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Review

Advances in multiplexed photoelectrochemical sensors for multiple components

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ABSTRACT

Multiplexed photoelectrochemical (M-PEC) sensors are transforming the landscape of analytical detection by offering unprecedented sensitivity and the ability to simultaneously detect multiple targets—ranging from biomolecules and small organic compounds to metal ions. These sensors represent a significant leap forward in key sectors such as biomedical diagnostics, environmental monitoring, and food safety, overcoming limitations of traditional single-signal PEC sensors, which often struggle with interference and selectivity in complex samples. Recent innovations in materials, such as quantum dots, metal–organic frameworks, and nanocomposites, have driven improvements in light-harvesting efficiency, signal amplification, and target specificity. Furthermore, advanced multiplexing strategies—such as wavelength-resolved, potential-resolved, spatial-resolved, and multimode sensing—have empowered these sensors to achieve enhanced performance in detecting multiple analytes with minimal crosstalk. Despite impressive progress, challenges remain, particularly in improving long-term stability, scalability, and real-world applicability. This review discusses cutting-edge advancements in M-PEC sensor detection strategies and the applications of M-PEC sensors for detecting multiple targets, while offering perspectives on future directions, including the push toward miniaturization, high-throughput screening, and ultra-sensitive trace-level detection, setting the stage for widespread practical implementation across various applications.

1. Introduction

Photoelectrochemical (PEC) sensors have been established as a versatile and powerful analytical tool, particularly valued for their ability to convert light into electrical signals that correspond to the presence of specific analytes [1–5]. The fundamental operation of PEC sensors is based on the photoelectric effect, where light-induced electron-hole pairs in a photoactive material generate a measurable current [6]. This capability allows for highly sensitive and selective detection of various chemical and biological substances, making PEC sensors attractive for applications ranging from environmental monitoring [7–9] to medical diagnostics [10–13]. However, traditional PEC sensors, often limited to detecting a single analyte, face significant challenges in complex sample matrices, including the risk of cross-reactivity, susceptibility to interference, and reduced accuracy when multiple analytes are present. Moreover, the reliance on a single detection signal makes it difficult to cross-validate results, which is a critical requirement in high-stakes applications like clinical diagnostics where accuracy and reliability are

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paramount.

To address these restrictions, the development of multiplexed PEC (M-PEC) sensors has gained significant attention [14–16]. Unlike single-target systems, M-PEC sensors are designed to simultaneously detect multiple analytes or signals by integrating various photoactive materials and recognition elements on a single platform. This multiplexing capability enhances the selectivity and sensitivity of the sensors, enables the concurrent analysis of multiple targets within a single assay, and reduces the likelihood of false positives by allowing for cross-validation through multiple detection pathways [17,18]. M-PEC sensors offer several additional advantages. First, their rapid photoelectric response facilitates the development of fast detection tools, while their diverse detection modes enhance flexibility and expand application scenarios [19]. Second, these sensors provide comprehensive information about target analytes in a single test, reducing testing costs [20], simplifying procedures [21], and minimizing sample requirements—particularly valuable for precious or hard-to-obtain samples [22]. Third, their two-in-one or multi-in-one detection capability supports device miniaturization and compactness, which is especially advantageous for applications such as cancer diagnostics, where simultaneous detection of multiple biomarkers can yield a more comprehensive and accurate assessment. The advancements in material science have been a driving force behind the development of M-PEC sensors. Innovations such as the incorporation of nanomaterials [23–28], quantum dots [29–32], and hybrid composites [33–35] have significantly enhanced the photoelectrochemical properties of these sensors. These materials contribute to improved charge separation [35], increased light absorption [36], and greater overall stability, which are essential for reliable performance in multiplexed detection.

Nevertheless, the transition from single target/signal to multiple target/signal detection introduces new challenges. Key issues include managing signal interference between different detection pathways, ensuring uniformity and reproducibility across multiple sensing sites, and maintaining stability in complex biological environments [14,16,37]. Overcoming these challenges is critical for the continued evolution and practical application of multiplexed PEC technology. In this review, we introduce the concept of M-PEC sensors, summarize emerging strategies in their development—focusing on various detection strategies—and highlight the exciting new applications in detecting various targets with high performance. We also discuss the challenges that remain and offer perspectives on the future direction of M-PEC sensor technology, emphasizing its potential to revolutionize various fields, particularly in biomedical diagnostics, environmental monitoring, and food safety.

2. Concept of multiplexed PEC sensors

M-PEC sensors have emerged as a sophisticated evolution of traditional single-analyte PEC systems, offering the ability to detect multiple targets simultaneously within a single platform (Fig. 1). For an original sample containing multiple components, the M-PEC sensor could produce multi-channel signals due to the specificity to different targets on the individual sites. The multi-channel signals can be resolved by the wavelength [38], the potential [12], and the spatial region [39]. This capability is particularly valuable in complex analytical environments where the simultaneous measurement of various analytes can provide a more comprehensive understanding of a sample's composition. The operation of M-PEC sensors hinges on three core principles: the integration of diverse photoactive materials, the employment of distinct signal transduction strategies, and the careful design of sensor architectures that minimize crosstalk while maximizing sensitivity and specificity.

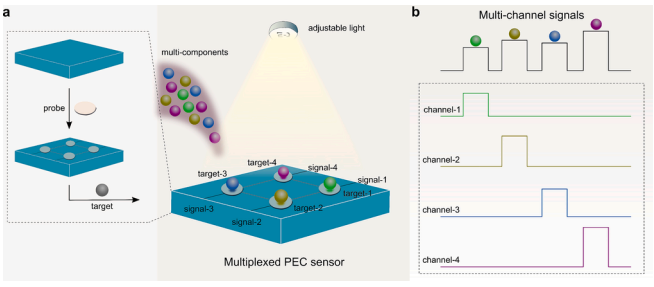

Fig. 1. Schematic of multiplexed PEC sensors for detecting multiple targets. a, Sensor preparation and detection for multiple components. b, Multi-channel signals from the sensor.

