

Metal–Organic Framework-Based Optical Biosensors: Recent Advances in Pathogen Detection and Environmental Monitoring

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Abstract

Metal–organic frameworks (MOFs) have emerged as highly versatile materials for the development of next-generation optical biosensors due to their tunable porosity, large surface area, and customizable chemical functionality. In recent years, MOF-based platforms have shown great promise in various optical transduction modalities, including fluorescence, luminescence, and colorimetric sensing, enabling highly sensitive and selective detection of biological analytes. This review provides a comprehensive overview of recent advancements in MOF-based optical biosensors with a focus on applications in pathogen detection and environmental monitoring. We highlight key design strategies, including MOF functionalization, hybridization with nanoparticles or dyes, and integration into microfluidic and wearable devices. Emerging trends such as point-of-care diagnostics, label-free detection, and real-time monitoring are also discussed. Finally, the review outlines current challenges and future directions for the practical deployment of MOF-based optical biosensors in clinical and field environments.

Keywords: Metal–organic frameworks (MOFs), Optical biosensors, Wearable biosensors, Environmental monitoring, Colorimetric sensors, Fluorescence sensing, Luminescent MOFs, Pathogen detection, Heavy metal sensing, Real-time detection.

1. Introduction

The global burden of infectious diseases and environmental pollution continues to challenge public health systems, food and water safety, and ecological stability [1,2]. Pathogenic microorganisms such as bacteria, viruses, and fungi are responsible for widespread morbidity and mortality, while contaminants like heavy metals, pesticides, and organic pollutants threaten ecosystems and human well-being [3–5]. Early, accurate, and on-site detection of these biological and chemical hazards is critical for controlling disease outbreaks, ensuring environmental compliance, and supporting timely intervention

strategies [6]. However, conventional analytical approaches, including culture-based microbiological assays, polymerase chain reaction (PCR), enzyme-linked immunosorbent assay (ELISA), atomic absorption spectroscopy (AAS), and high-performance liquid chromatography (HPLC), though highly reliable in laboratory settings, often fall short in field applications due to their reliance on expensive instrumentation, time-intensive workflows, and the need for skilled personnel [7,8].

In this context, biosensors have emerged as transformative tools that combine biological recognition elements with signal transduction mechanisms to detect target analytes with high specificity and sensitivity [9]. Among various types of biosensors, optical biosensors have gained considerable attention due to their unique advantages [10]. These systems transduce molecular recognition events into optical signals typically via fluorescence, luminescence, chemiluminescence, surface plasmon resonance, or colorimetric changes that are readily detectable, often in real-time [11,12]. Optical biosensors offer several benefits over electrochemical or piezoelectric counterparts, including rapid signal generation, minimal interference from sample matrices, and compatibility with visual and smartphone-based detection platforms [13]. Their capacity for multiplexing, miniaturization, and non-contact readouts further supports their deployment in decentralized, point-of-care (POC), and resource-limited settings [14].

The effectiveness of optical biosensors in pathogen detection is largely attributed to their ability to provide rapid, highly sensitive, and selective analysis with minimal sample processing [15]. By targeting pathogen-specific biomarkers such as nucleic acids, proteins, lipopolysaccharides, or whole cells, these biosensors can discriminate between closely related species and strains [16]. Fluorescence-based sensors, for instance, can exploit hybridization probes, aptamers, or antibody-antigen interactions to trigger measurable emission changes upon binding with the target [17,18]. Similarly, colorimetric biosensors enable naked-eye detection through visually discernible color shifts induced by enzyme-catalyzed reactions or nanoparticle aggregation [19]. Such attributes not only enable early diagnosis and environmental warning systems but also facilitate continuous monitoring in real time, which is particularly important during disease outbreaks or exposure to dynamic pollution sources [20].

Despite these advantages, the performance of optical biosensors is heavily dependent on the materials used for signal generation, amplification, and biorecognition [21]. This has led to intensive research into advanced materials capable of enhancing sensitivity, selectivity, and operational stability [22]. Among these, metal-organic frameworks (MOFs) have emerged as a highly promising class of materials for next-generation biosensor development [23]. MOFs are crystalline porous materials composed of metal ions or clusters coordinated with organic linkers, yielding tunable three-dimensional architectures [24]. They exhibit exceptionally high surface areas (often exceeding 5000 m²/g), adjustable pore sizes, and a high degree of chemical modularity [25]. These features make MOFs uniquely suited for hosting functional molecules, facilitating molecular interactions, and enhancing signal transduction in optical biosensing platforms.

