex targets, can output signals through stepwise catalysis of the targets (Figure 4A). An early example of this strategy involves synthesizing a Pd-N-C nanozyme with NIR responsiveness and oxidase-like activity through microwave pyrolysis. By integrating acetylcholinesterase (AChE) with the Pd-N-C nanozyme, they developed a sensor for detecting AChE activity. Specifically, AChE catalyzed the hydrolysis of acetylthiocholine, generating thiocholine, which inhibited the oxidase-like activity of the Pd-N-C nanozyme. The activity of AChE was calculated by monitoring the signal changes of the chromogenic substrate (Figure 4B) [49]. Furthermore, nanozymes with multi-enzyme activities can replace natural enzymes and reduce the synthetic steps of catalysts, enhancing the efficiency of cascade catalysis. However, due to the absence of the specific substrate recognition capability inherent to natural enzymes, the accuracy of the signal output may be compromised. The emergence of multi-enzyme cascade detection platforms has further expanded the range of detectable substrates and demonstrated strong anti-interference capabilities. However, issues such as the need for frequent switching of reaction environments have increased the complexity of platform operation, making rapid detection difficult to achieve.

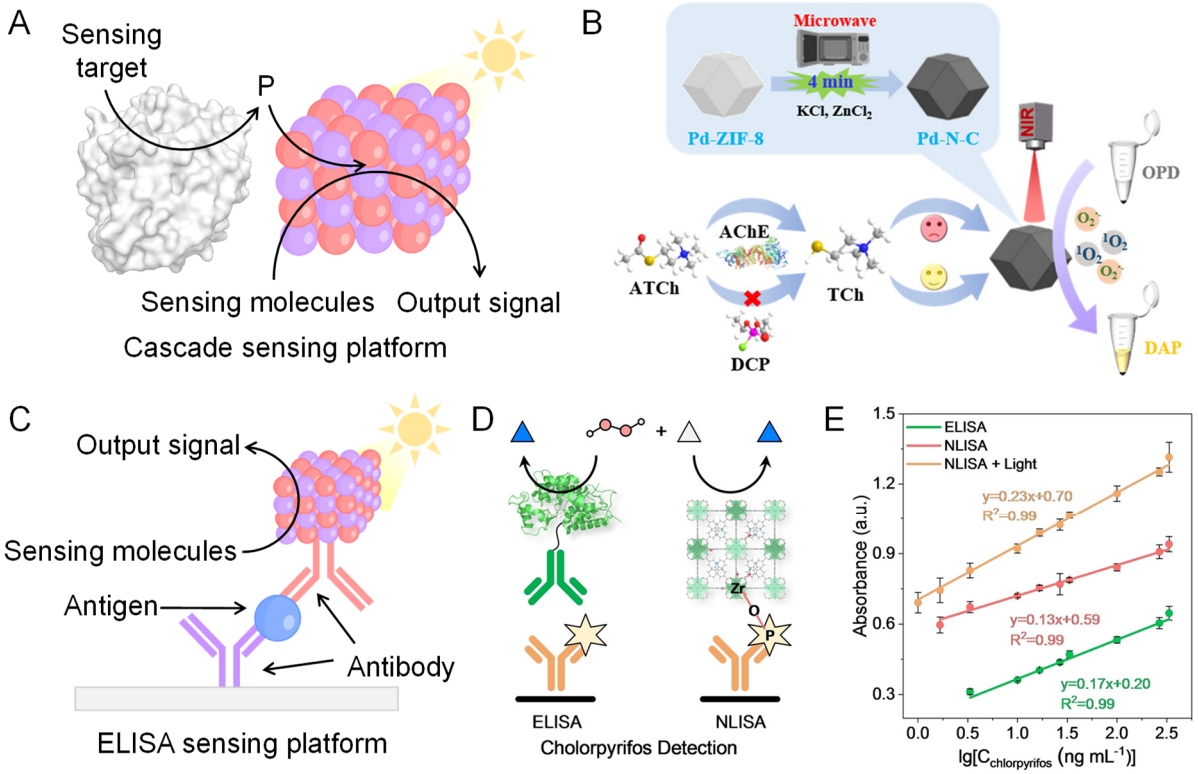

Figure 4. (**A**) Schematic illustration of the cascade sensing platforms constructed by photo-regulated nanozymes. (**B**) Schematic illustration of the cascade sensing platforms constructed by Pd-N-C for the AChE activity [49]. Copyright 2025, American Chemical Society. (**C**) Schematic illustration of the ELISA sensing platforms constructed by photo-regulated nanozymes. (**D**) Schematic illustration of the ELISA sensing platforms constructed by UiO-67-Fe for chlorpyrifos. (**E**) Linear curves of ELISA, NLISA, and NLISA+Light [50]. Copyright 2024, Wiley.