At the heart of M-PEC sensors is the use of multiple photoactive materials, each designed to respond uniquely to specific stimuli, such as different light wavelengths or distinct electrochemical potentials. By selecting materials with complementary optical and electronic properties, it is possible to generate distinct photoelectrochemical signals for each target analyte within the same sensor system. Notably, the geometry of photoactive materials or related electrode could significantly affect the photocurrent by engineering light absorption [40], electric field distribution [41], the contract area [42], and carrier transport [43]. After selecting the target-oriented photoactive materials, it is vital to employ sophisticated signal modulation strategies that prevent interference between the signals corresponding to different analytes. Typically, wavelength-resolved multiplexing [38,44,45] utilizes the unique optical properties of photoactive materials, where different materials absorb and emit light at distinct wavelengths, enabling the separation of signals based on their spectral characteristics. Potential-resolved multiplexing [12,46,47], on the other hand, leverages the electrochemical characteristics of the materials, applying different potentials to selectively trigger specific responses from each analyte. For multiplexing, the sensor performance is directly derived from the sensor architecture and design [12] to ensure that each analyte can be detected independently and accurately. Spatial resolution techniques [48,49], dividing the sensor surface into distinct regions, each functionalized with different recognition elements, enable the independent operation of multiple detection channels. This approach reduces the risk of crosstalk between signals, allowing for more precise and reliable measurements.

3. Emerging strategies for developing advanced multiplexed PEC sensors

The development of M-PEC sensors has been a gradual evolution, due to the merits in simultaneous detection of multi-components with high sensitivity and low crosstalk. As mentioned previously, the choice of photoactive materials is the foundation to construct rational and efficient strategies for M-PEC sensors. Nanomaterials such as quantum dots (QDs), graphene, and metal nanoparticles have been at the forefront of PEC sensor development. QDs, in particular, are favored for their size-dependent optical properties, which can be finely tuned for wavelength-specific responses, essential for multiplexing [50]. Graphene and its derivatives [7,51–53] are used to improve electron transport and surface functionalization, enabling the immobilization of various recognition elements on a single sensor platform. The combination of different materials to create hybrid systems has proven to be an effective strategy for enhancing sensor performance. For example, metal–organic frameworks (MOFs) combined with conductive polymers or metal nanoparticles offer synergistic properties, such as enhanced light absorption, improved charge separation, and increased surface area for biomolecule attachment [54,55]. These hybrid materials are particularly effective in spatially resolved multiplexed sensors, where distinct regions of the sensor surface can be functionalized with different materials. Semiconductors [32,56] like titanium dioxide (TiO_2) and cadmium sulfide (CdS) remain staples in PEC sensor design due to their strong photoelectrochemical properties. These materials are often used in tandem with other semiconductors or nanomaterials to form heterojunctions, which facilitate efficient charge transfer and enhance the

sensor's ability to generate distinct signals for different analytes.

3.1. Wavelength-resolved strategy

The wavelength-resolved strategy leverages the unique optical properties of photoactive materials that respond to different wavelengths of light (Fig. 2a). By using materials of QDs with tunable emission properties, researchers have developed sensors capable of detecting multiple analytes simultaneously through wavelength-specific signals. This has proven particularly effective in applications like DNA and protein detection, where different targets can be labelled with distinct fluorophores for precise identification.

The most common method to realize a wavelength-resolved strategy is obtaining anodic and cathodic photocurrent signals under different illuminations (Fig. 2b). A noteworthy example [58] is the work of Jiang et al. who developed TiO_2-Ag/nitrogen doped graphene (TiO_2-Ag/NDG) nanocomposites capable of switching photocurrent direction between anodic and cathodic responses by adjusting the irradiation wavelength. This enabled the simultaneous detection of chloramphenicol and tetracycline, two important contaminants, by utilizing their different photocurrent responses under specific wavelengths. The high sensitivity, specificity, and reliability make the M-PEC sensor suitable for food safety biosensing and environmental monitoring. Similarly, Deng et al. proposed a wavelength-resolved dual-signal output PEC biosensor [59] based on click-response mechanisms and DNAzyme-assisted signal amplification. This innovative sensor enabled the simultaneous detection of three metal ions—Pb^{2+}, Mg^{2+}, and Cu^{2+}—using a click-reaction strategy that amplified the signal by cycling DNA outputs. Enhanced sensitivity allows for more precise detection of low-abundance heavy metal ions. Zhang et al. introduced another important advancement [45] using titanium dioxide nanotubes (NTs) as a template to create molecularly imprinted polymers (MIPs) for the selective detection of ascorbic acid and uric acid. By employing spectrally resolved differential mode, they achieved simultaneous detection of ascorbic acid (AA) and uric acid (UA) with minimal interference, showing how excitation at specific wavelengths could distinguish between these analytes in complex matrices.

Dong et al. took this approach further by designing a polarity-switchable dual-wavelength PEC biosensor [38]. Using a covalent organic polymer (TPAPP-PTCA PCOP) as the template, combined with ferrocene and hydrogen peroxide as regulators, they achieved dual-wavelength excitation (Fig. 2c). This setup allowed for the sensitive and accurate detection of aflatoxin M1, a potent carcinogen, demonstrating how polarity-switching characteristics can enhance detection performance.

In a more unconventional application, Fathabadi et al. developed a wavelength-distinguishable PEC photodetector [44] capable of operating in the visible (405 nm) and UV (302 nm) range (Fig. 2d). The photodetector exhibited high responsivity and ultra-fast response times, enabling its use in secure data transmission in underwater wireless sensor networks. This study highlights the versatility of wavelength-resolved PEC systems beyond traditional sensing applications.