The intrinsic and tunable optical properties of MOFs further contribute to their utility in this field [26]. Some MOFs exhibit intrinsic luminescence due to the electronic transitions of metal clusters or organic linkers, while others can serve as protective carriers for fluorescent dyes, quantum dots, or nanoparticles, preventing photobleaching and quenching [27]. MOFs can also act as signal amplifiers through mechanisms such as fluorescence resonance energy transfer (FRET), photoinduced electron transfer (PET), or inner filter

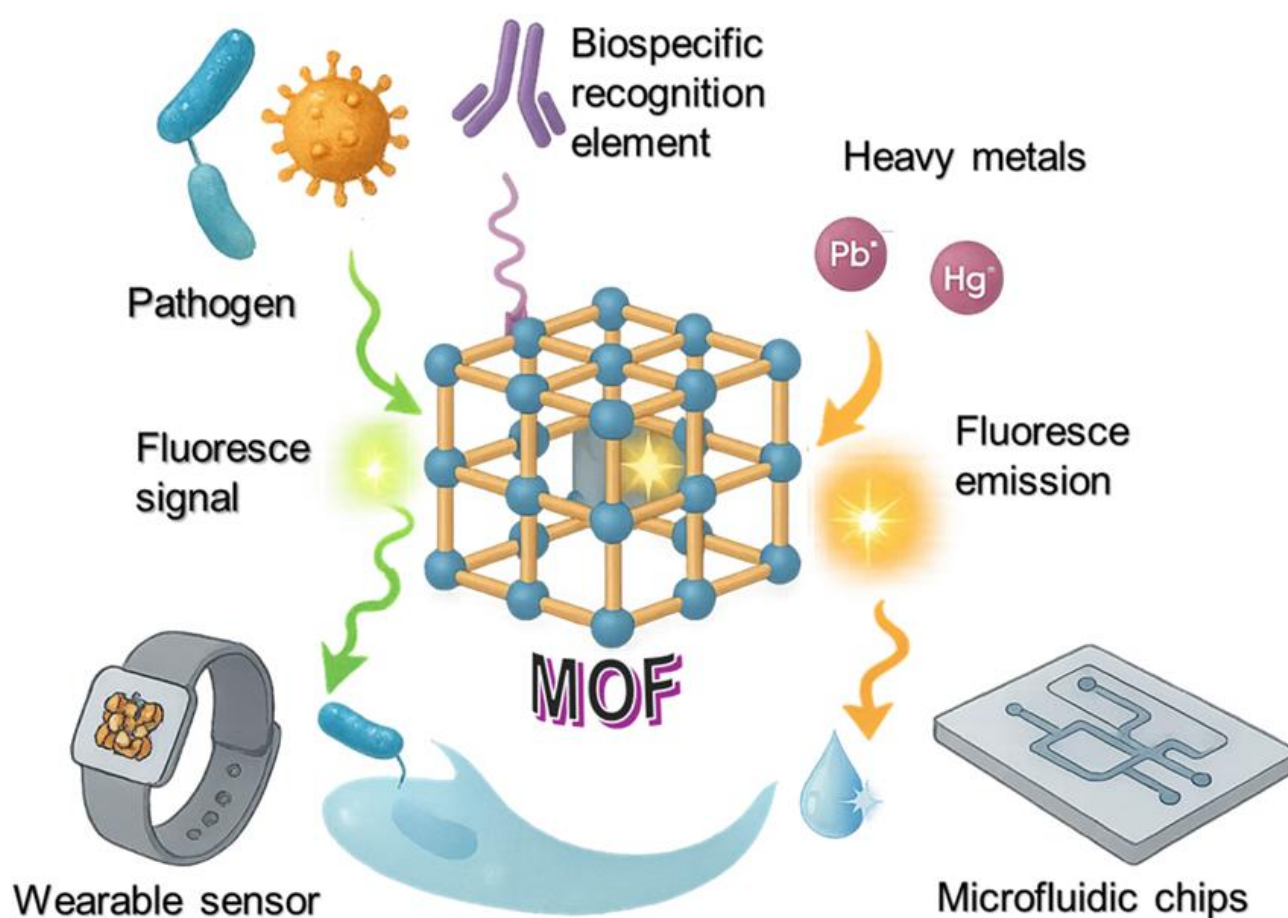
effects (IFE), depending on their structural and electronic characteristics [28,29]. Moreover, the surface of MOFs can be readily functionalized with aptamers, DNA strands, peptides, or antibodies, providing specificity toward targeted biological or environmental analytes [30]. These combined properties enable the design of highly sensitive, selective, and versatile optical biosensors with low detection limits and excellent performance in complex sample matrices [31].