The enzyme-linked immunosorbent assay (ELISA) represents one of the most common and highly efficient methods in sensing. The high specificity of antibodies or aptamers endows ELISA sensing platforms with exceptional selectivity, while natural enzymes confer robust catalytic sensing performance. However, the low stability and cost-inefficiency of natural enzymes make them difficult to be widely applied. The substitution of natural enzymes with nanozymes possessing the same catalytic activities holds promise for addressing these issues (Figure 4C). Our group integrated multiple enzyme-like cofactors into the MOF material UiO-67-Fe, enabling it to exhibit excellent peroxidase-like activity. Considering the strong adsorption of Zr sites for phosphate ester bonds, UiO-67-Fe was employed as a substitute for natural horseradish peroxidase in the specific detection of chlorpyrifos (Figure 4D). The constructed nanozyme-linked immunosorbent sensing assay (NLISA) platform demonstrated a detection limit of 0.46 ng mL^{-1} under irradiation, significantly lower than that of the natural enzyme-based immunosorbent sensing assay platform (1.91 ng mL^{-1}) (Figure 4E). This result demonstrated the great prospects of nanozymes in sensing applications [50].

3.2. Interference Pretreatment

Point-of-care testing (POCT) has emerged as one of the most promising sensing modalities due to its operational simplicity and rapid response. Despite its notable advantages, POCT often compromises its anti-interference performance, leading to false-positive or false-negative results. Although pretreatment of complex samples can eliminate the influence of interferents, it requires specialized equipment, which contradicts the fundamental concept of POCT. To address this issue, a strategy utilizing nanozymes for interferent pretreatment has emerged. As shown in Figure 5A, unlike natural enzymes with single catalytic activity, nanozymes possess multi-enzyme activities that enable simultaneous catalysis of multiple substrates. This feature holds promise for the pretreatment of various interferents in complex samples under irradiation. When photo-regulated nanozymes are added to a complex sample containing the target substance and multiple interferents, followed by irradiation, the interferents can be rapidly eliminated. Subsequently, signals are output through a colorimetric reaction, thereby avoiding the occurrence of false-negative and false-positive results. As a typical example, the ability of Cu SA/NC nanozyme was utilized to express multiple enzyme-like activities under irradiation to develop a pretreatment-and-sensing integration kit (PSIK). Specifically, Cu SA/NC first switched to a pretreatment mode under NIR light, where its expressed peroxidase-like, oxidase-like, and catalase-like activities collectively eliminate interferents in the sample (Figure 5B). Upon removal of the light source, Cu SA/NC switched to a detection mode, which only expressed peroxidase-like activity. Based on this, Cu SA/NC was coupled with glucose oxidase to construct a tandem reaction system, which was further developed into a PSIK, demonstrating exceptional anti-interference capability in glucose assays (Figure 5C). Furthermore, using A549 human lung carcinoma cells and PC12 rat pheochromocytoma cells as a model, the efficient pretreatment performance of the PSIK successfully cleared endogenous interferents, enabling precise glucose detection in actual samples (Figure 5D,E) [51]. The emergence of the PSIK kit enables effective pretreatment of interferents, yet its requirement for specific light sources and the addition of extra natural enzymes complicate the detection process.