Despite these advancements, a key challenge in wavelength-resolved PEC detection lies in identifying and designing electrode materials that produce distinct and non-interfering photocurrent responses at different wavelengths. This crosstalk between responses can compromise the accuracy of the sensor, especially when different analytes are detected simultaneously. To address this, it is essential to develop electrode materials with well-defined and significantly different wavelength responses. Strategies such as bandgap-tuning in materials like quantum dots and advanced surface engineering techniques can help reduce spectral overlap and enhance wavelength selectivity, thereby improving the overall performance of wavelength-resolved PEC sensors.

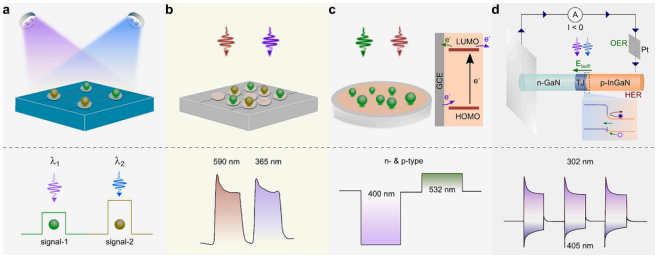

Fig. 2. Wavelength-resolved multiplexed PEC sensors. a, Schematic of the wavelength-resolved method. b, General strategy to realize the wavelength-resolved sensor by distinguishing signal via different wavelength light. Adapted from Zheng et al. [57]. c, Polarity-switchable dual-wavelength sensor with both n-type and p-type semiconductor. Adapted from Dong et al. [38]. d, Wavelength distinguishable sensor with a p-n heterojunction. Adapted from Fathabadi et al. [44].

3.2. Potential-resolved strategy

Potential-resolved detection involves applying distinct electrochemical potentials to selectively activate responses from different photoactive materials (Fig. 3a). This strategy is particularly advantageous in minimizing signal crosstalk, making it highly effective for detecting multiple analytes simultaneously. By adjusting the applied potential for each separate analyte (Fig. 3b), this approach offers versatility and precision, especially in clinical diagnostics where multiple biomarkers need to be detected independently in a single system.

Instead of using two separate electrodes, most potential-resolved M-PEC sensors are based on a simpler configuration of a modified electrode (Fig. 3c). Dai et al. realized the potentiometric addressable strategy by employing graphitic carbon nitride (g-C_3N_4) and chitosan-silver iodide (CS-AgI) on a dual-disk electrode, which allows for simultaneous detection of namely prostate-specific antigen (PSA) and human interleukin-6 (IL-6) without signal interference. In this sensor, g-C_3N_4 generates an anodic photocurrent for PSA detection, while CS-AgI generates a cathodic photocurrent for IL-6 detection [60]. By using three-dimensional nitrogen-doped graphene-loaded copper indium disulfide ($CuInS_2$/3DNG) and Bi^{3+}-doped black anatase titania nano- particles decorated with reduced graphene oxide (Bi^{3+}/B-TiO_2/rGO) materials, Zhang et al. constructed a PEC aptamer sensor for the simultaneous detection of enrofloxacin and ciprofloxacin through a regulated bias strategy [46]. Similarly, Cao et al. utilized cadmium sulfide nanowires (NWs) and Tin niobate hexaoxide ($SnNb_2O_6$) nanosheets as photoactive materials, each exhibiting distinct critical voltages that generate anodic and cathodic photocurrents, respectively [62]. By applying specific bias voltages, they achieved independent detection of myoglobin and cardiac troponin I within the same system. Hao et al. extended this approach [47] by designing partitioned substrates using cadmium telluride loaded carbon nitride nanosheets (CdTe-C_3N_4) and CdTe loaded 3D graphene hydrogel (CdTe-3DGH) nanocomposites. These materials produced

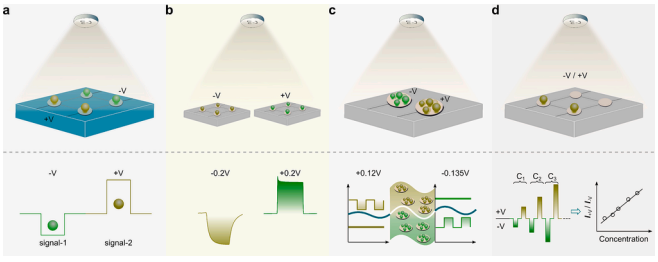

Fig. 3. Potential-resolved multiplexed PEC sensors. a, Schematic of wavelength-resolved strategy. b, Dual-signal PEC sensor with switching electrodes for multiple cancer markers. Adapted from Zhong et al. [12]. c, Potentiometric addressable PEC sensor for multiple biomarkers by varying the applied bias. Adapted from Dai et al. [60]. d, Sunlight-powered potentiometric PEC sensor for detecting antibiotic. Adapted from Hao et al. [61].

distinguishable photocurrent responses at specific bias voltages, allowing for the quantitative detection of microRNAs (miRNA141 and miRNA21).

Additionally, Hao et al. present a portable potentiometric PEC biosensor [61] (Fig. 3d) that utilizes sunlight as the light source for detecting aflatoxin B1 (AFB1). Interestingly, this work creatively eliminates the interference caused by unstable sunlight intensity using the potentiometric resolve ratiometric principle, allowing the biosensor to accurately detect analytes under varying sunlight conditions by using two nanomaterials, Ag/TiO_2/3DNGH and carbon nitride nanosheets (CNNSs).

Collectively, these studies underscore the versatility and effectiveness of potential-resolved detection in multi-analyte sensing. However, the success of this approach hinges on selecting and integrating photoactive materials that generate distinct, non-overlapping responses at specific potentials. A key challenge arises when the applied potential repeatedly regulating the photocurrent of photoactive material affects the intrinsic properties of both photoactive material and other material on the same electrode, leading to signal interference. To address this, creating spatially resolved zones where each material is confined to a distinct region may be necessary, in addition to carefully selecting stable materials with distinct redox potentials.