Recent advances have demonstrated the successful application of MOF-based optical biosensors in detecting a wide range of pathogens, including *Escherichia coli*, *Staphylococcus aureus*, *Salmonella enterica*, and SARS-CoV-2, as well as in monitoring toxic environmental contaminants such as Pb^{2+} , Hg^{2+} , Cr^{6+} , organophosphates, and nitroaromatic compounds [32–34]. These sensors have exhibited outstanding analytical performance with detection limits in the femtomolar to picomolar range, rapid response times, and strong resistance to interference [35]. Notably, the incorporation of MOFs into portable devices, paper-based sensors, microfluidic chips, and wearable formats has opened new avenues for decentralized monitoring, offering low-cost, user-friendly, and field-deployable sensing solutions [36,37]. Such innovations are particularly valuable for epidemiological surveillance, water quality assessment, agricultural monitoring, and early warning systems in underserved regions [20,38].

This review provides a comprehensive examination of recent developments in MOF-based optical biosensors with a focus on their applications in pathogen detection and environmental monitoring. We begin by introducing the fundamental principles of optical biosensing and the rationale for using MOFs as functional materials. The review then explores various design strategies including MOF functionalization, hybridization with nanomaterials, and structural tailoring for enhancing sensing performance. Representative examples across different optical modalities such as fluorescence, luminescence, and colorimetry are discussed in detail. Special attention is given to emerging trends such as label-free detection, smartphone integration, wearable sensors, and real-time monitoring. Finally, we address key challenges in the field, including MOF stability under physiological conditions, reproducibility, scalability, and regulatory acceptance, and outline future research directions for advancing the practical implementation of MOF-based optical biosensors.

2. Fundamental Mechanisms Underpinning MOF-Based Optical Biosensors

Metal–organic frameworks (MOFs) are an emerging class of crystalline hybrid materials composed of metal ions or clusters coordinated to organic linkers [39]. Their high surface area, structural order, and synthetic tunability make them ideal platforms for biosensing. In optical biosensing, MOFs offer unique benefits, including facile integration of signal elements (e.g., fluorophores), high analyte adsorption capacity, and modularity for engineering molecular recognition and transduction pathways. These properties underpin their roles in developing sensitive, selective, and versatile biosensing platforms (Scheme 1).



Scheme 1. MOF-based optical biosensor detecting pathogens and heavy metals via fluorescence and color changes in environmental samples.

2.1. Structural and chemical tunability

One of the most advantageous features of MOFs is their structural and chemical tunability, which allows precise control over pore size, surface chemistry, and framework topology [40]. These properties are critical in biosensing, governing analyte accessibility and interaction dynamics within the sensing matrix [41]. The organic linkers and metal nodes can be systematically modified or replaced by introducing functional groups or coordination sites tailored for specific targets such as nucleic acids, proteins, or small molecules [42]. Post-synthetic modification techniques ligand exchange, covalent grafting, and metal ion doping expand the chemical diversity and functional capabilities of MOFs, facilitating enhanced binding affinities and selective recognition [43].

Building on this concept, Yan et al. demonstrated that a MIL-53(Al)-NH₂ framework could be engineered to capture FcMBL-conjugated elements for *Bacillus cereus* detection (Figure 1) [44]. Through aptamer-functionalized magnetic beads and a dual-recognition mechanism, the MOF biosensor achieved rapid detection (LOD: 4 CFU/mL) across a wide dynamic range (20–2 × 10⁸ CFU/mL). This example underscores how structural flexibility allows the integration of both recognition and optical transduction components within the same sensing matrix. This illustrates how structural flexibility enables synergistic incorporation of capture and signal elements.