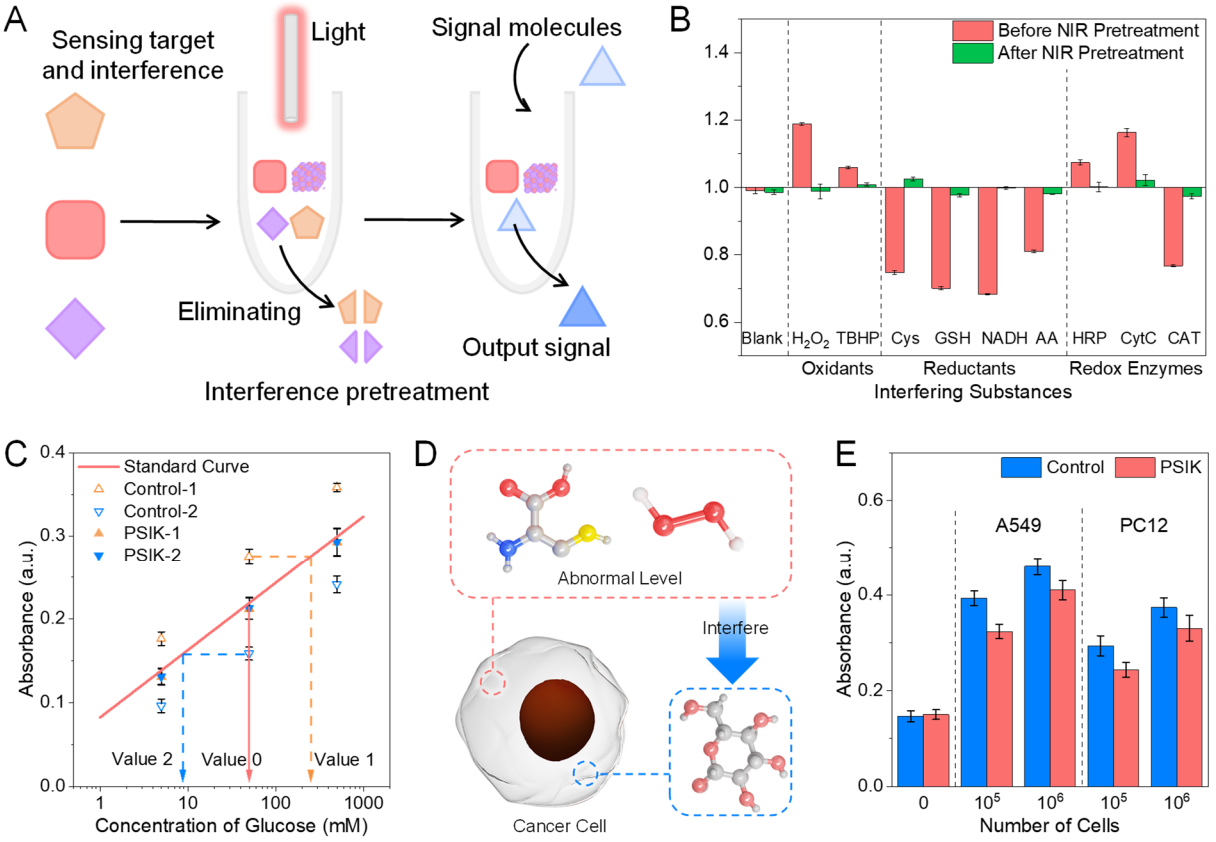

Figure 5. (**A**) Schematic illustration of interference pretreatment by using photo-regulated nanozymes. (**B**) The scavenging performances of Cu SA/NC for interfering substances. (**C**) Detection of glucose using PSIK in the presence of different interferences. (**D**) Schematic illustrating the abnormal expression in cancer cells and their interference with the sensing target. (**E**) Detection of glucose in A549 and PC12 using classic methods and PSIK [51]. Copyright 2023, Wiley.

3.3. Feature Discrimination

Due to the absence of the active pockets, nanozymes are unable to replicate the specific recognition and catalytic functions of natural enzymes towards substrates. Only relying on a single active site and catalytic mechanism, traditional nanozymes often fail to achieve feature discrimination among substrates of the same category. By exploiting the differences in functions and catalytic mechanisms between photo-regulated nanozymes and traditional nanozymes, it becomes feasible to construct substrate feature fingerprints through the output of multiple signals, thereby enabling the differentiation of substrates within the same category (Figure 6A). Our group reported a Ga doped carbon nitride nanozyme (Ga-CN), wherein the introduction of Ga sites modulated the electronic structure of the cyano groups and formed Ga-CN dual sites, thereby synergistically enhancing the peroxidase-like activity. The addition of thiol-containing drugs can inhibit the oxidation of hydrogen peroxide at the Ga-CN dual sites, thereby reducing the intensity of the chromogenic signal (Figure 6B). Different thiol-containing drugs exhibit distinct inhibitory mechanisms on the activity of the Ga-CN nanozyme, and even the same drug demonstrates varying inhibitory mechanisms with irradiation and without irradiation. Based on this, by evaluating the kinetics of the nanozyme reaction after adding thiol-containing drugs, such as Tapazole (TAP) and Tiopronin (TP), the kinetic parameters can be obtained, respectively, under irradiation or not (Figure 6C). Subsequently, a Ga-CN nanozyme sensor array was developed for the feature discrimination of thiol-containing drugs. This sensor array was also integrated with the machine learning technology based on a support vector machine (SVM) algorithm (Figure 6D). On one hand, through algorithms, the adaptive learning mode of machine learning can construct optimal models based on limited samples, thereby accelerating the screening of large-scale drug candidates and overcoming the cumbersome data processing drawbacks of traditional methods. On the other hand, the advantage of automated feature extraction in machine learning enables rapid processing of complex samples, avoiding human-induced errors in traditional data identification and further improving the accuracy of results. Compared to previous approaches that employed multiple materials to generate multiple signals, this strategy effectively avoids interference introduced by heterogeneous components and simplifies the construction of the sensing platform, holding promise for facilitating early-stage drug discovery [52]. However, this machine learning-based sensor array faces challenges in optimal model identification and requires specialized expertise, which undoubtedly limits its broad application.