3.3. Spatial-resolved strategy

Spatially resolved detection involves segmenting the sensor electrode into multiple areas, each tailored with specific recognition elements or photoactive materials, which generate signals when illuminated by light (Fig. 4a). It is particularly useful in microarray-based PEC sensors, enabling high-throughput screening for large-scale applications such as environmental monitoring, drug discovery, and clinical diagnostics. One of the most promising advancements in this area is the automatic light-addressable PEC (ALA-PEC) platform [63] developed by Xu et al. which utilized Au nanoparticle-modified TiO_2 nanotube photonic crystals as photoelectrodes. This platform targeted eight antibiotics, achieving rapid, automated detection of multiple molecules in a short period of time. Wang et al. further demonstrated the utility of spatially resolved detection in a label-free, addressable photoimmunosensor array [39]. This sensor array, based on magnetic separation and self-calibration strategies, used $Na_2Ti_6O_{13}$@Fe_3O_4@CdS as a substrate to enrich amyloid β (Aβ) into distinct regions for detection. The system exhibited high stability, specificity, and selectivity, enabling high-precision and high-throughput analysis for disease diagnostics. In another example, Wang et al. designed an electrochemical sandwich-type immunosensor [20] that used a bovine serum albumin (BSA) matrix with glutaraldehyde (BSA@GA) modified silicon photoelectrode. The device employed a light-addressable electrochemical immunoassay for multiplexed PSA detection, offering opportunities for miniaturizing and functionalizing the sensor platform.

In addition to the detection of multi-targets, this strategy also works well in analyzing the concentrations of one target (Fig. 4b). Cao et al. developed a spatially resolved PEC platform [49] for high-throughput protein analysis using CdS@g-C_3N_4. Their system employed a rotating disk substrate to spatially record PEC signals from an electrode array, enabling both single-analyte and multiplexed detection. This high-sensitivity, high-throughput approach underscores the potential for developing efficient, automated, portable, and low-cost multiplexed electrochemical immunoassays for multi-target analysis.

Spatially resolved M-PEC sensors utilizing a light-addressable strategy expand the construction area from individual electrode surfaces to larger microdevices by integrating multiple signaling pathways within a unified microreaction system. This approach enables high-throughput detection, greatly enhancing the efficiency of detecting multiple components in complex matrices. Furthermore, it facilitates the fabrication of microarray devices, making them highly suitable for portable, real-time, and on-site environmental monitoring. However, signal variations arising from engineering challenges, such as precise spatial control of the working electrodes and shared reference, must also be addressed to ensure reliable performance. Advances in laser-induced nanofabrication technologies [64] offer promising solutions to overcome these limitations.

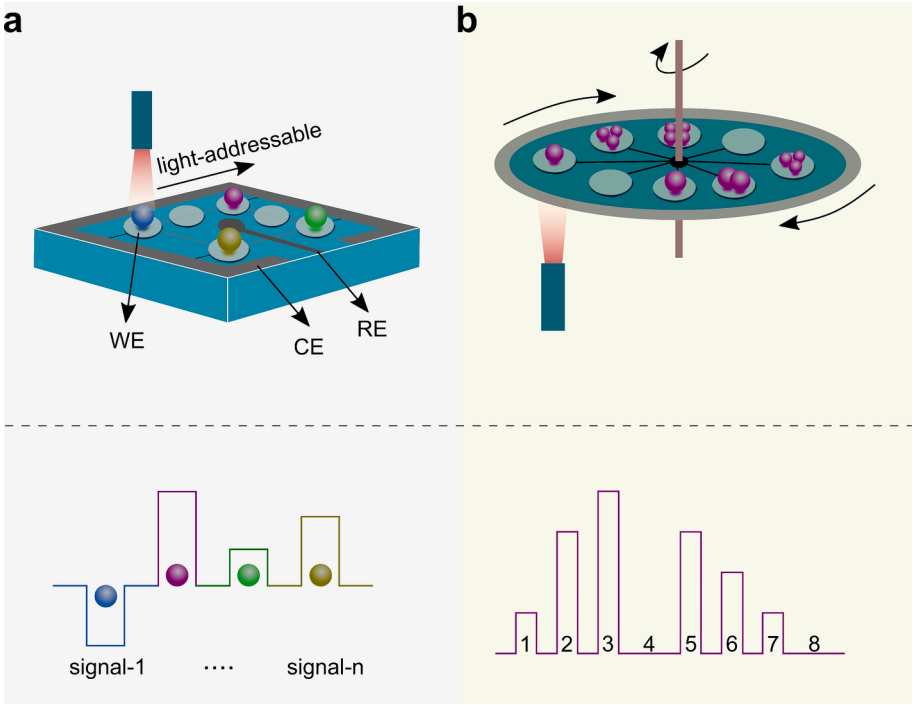

Fig. 4. Spatial-resolved multiplexed PEC sensors. a, General configuration of spatial-resolved strategy. b, High-throughput spatial-resolved rotatable PEC sensor for protein analysis.
Adapted from Cao et al. [49].

3.4. Multi-mode strategy

The multi-mode strategy integrates multiple detection techniques—such as electrochemistry, colorimetry, and spectroscopy—into a single sensor platform. This enhances the sensor's accuracy and reliability by allowing cross-validation between different modes, reducing the likelihood of false-positive or false-negative results. By leveraging the unique strengths of each method, multi-mode PEC sensors provide more comprehensive analytical capabilities, particularly in complex diagnostic applications.