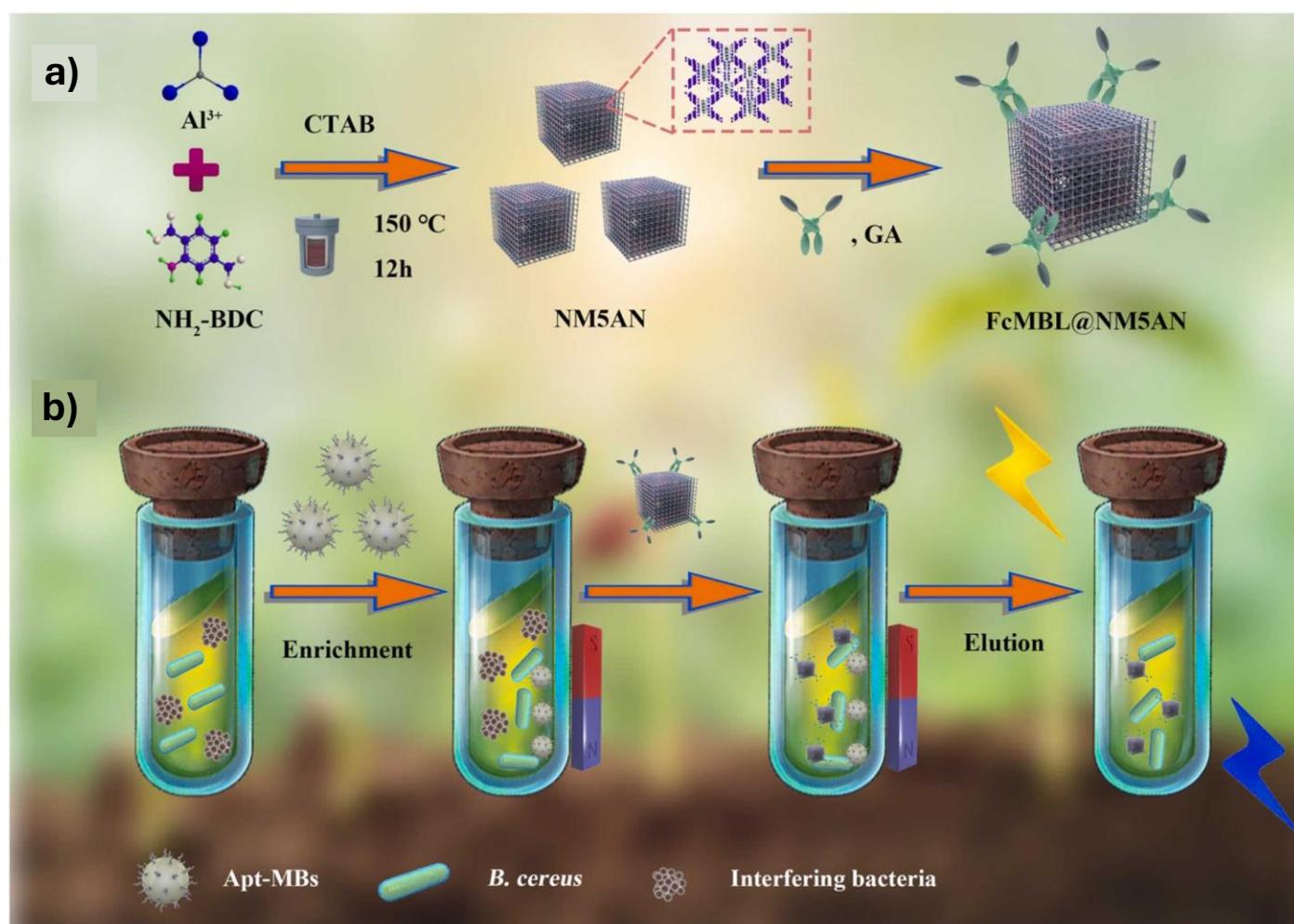


Figure 1. a) Fabrication of FcMBL@NM5AN; b) Detection of *B. cereus* in mixed samples employing a dual recognition approach. Copyright 2023 Elsevier [44].

Expanding on the idea of multifunctionality, another study used a MOF-based gated nanoprobe integrated with hairpin DNA sequences to differentiate wild and vaccine strains of *Brucella* [45]. The MOF matrix acted as a protective scaffold for fluorophores, enabling precise and gated fluorescence release upon DNA hybridization. The dual-signal platform achieved a LOD of 6.4×10^{-10} M with over 90% detection accuracy, showcasing how framework integrity enhances selectivity and minimizes background interference. This highlights the dual role of MOFs in molecular protection and signal responsiveness.

In addition to biochemical detection, MOFs are increasingly being employed in early disease diagnosis. El-Sheikh et al. reported Zn-MOF nanoparticles (~118 nm) with tunable photoluminescence and thermal stability for detecting prostate-specific antigen (PSA) [46]. The sensor achieved a detection limit of 0.145 fg/mL over a linear range of 0.1 fg/mL to 20 pg/mL, demonstrating the feasibility of ultra-sensitive MOF-based clinical diagnostics.

While fluorescence-based detection dominates current applications, MOFs' responsive frameworks are also exploited in colorimetric sensing. A notable example is the flexible MIL-53(Al) framework, which exhibits reversible structural transformations upon interaction with VOCs like ketones, alcohols, and water [47]. These guest-induced changes in pore geometry influence its photoluminescence, allowing selective visual detection.

Though not quantitative in terms of LOD, this qualitative shift reinforces the utility of framework responsiveness in environmental monitoring.

Bridging the gap between structural engineering and signal enhancement, future directions may involve combining MOFs with LSPR-based fiber optic biosensors for real-time and label-free detection [48]. Although not inherently MOF-based, LSPR systems could benefit significantly from MOFs' porous, tunable architecture, enabling better molecular recognition, reduced noise, and signal amplification in portable diagnostic formats. As the examples above illustrate, structural and chemical tunability is foundational for optimizing the sensitivity, selectivity, and responsiveness of MOF-based optical biosensors.