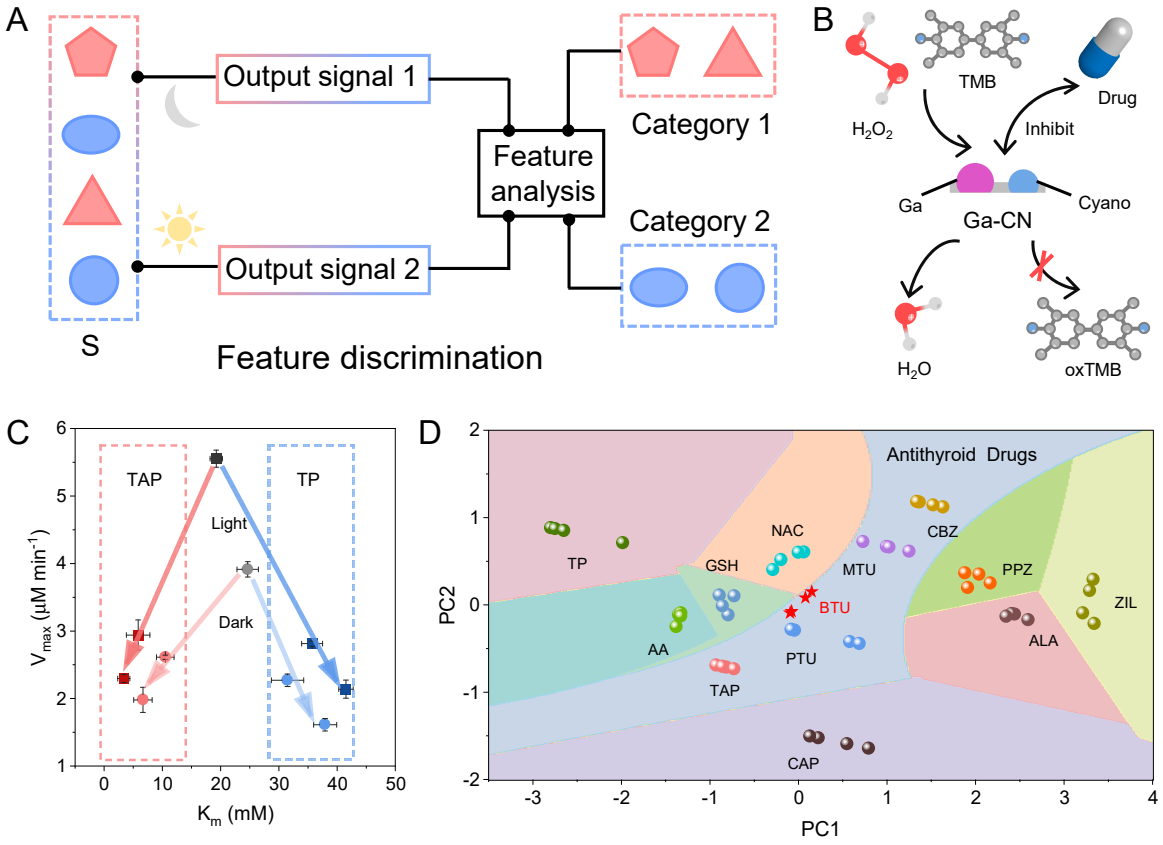

Figure 6. (**A**) Schematic illustration of feature discrimination by using photo-regulated nanozymes. (**B**) Schematic diagram of drug inhibition on Ga-CN. (**C**) The changes in K_m and V_{max} of Ga-CN nanozyme with irradiation or not after adding TAP and TP. (**D**) SVM classification in PCA space [52]. Copyright 2025, American Chemical Society.

4. Challenges and Limitations in Translating to Practical Sensing Applications

Due to the significantly superior stability and broader wavelength range of response exhibited by photo-regulated nanozymes compared to natural photo-regulated enzymes, their range of applications is wider than that of natural enzymes. However, certain foreseeable limitations, such as catalytic activity and specificity, still make them hard to match up to natural enzymes. Furthermore, the absence of photosensitive units in most photo-regulated nanozymes results in significantly longer light-response times than those of natural enzymes, further hindering the development of photo-regulated nanozymes. In this section, some personal perspectives on the potential challenges and corresponding strategies for reference are presented to promote the translation of photo-regulated nanozymes into practical applications.