Generally, electrochemical (EC) detection is often combined with PEC to achieve multi-mode detection for the target analytes (Fig. 5a). Zhang et al. constructed a dual-mode EC and PEC biosensor [65] for the detection of the lung cancer biomarker cytokeratin 19 fragment 21-1 (CYFRA21-1). This sensor capitalizes on the photoelectronic properties of methylene blue (MB) on gold nanoparticles/3,4,9,10-perylenetetracarboxylic dianhydride (PTCDA)@C60/indium tin oxide (Au NPs/PTCDA@C_{60}/ITO) electrodes, allowing the independent detection of CYFRA21-1 based on different electrochemical activities at specific potentials. Li et al. introduced a bifunctional PEC and electrochemiluminescent (ECL) biosensor [55] for detecting microRNA-126. Their system, based on a V_2CT_x MXene-derived porphyrin metal–organic framework embedded with silver nanoparticles (AgNPs@V-PMOF), enables sensitive and selective detection of miRNAs in living cancer cells, underscoring its utility in cancer diagnostics and expanding the scope of multi-mode biosensing applications.

Additionally, Liu et al. designed an integrated platform [56] that facilitates simultaneous PEC and surface-enhanced Raman spectroscopy (SERS) measurements (Fig. 5b), using quantum dots and metal–organic framework nanocomposites (CdTe/YbTCPP). This combination enables both PEC and SERS analyses to be performed on the same sensor, offering valuable insights into semiconductor–metal interfaces and providing a pathway for developing high-performance biosensors.

Furthermore, more detection methods can be combined with PEC. Meng et al. developed a multifunctional TiO_2/ZIF-8/Cu(II) chip [66] that combines PEC, colorimetric, and photothermal imaging for the accurate detection of prostate-specific antigen (PSA). This system improves detection reliability by switching between modes, allowing multiple assays to be conducted on the same sample, reducing the risk of error and providing enhanced diagnostic information for clinical use.

While these multi-mode systems present promising advancements, several challenges remain. The nano-engineering of multifunctional photoactive materials and the integration of distinct signaling pathways can introduce compatibility issues and signal interference. Most multimodal systems are currently limited to bimodal detection, and further research is necessary to overcome the complexity of combining multiple components and reaction processes without compromising performance through advanced nanofabrication, photoactive materials, and electrode preparation.

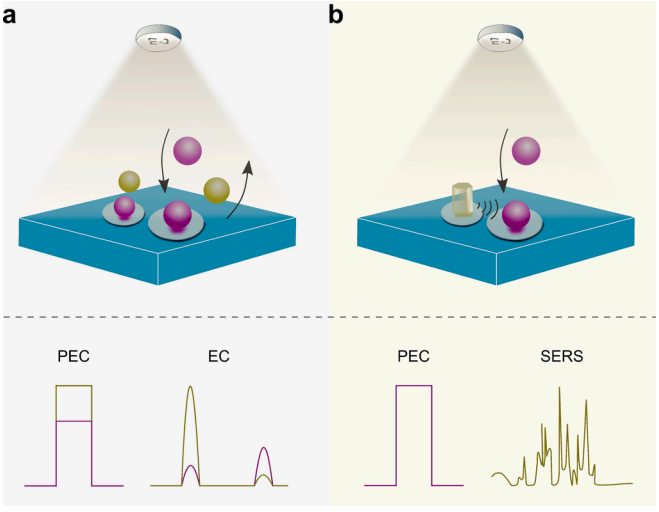

Fig. 5. Multi-mode multiplexed PEC sensor. a, PEC-EC dual-mode M-PEC strategy. Adapted from Zhang et al. [65]. b, SERS-enhanced dual-mode M-PEC strategy. Adapted from Liu et al. [56].

4. Multiple targets detection by multiplexed PEC sensors

As a robust platform, M-PEC sensor offer superiority in simultaneous detection, high sensitivity, and broad applicability for a range of biomolecules, organic molecules, and ions within complex matrices across various fields of biomedical diagnostics [10–13], environmental monitoring [7–9], and food safety [4,74,90]. In this section, we show the advances of two key parameters of M-PEC sensors in limits of detection (LOD) and detection range (Fig. 6 and Table 1).

The key aspect driving the success of M-PEC sensors is their ability to detect analytes with extremely low LOD, often reaching femtomolar (fM) or femtograms per milliliter (fg/mL) sensitivity. In biomedical diagnostics, where early detection of disease biomarkers is essential, multiplexed PEC sensors excel. A prime work [78] developed a multiplexed PEC sensor capable of detecting miRNA-21 and miRNA-141 using a target-triggered polarity-switchable mechanism. This innovation allows the sensor to shift between anodic and cathodic signals based on the target analyte by engineering photosensitive materials of Cu_2O/AuNPs/TiO_2 and CdS/AuNPs/TiO_2, resulting in attomolar-level sensitivity and overcoming the challenge of cross-interference between different targets. The sensor's integration with smartphone-based platforms further enhances its practicality for community-based diagnostics, offering both affordability and portability in real-world bioassays. In addition to genes, M-PEC sensors exhibit excellent performance in detecting some specific proteins. Dai et al. reported the sensitive detection of two important biomarkers of PSA and IL-6 via the potentiometric addressable strategy [60]. This biosensor leverages the unique capability of tuning the applied bias-induced polarities to selectively and simultaneously detect two biomarkers on a single dual-disk electrode, meanwhile eliminating interference between signals from different targets. A significant milestone achieved by this study is the application of two distinct photoactive materials—g-C_3N_4 (graphitic carbon nitride) with anodic photocurrent and CS-AgI (chitosan-silver iodide) with cathodic photocurrent—on the same electrode. This configuration allows for precise and simultaneous detection of both PSA and IL-6, with impressive detection limits in the picomolar range, offering a promising platform for early cancer detection and other clinical diagnostics.