2.2. Optical transduction mechanisms (e.g., fluorescence, colorimetry, SERS)

Transitioning from structure to function, MOFs' ability to convert biological recognition events into measurable optical signals is key to their biosensing utility. The primary optical transduction mechanisms include fluorescence, colorimetric changes, and surface-enhanced Raman scattering (SERS) [49–51]. Among these, fluorescence is the most widely utilized, where MOFs either possess intrinsic luminescence or act as hosts for fluorophores and quantum dots. Signal modulation occurs via mechanisms such as FRET, PET, or IFE, enabling precise "turn-on" or "turn-off" sensing modes [52,53].

One exemplary system used a copper-based MOF to develop a fluorescence biosensor for aflatoxin B1 detection [54]. The MOF simultaneously acted as a Cu^{2+} ion reservoir and antigen carrier. A target-induced click reaction triggered hybridization of fluorescent DNA strands, producing an amplified signal with an ultralow LOD of 0.48 pg/mL and a 670-fold improvement in sensitivity over conventional ELISA, emphasizing MOF-enabled transduction efficiency.

Expanding from simple fluorescence signaling, light-responsive nanoscale MOFs (NMOFs) are gaining traction due to their ability to undergo optical changes in response to external stimuli [55]. Originally designed for cancer imaging, these NMOFs now serve biosensing roles by enabling spatiotemporally controlled optical outputs, further enriching the design space for smart biosensors.

The development of ratiometric fluorescence systems has also advanced biosensor reliability. A hybrid CD/Co-MOF nanocoral served as a dual-channel sensor for alkaline phosphatase (ALP) detection [56]. The phosphate-triggered ligand exchange disrupted the MOF, releasing carbon dots (restoring fluorescence) and diminishing the second-order scattering signal. This allowed for a ratiometric optical output with an LOD of 0.6 mU/L and a linear range spanning six orders of magnitude, significantly enhancing precision and reproducibility.

Moreover, tuning the photophysical property of MOFs provides sensitive guest molecule loading capacity and overall improved sensing efficiency. MOFs exhibit highly tunable photoluminescent properties arising from their metal nodes, organic linkers, or encapsulated guest species, making them excellent candidates for optical transduction in biosensors [57]. By judicious selection of metal ions, organic ligands, and synthetic conditions, the fluorescence behavior of MOFs can be precisely engineered to enable sensitive and selective detection of a wide range of analytes. Fluorescence-based MOF sensors typically operate via "turn-on" or "turn-off" mechanisms, with "turn-on" systems being particularly valuable for real-time sensing due to their enhanced signal-to-noise performance. These tunable optical responses facilitate the development of MOF-based sensors capable of detecting hazardous chemicals, biological molecules, and environmental contaminants, thus showcasing their potential as versatile platforms for fluorescence-based biosensing.

2.3. Functionalization strategies for specificity and sensitivity

While MOFs inherently offer high porosity and modularity, specificity in biosensing is typically achieved through functionalization. This includes covalent attachment or adsorption of recognition elements (e.g., aptamers, antibodies, peptides, nucleic acids) and surface engineering via molecular imprinting or electrostatic interactions [58–60].

In a notable example, a gold nanoparticle-loaded ZIF-MOF (Au NPs@ZIF) was functionalized with DNA aptamers to construct a ratiometric fluorescence sensor for detecting *Staphylococcus aureus* [61]. The platform integrated methylene blue and ferrocene fluorophores, achieving intrinsic signal calibration and detecting *S. aureus* with a LOD of 1 CFU/mL and a broad linear range of 5 to 10^8 CFU/mL. This highlights the impact of combining biorecognition and ratiometric signaling.

Complementing this strategy, a lateral flow immunoassay (LFIA) was developed using a bimetallic Au/Ir@Cu/Zn-MOF functionalized with anti-*S. aureus* antibodies [62]. The porous MOF structure enhanced signal intensity through nanoparticle dispersion and photothermal synergy, achieving a visual detection limit of 10^3 CFU/mL a 100-fold improvement over non-MOF probes. Beyond detection, this functionalized MOF exhibited bactericidal effects, expanding its application to combined diagnostics and therapy.

Functionalization also plays a central role in small molecule detection, as shown by a dual-emission ratiometric sensor for adenosine triphosphate (ATP) [63]. The MOF core encapsulated $\text{Ru}(\text{bpy})_3^{2+}$ as a stable fluorescent reference, while dsDNA on the surface allowed SYBR Green I intercalation. ATP presence disrupted the DNA duplex, selectively quenching the SGI signal while preserving the Ru signal. This enabled an LOD of 0.63 μM . Embedded into agarose hydrogel and paired with a smartphone fluorescence reader, the sensor achieved real-time bacterial detection down to 10 CFU/mL in milk samples.