Given the highly efficient catalytic activity and specificity of natural enzymes, the design and synthesis of photo-regulated nanozymes predominantly follow structural guidance from natural enzymes. However, great differences in composition and structure make it challenging for photo-regulated nanozymes to effectively mimic natural enzymes. Current photo-regulated nanozyme development primarily focuses on mimicking specific metal catalytic sites of enzymes, often neglecting the critical role of coordination microenvironments. Precisely tuning the coordination environment or introducing synergistic catalytic groups represents an effective strategy to enhance the catalytic activity of photo-regulated nanozyme, yet its realization remains a significant challenge. *In situ* spectroscopic techniques, such as *in situ* infrared spectroscopy, *in situ* Raman spectroscopy, and *in situ* synchrotron radiation, have significantly advanced the understanding of coordination environments and synergistic catalytic groups in photo-regulated nanozymes. It has guided the design of novel photo-regulated nanozymes with superior performance and well-defined mechanisms. Furthermore, the emergence of machine learning-based predictive technologies has transformed traditional trial-and-error approaches, providing novel strategies for developing advanced photo-regulated nanozymes. However, as machine learning technologies remain in the exploratory phase and require specialized knowledge and technical expertise, they can only serve as an auxiliary tool in the design and synthesis of photo-regulated nanozymes.

As a class of nanomaterials with enzyme-like activities, photo-regulated nanozymes typically exhibit novel catalytic functions distinct from those of natural enzymes. Although this characteristic has facilitated the applications of photo-regulated nanozymes, these functions may also impact the enzyme-like catalytic activities, which further complicates the mechanism of photo-regulated nanozymes. To facilitate further advancement, a deep investigation into the catalytic mechanisms of photo-regulated nanozymes is imperative. There remains a lack of characterization methods for monitoring the catalytic reaction processes of photo-regulated nanozymes, necessitating the development of advanced techniques to address this issue. *In situ* spectroscopic techniques not only enable material characterization but also facilitate the investigation of catalytic mechanisms. Notably, the development of photo-regulated nanozymes represents an integration of nanotechnology and biotechnology. Researchers should concurrently consider both the catalytic properties of enzymes and nanomaterials during the investigation of catalytic mechanisms. Moreover, theoretical computational simulations of catalytic reaction processes facilitate the investigation into the catalytic mechanisms of photo-regulated nanozymes. However, most theoretical models exhibit significant discrepancies from actual reaction conditions, necessitating further integration with experimental data for comprehensive analysis.

With the advancement of the sensing field, the application scope of photo-regulated nanozymes has become increasingly broad. To address the growing diversity of detection scenarios, it is imperative to further expand the range of enzyme-like activities in photo-regulated nanozymes. Most reported photo-regulated nanozymes only exhibit redox-like or hydrolase-like activities. There remains a great challenge in mimicking natural photo-regulated enzymes such as DNA photolyases and decarboxylases, which hinders the development of photo-regulated nanozymes. Addressing this limitation requires urgent exploration of novel catalytic activities through innovative material utilization and reaction conditions. Notably, beyond their photo-responsive properties, photo-regulated nanozymes exhibit other unique physicochemical characteristics, such as acoustic, magnetic, and electrical responsiveness. Leveraging these properties enables photo-regulated nanozymes to surpass the catalytic limitations and broaden the application scope of sensors. Furthermore, integrating artificial intelligence technologies into sensors is expected to drive innovation in sensing modalities and accelerate data processing, thereby advancing the development of novel and efficient sensing platforms.

5. Conclusions

Photo-regulated nanozymes represent a novel class of nanozymes that perfectly integrate the unique physicochemical properties of nanomaterials with enzyme-like catalytic activities, exhibiting the unique functions that are not possessed by natural enzymes. In this review, we propose various design principles for photo-regulated

nanozymes based on their catalytic mechanisms. The systematic compilation of their sensing applications and critical analysis of current limitations and corresponding solution strategies is anticipated to significantly enhance their transition from conceptual frameworks to real-world applications. The emergence of photo-regulated nanozymes has facilitated a transition from passive catalysis to active regulation strategies in nanozymes, opening up new avenues for the application in the field of sensing.

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Conflicts of Interest

The authors declare no conflict of interest.

Use of AI and AI-Assisted Technologies

No AI tools were utilized for this paper.

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