M-PEC sensors are equally effective in detecting organic molecules with low LOD, particularly antibiotics and pesticides in environmental and food safety monitoring. Zhang et al. reported the development of a band alignment modulated polarity-switchable PEC ratiometric sensor [73] for detecting ochratoxin A (OTA), a food safety contaminant. The sensor's ability to integrate a pH-responsive CuTCPP MOF with i-motif DNA allowed for a "one-to-two" ratiometric response, achieving a LOD as low as 0.79 fM (0.32 fg/mL). This innovative design enhances detection accuracy by minimizing cross-interference, making it highly effective for food safety applications.

In the detection of ions, in particular metal ions, M-PEC sensors have demonstrated their utility in addressing heavy metal contamination. Yang et al. developed a dual-modal PEC/EC biosensor [69] for detecting mercuric ions (Hg^{2+}). This sensor incorporates a Cu_2O@Cu_2S/2D ultrathin covalent organic framework (Cu_2O@Cu_2S/D-TA COF) heterojunction with catalase-like properties, amplifying the photocurrent signals and achieving 3.15 fM sensitivity. The dual-mode detection system, which leverages both PEC and DPV signals, provides enhanced accuracy and significantly reduces the risk of false positives, making it ideal for the monitoring of heavy metal pollutants.

Beyond their impressive sensitivity, M-PEC sensors offer wide detection ranges, typically spanning several orders of magnitude from

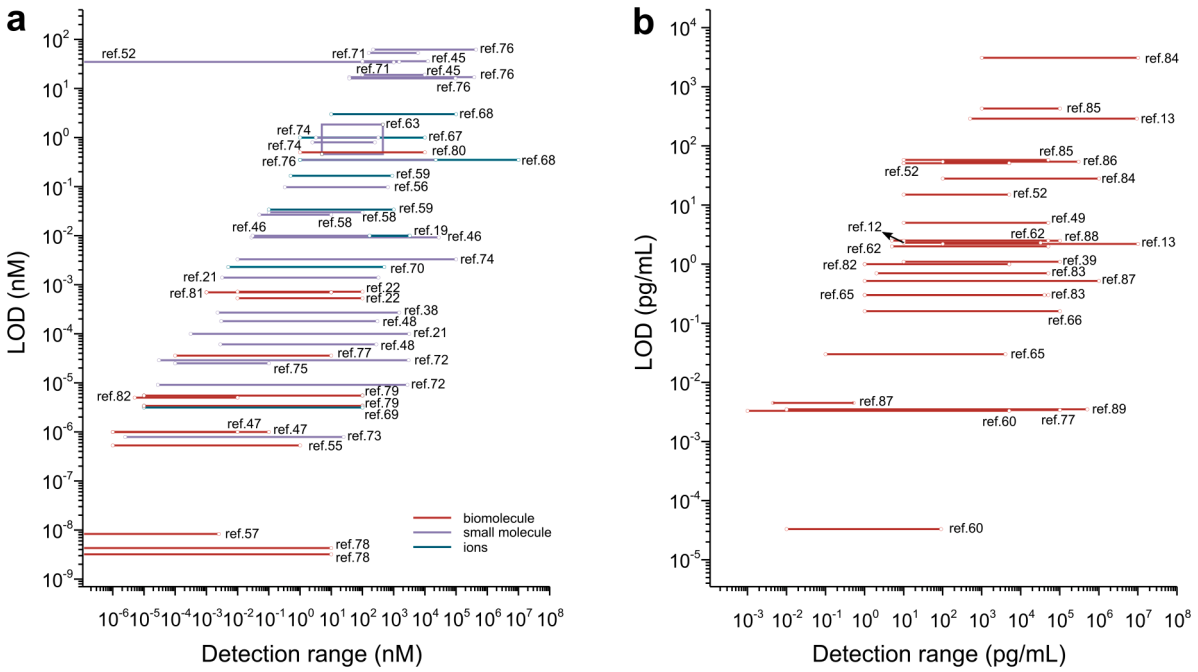

Fig. 6. Detection performance of M-PEC sensors for various targets. a, Performance for three kinds of targets including ions (blue), small molecules (purple) and biomolecules (red) based on the molar concentration (mol/L). b, Performance for biomolecules mainly some proteins, DNA and virus based on the mass concentration (pg/mL).

very low to millimole or from sub-pg/mL to tens of micrograms (Fig. 6). For example, Ma's miRNA detection approach [78] effectively covers a range from 10 aM to 100 nM, while other systems designed for detecting organic molecules and ions extend their detection capabilities to μM concentrations, and even to mM concentrations. Yue et al. reported a light-addressable AuNCs-GO-based PEC sensor [52] capable of detecting Glypican-1 (GPC1), carcinoembryonic antigen (CEA), and glutathione (GSH), with detection capabilities extending up to 1.5 μM for GSH whilst remaining high sensitivity (21.42nA/μM), although the LOD is not perfect enough.

M-PEC sensors have shown great promise for detecting a wide array of targets, yet their future lies in enhancing these capabilities further. As illustrated in Fig. 6a, a disparity remains between the LODs for organic molecules, metal ions, and biomolecules. Lowering LODs for M-PEC sensors will not only meet the demands of real-world applications but also contribute to a healthier and safer environment. Improvements in sensor materials and designs are anticipated to push both detection limits and the range of detectable targets, positioning multiplexed PEC sensors as indispensable tools for high-throughput detection in areas such as biomedical diagnostics, environmental monitoring, and food safety. Continuous advancements in this field will ensure that these sensors remain essential in overcoming critical analytical challenges in modern science.

5. Challenge and perspective

The development of M-PEC sensors has seen remarkable progress in recent years, with innovations in material science, detection strategies, and sensor design expanding their potential applications. However, there remain several vital challenges that must be addressed to bring this technology closer to widespread practical use. These challenges span material stability, signal interference, and scalability considerations. At the same time, future advancements in standardization, miniaturization, high-throughput capabilities, and trace-level sensitivity hold immense promise for the evolution of M-PEC sensors.