Finally, MOF-based systems also enable multiplexed biosensing, as shown in a dual-channel electrochemical biosensor using Au@CuMOF and Au@PbMOF nanotags (**Figure 2**) [64]. Functionalized with DNA probes targeting *Salmonella typhimurium* (*invA* gene) and *Listeria monocytogenes* (*inlA* gene), the platform produced distinct DPV signals for each ion (Cu^{2+} and Pb^{2+}), achieving LODs of 2.33 CFU/mL for *S. typhimurium* and 6.61 CFU/mL for *L. monocytogenes*, with wide linear ranges and minimal cross-reactivity (**Table 1**).

These studies collectively underscore how surface functionalization strategies empower MOFs with high analyte specificity, minimal background interference, and versatile transduction formats for real-world biosensing applications.

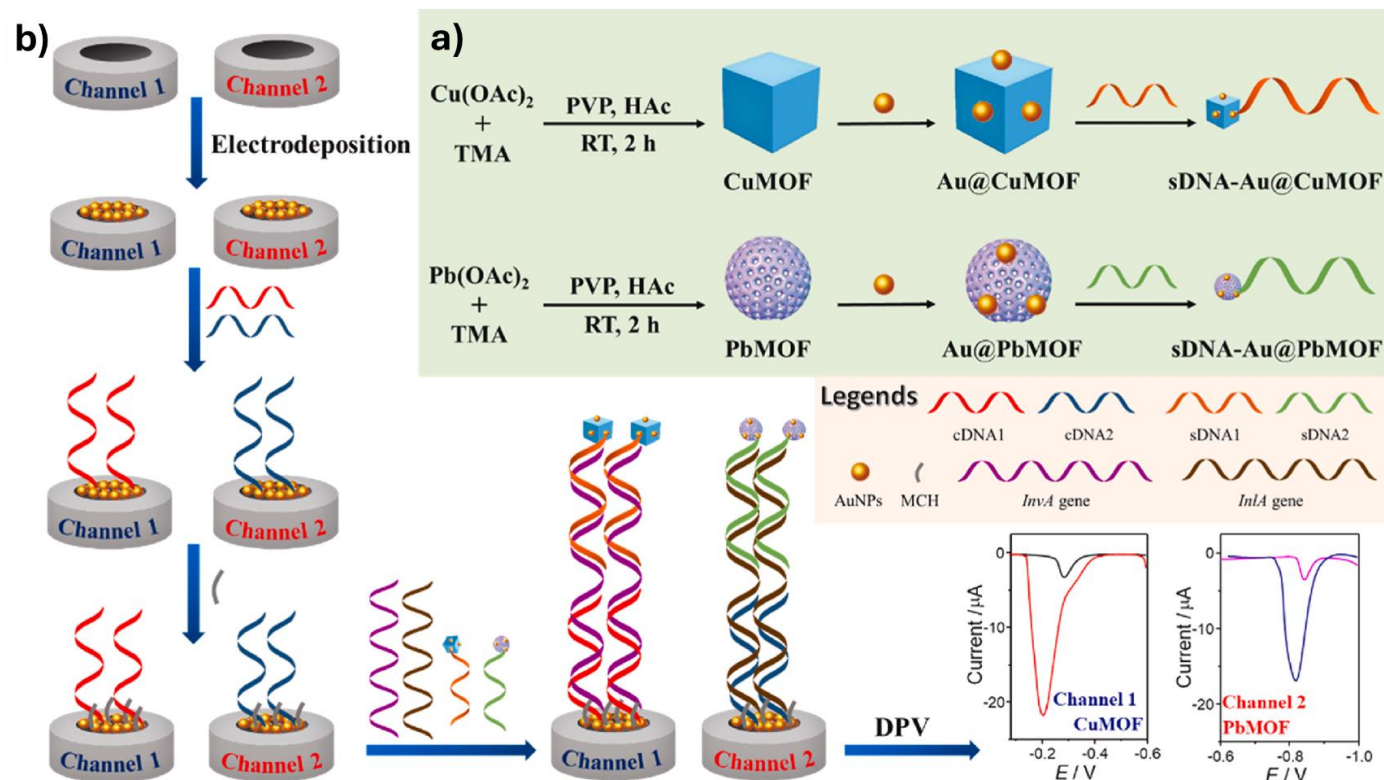


Figure 2. a) Schematic illustration of the synthesis steps for CuMOF, PbMOF, Au@CuMOF, and Au@PbMOF, b) Diagram showing the working principle of the dual-channel electrochemical biosensor for detecting *S. typhimurium* (*invA* gene) and *L. monocytogenes* (*inlA* gene). Copyright 2023 Elsevier [64].

Table 1. Summary of MOF-Based Optical Biosensors.

Design Strategy	Target Microorganism / Analyte	Detection Method	Advantages	Ref.
MIL-53(Al)-NH ₂ with FcMBL and aptamer-functionalized beads	<i>Bacillus cereus</i>	Fluorescence	Dual-recognition; LOD: 4 CFU/mL; wide linear range (20–2 × 10 ⁸ CFU/mL); rapid detection	[44]
MOF with hairpin DNA for gated dye release	<i>Brucella</i> (wild vs. vaccine strain)	Fluorescence	DNA-responsive release; LOD: 6.4 × 10 ⁻¹⁰ M; >90% accuracy; minimal cross-reactivity	[45]
Zn-MOFs with modifiable chemistry	Prostate-Specific Antigen (PSA)	Fluorescence	LOD: 0.145 fg/mL; linear range: 0.1 fg/mL–20 pg/mL; stable and selective	[46]
Cu-MOF with antigen and click-reaction signal amplification	Aflatoxin B1	Fluorescence	LOD: 0.48 pg/mL; 670× sensitivity over ELISA; proximity-triggered amplification	[54]
CD/Co-MOF nanocoral (ratiometric probe)	Alkaline Phosphatase (ALP)	Fluorescence	Dual-signal response; LOD: 0.6 mU/L; broad linear range; reduced background interference	[56]
Au NPs@ZIF-MOF functionalized with aptamers	<i>Staphylococcus aureus</i>	Fluorescence	LOD: 1 CFU/mL; wide dynamic range (5–10 ⁸ CFU/mL); intrinsic signal calibration	[61]

Au/Ir@Cu/Zn-MOF with anti- <i>S. aureus</i> antibodies	<i>Staphylococcus aureus</i>	Immunoassay	LOD: 10 ³ CFU/mL; 100× more sensitive; multifunctional (biosensing + antibacterial)	[62]
Ru(bpy) ₃ ²⁺ @Zr-MOF with dsDNA and SYBR Green I	ATP (viable bacterial marker)	Fluorescence	LOD: 0.63 μM; real-time pathogen detection (down to 10 CFU/mL in milk); smartphone-readout capability	[63]
Au@CuMOF and Au@PbMOF functionalized with DNA probes	<i>S. typhimurium</i> and <i>L. monocytogenes</i>	Electrochemical	Dual-pathogen detection; LOD: 2.33 & 6.61 CFU/mL; high selectivity; broad linear range	[64]

3. MOF-Based Electrochemical and Optical Biosensors for Pathogen Detection

The emergence of infectious diseases and antimicrobial resistance has heightened the urgency for rapid, sensitive, and portable pathogen detection technologies. MOFs, owing to their modularity, high porosity, and tunable optical/electrochemical properties, have gained prominence in biosensor design [65,66]. MOFs can be tailored for diverse transduction strategies including fluorescence, colorimetry, surface-enhanced Raman scattering (SERS), and electrochemical readouts [67]. This section reviews recent progress in MOF-based biosensors for microbial detection, focusing on three aspects: (i) microbial targets (bacteria, viruses, fungi), (ii) detection strategies (label-free vs. labeled), and (iii) performance metrics such as sensitivity and limit of detection.

3.1. Bacteria, viruses, fungi

Recent advancements highlight the broad utility of MOF-based biosensors in targeting bacterial, viral, and fungal pathogens [68]. By tailoring the pore environment, surface functional groups, and framework composition, MOFs can be functionalized with aptamers, antibodies, and enzymes to achieve highly specific and sensitive detection. A notable example is a zirconium-based MOF functionalized with DNA aptamers for the fluorescence-based detection of *Escherichia coli* O157:H7. The system exploited a fluorescence “turn-on” mechanism triggered by the specific binding between aptamer and pathogen, providing a highly selective and responsive readout [69]. Similarly, lanthanide-doped MOFs enabled time-resolved fluorescence sensing of *Staphylococcus aureus*, minimizing autofluorescence and background interference. For viral targets, MOFs integrated with gold nanoparticles (AuNPs) and antibody tags were employed in a colorimetric platform for the detection of SARS-CoV-2 antigens. This system enabled visual detection within 15 minutes, making it a viable option for rapid point-of-care testing [70]. Though less explored, fungal diagnostics have also benefited from MOF integration. In one case, MOFs functionalized with lectins or enzyme mimics enabled SERS-based fingerprinting of *Candida albicans*, demonstrating the material’s adaptability even in fungal biosensing [71].