One of the primary concerns in the development of M-PEC sensors is the stability and selectivity of the materials used. While advanced materials such as quantum dots, MOFs, and hybrid composites have been widely employed due to their sensitivity and multiplexing capabilities, these materials often face long-term stability issues [91,92], especially in challenging environmental or biological conditions. Additionally, ensuring high selectivity in complex matrices remains a significant hurdle. Non-specific binding or interference from similar analytes can lead to compromised accuracy, limiting the practical application of these sensors in fields where precision is critical, such as clinical diagnostics. To address this concern, future research must focus on the development of robust and durable materials capable of withstanding environmental stressors while maintaining high selectivity. A promising approach involves synthesizing hybrid composites that combine the stability of traditional materials like metal oxides with the high sensitivity of nanomaterials. In addition, the designed hybrid composite would benefit from the surface engineering through functionalization techniques [93,94] for a significantly improved stability and the specificity of recognition elements. Other considerations, such as effective device encapsulation, can also play a crucial role in improving the stability of M-PEC sensors. All the efforts will drive the reliability and utility of M-PEC sensors in real-world applications.

Another major challenge is signal interference and crosstalk between different detection channels, which is inherent in multiplexed systems [15,95]. This issue is particularly pronounced when analytes exhibit similar electrochemical or optical properties, making it difficult to differentiate between signals. The resulting crosstalk can diminish the accuracy of the sensor, especially when precise quantification of multiple analytes is required. Addressing this challenge will require innovations in signal processing and sensor architecture. Future efforts could focus on developing more sophisticated signal modulation techniques, such as machine learning algorithms [95], to accurately deconvolute complex signals and interpret data from multiple detection channels. Refining spatial or potential-resolved strategies will also help reduce interference, further improving signal fidelity and sensor reliability.

In practical applications, particularly in point-of-care diagnostics and environmental monitoring, miniaturized and portable sensors are highly desirable. However, current M-PEC sensors tend to be relatively

Table 1
Detection performance of M-PEC sensors for ions, small molecules and biomolecules.

Type	Chemical	Detection range (nM)	Detection limit (nM)	Refs.
Ion	Pb^{2+}	0.5–900	0.166	[59]
	Mg^{2+}	0.1–1000	0.034	[59]
	Hg^{2+}	170–3300	0.01	[19]
	S^{2-}	1–10000	1	[67]
	Cd^{2+}	1–10000000	0.35	[68]
	Cu^{2+}	10–100000	3	[68]
	Hg^{2+}	0.00001–100	0.00000315	[69]
	Hg^{2+}	0.005–500	0.0023	[70]
Small molecule	AFB1	0.0032–320	0.0014	[21]
	ZEN	0.0003141–3140	0.0001	[21]
	dopamine	160–6000	53	[71]
	glutathione	100–1000	34.3	[71]
	ENR	0.0278–27800	0.0092	[46]
	CIP	0.0302–3000	0.00996	[46]
	ENR	0.0000278–2780	0.0000091	[72]
	CIP	0.0000302–3000	0.000029	[72]
	CIP	0.003–301.8	0.000181	[48]
	OFL	0.0028–276.7	0.0000609	[48]
	OTA	0.0000025–24.8	0.00000079	[73]
	OTA	2.5–250	0.8	[74]
	lincomycin	0.01–100000	0.0033	[74]
	edifenphos	3.22–322	1	[74]
	CAP	0.05–10	0.0267	[58]
	TET	0.1–100	0.03	[58]
	sulfamethazine	0.0001–0.1	0.000025	[75]
	DDVP	1–22500	0.35	[76]
	Methylparathion	38–380000	17	[76]
	Trichlorfon	38–95000	16	[76]
	dimethoate	220–436000	62	[76]
	AFM1	0.0023–1500	0.0002711	[38]
	PAT	0.3244–648.8	0.0973	[56]
	AA	100–10000	19	[45]
	UA	100–12500	36	[45]
	Antibiotic	5–450	0.46–1.84	[63]
	GSH	0–1500	34.9	[52]
		Unit (fM)	Unit (fM)	
Biomolecule	miRNA21	1–100000	1	[47]
	miRNA-21	100–10000000	36	[77]
	miRNA-21	0.01–10000000	0.0032	[78]
	miRNA-21	10–100000000	3.4	[79]
	miRNA-126	1–1000000	0.53	[55]
	miRNA141	1–10000	1	[47]
	miRNA-141	0.01–10000000	0.0043	[78]
	miRNA-141	10–100000000	5.5	[79]
	ARGs	1000000–10000000000	500,000	[80]
	virus-Norovirus	10000–100000000	720	[22]
	virus-Rotavirus	10000–100000000	530	[22]
	p53 gene	0.025–2500	0.00833	[57]
	HBV	1000–10000000	700	[81]
	HCV	1000–10000000	700	[81]
	HIV	1000–10000000	700	[81]
	thrombin	5–10000	5	[82]
		Unit (pg/mL)	Unit (pg/mL)	
	PSA	1–50000	0.3	[83]
	PSA	1–5000	1	[82]
	PSA	0.001–5000	0.0033	[60]
	PSA	1–100000	0.16	[66]
	PSA	100–1000000	28	[84]
	CEA	10–5000	51	[52]
	CEA	10–32000	2.3	[12]
	CEA	1–5000	1	[82]
	CEA	10–50000	58	[85]
	CEA	1000–10000000	3100	[84]
	AFP	2–50000	0.7	[83]
	AFP	100–300000	54	[86]
	HIgG	100–10000000	2.2	[13]
	HIgG	500–9375000	290	[13]
	Myo	5–50000	2	[62]
	IcTnI	5–50000	2.5	[62]
	CYFRA21-1	1–40000	0.3	[65]
	CYFRA21-1	0.1–4000	0.03	[65]
	mucin 1	0.01–100000	0.0034	[77]

(*continued on next page*)

Table 1 (*continued*)

Type	Chemical	Detection range (nM)	Detection limit (nM)	Refs.
	IL-6	0.01–90	0.000033	[60]
	Aβ42	0.0045–0.52	0.0045	[87]
	Aβ40	1–1000000	0.52	[87]
	Ab1	10–50000	5	[49]
	mucin-1	1000–100000	430	[85]
	GPC1	10–5000	15	[52]
	NSE	10–100000	2.49	[88]
	CYFRA21-1	0.01–500000	0.0035	[89]
	Amyloid β–Protein	10–100000	1.1	[39]

Note. AFB1, aflatoxin B1, ZEN, zearalenone, ENR, enrofloxacin, CIP, ciprofloxacin, OFL, ofloxacin, OTA, ochratoxin A, CAP, chloramphenicol, TET, tetracycline, AFM1, aflatoxin M1, PAT, patulin, AA, ascorbic acid, UA, uric acid, GSH, glutathione, mRNA, microRNA, antibiotic ARGs, resistance genes, HBV, hepatitis B, HCV, hepatitis C, HIV, human immunodeficiency, PSA, prostate-specific antigen, CEA, carcinoembryonic antigen, AFP, a-fetoprotein, HigG, Human immunoglobulin G, Myo, myoglobin, IcTnI, cardiac troponin, IL-6, human interleukin-6, Aβ42, amyloid-beta 42, Aβ40, amyloid-beta 40, Ab1, antibodies, MUC1, mucin-1, GPC1, Glypican-1, NSE, neuron specific enolase.

large and complex, limiting their portability, despite the use of nanoscale materials. Advances in micro-/nanofabrication, such as direct laser writing [64], offer the potential to create compact, integrated M-PEC devices without compromising sensitivity or multiplexing capabilities. The development of portable, handheld sensors could transform the use of PEC technology, enabling its deployment in remote locations and on-site testing. Additionally, integrating M-PEC sensors with user-friendly devices, such as smartphones [13,54,78,96], could further enhance their accessibility, making these advanced sensors available for broader use in clinical, environmental, and industrial settings.

Achieving true high-throughput detection is another key goal for the future of M-PEC sensors. Although some sensors [63,74] have demonstrated the ability to detect multiple analytes simultaneously, the current scale—often limited to less than 10 samples per assay—falls short of the requirements for high-throughput applications in areas like drug discovery and environmental screening. Future research should aim to develop sensors that can analyze hundreds or even thousands of samples simultaneously. This will require innovations in sensor array design, increasing the density of detection sites, as well as more efficient data processing algorithms to manage the large amounts of data generated. Combining these innovations with scalable manufacturing processes will enable the creation of high-throughput sensors that meet the demands of large-scale applications.

Currently, PEC sensors rely on multiple external inputs, such as different applied potentials or wavelengths of light, to perform multichannel detection. This complexity may hinder ease of use. The design of materials and systems that allow for a single excitation input to trigger multiple analyte-specific responses would significantly simplify sensor operation. Multifunctional photoactive materials, capable of responding to a single stimulus while generating distinct signals, could streamline detection, making multiplexed PEC systems more user-friendly and efficient. Innovations in this area could also reduce signal interference, further improving the accuracy and usability of these sensors.

Another frontier in the development of multiplexed PEC sensors is achieving trace-level sensitivity. To compete with established techniques like surface-enhanced Raman scattering [97–100], M-PEC sensors must be capable of detecting extremely low concentrations of analytes. This is pivotal for applications such as detecting illicit drugs at border crossings, monitoring environmental pollutants, and diagnosing diseases at early stages. Achieving this level of sensitivity will require a combination of advanced nanomaterials, improved surface modification techniques, and novel signal amplification strategies. These innovations could push M-PEC sensors toward ultra-sensitive detection, opening new opportunities for their application in fields requiring rapid, on-site analysis of trace substances.

Lastly, as M-PEC sensors move closer to real-world applications, particularly in healthcare and environmental monitoring, regulatory and ethical considerations will become increasingly important. Ensuring the accuracy, safety, and reliability of these sensors is paramount, especially when they are used for critical decisions in clinical diagnostics or public safety. Early engagement with regulatory bodies will help establish the necessary standards for sensor validation and deployment. Moreover, ethical considerations such as data privacy, informed consent, and equitable access must be carefully addressed, particularly when these sensors are used to collect sensitive information.

In conclusion, while multiplexed PEC sensors have made impressive advances, addressing the challenges of material stability, signal interference, scalability, and trace-level sensitivity is essential for their future success. At the same time, innovations in miniaturization, high-throughput detection, and one-to-all strategies offer exciting opportunities for expanding the capabilities of these sensors. By continuing to refine materials, sensor designs, and signal processing techniques, multiplexed PEC sensors have the potential to revolutionize fields such as diagnostics, environmental monitoring, and industrial analysis. Collaboration with industry partners and engagement with regulatory bodies will be crucial in ensuring that these sensors transition from research tools to commercially viable technologies with widespread impact.

CRediT authorship contribution statement

Lei Ding: Writing – review & editing, Writing – original draft, Visualization, Supervision, Investigation, Data curation, Conceptualization. **Zhaoxiang Zhong:** Investigation, Data curation, Conceptualization. **Chaohao Chen:** Writing – review & editing, Funding acquisition. **Baolei Liu:** Writing – review & editing, Funding acquisition. **Zhijie Chen:** Writing – review & editing. **Ling Zhang:** Writing – review & editing. **Jie Mao:** Funding acquisition, Writing – review & editing. **Min Zhang:** Writing – review & editing. **Qian Peter Su:** Writing – review & editing, Funding acquisition. **Faliang Cheng:** Writing – review & editing, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

Data will be made available on request.

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