To expand the scope to broader detection targets, a phage-functionalized Fe-MOF nanozyme (Fe-MOF@SalmpYZU47) was developed for colorimetric detection of multiple *Salmonella enterica* serovars [72]. This platform used a broad-host-range bacteriophage (SalmpYZU47) immobilized on an Fe-based MOF, imparting both biorecognition and enzymatic mimicry. The peroxidase-like activity of the MOF nanozyme was selectively inhibited in the presence of *S. enterica*, yielding a colorimetric signal with a linear range of

1.0×10^2 to 1.0×10^8 CFU/mL and a detection limit of 11 CFU/mL. The system achieved recovery rates of 91.88–105.34% in food samples, underscoring its practical utility (**Figure 3**).

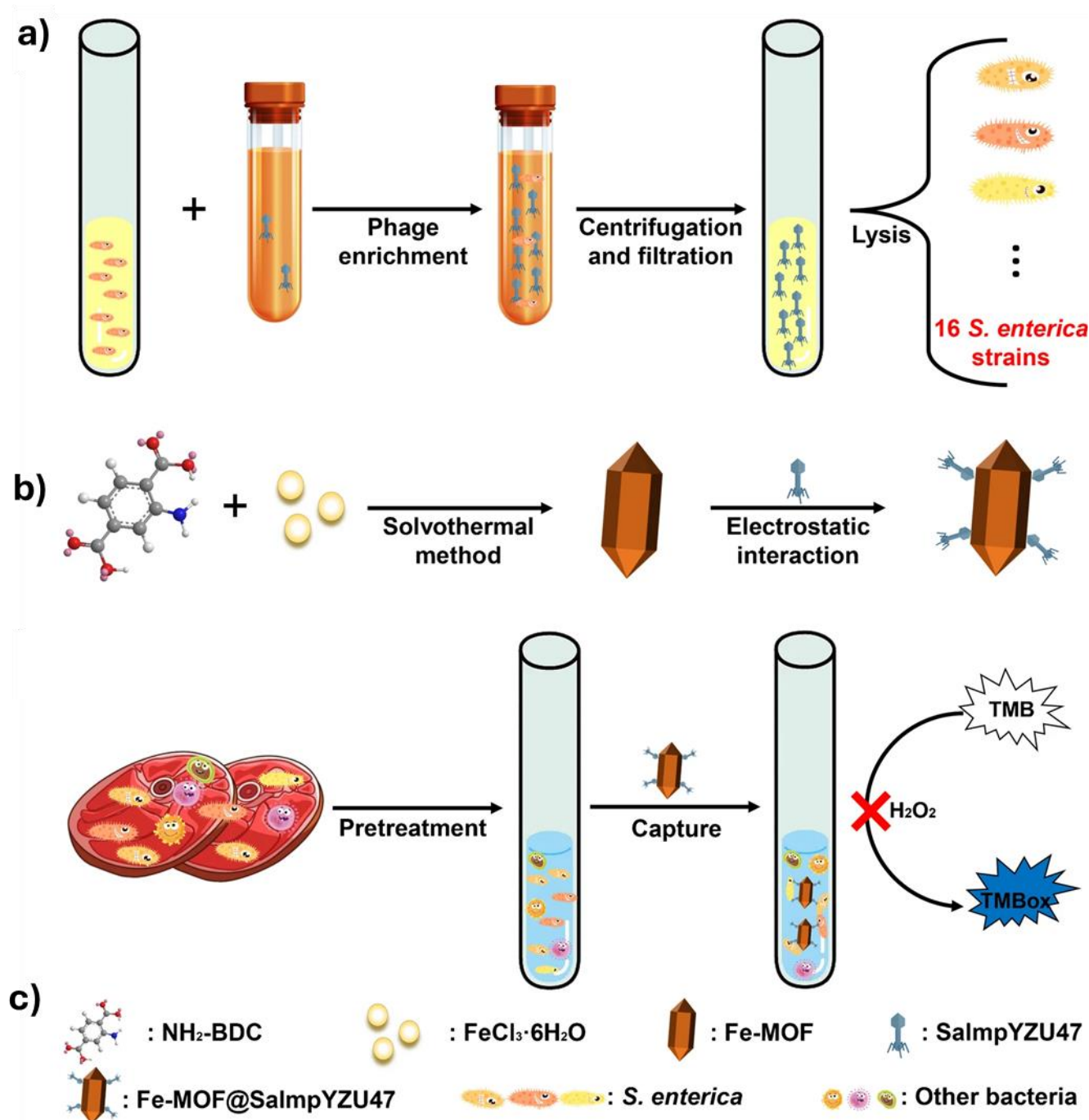


Figure 3. a) Isolation and purification process of phage SalmpYZU47; b) synthesis pathway of the Fe-MOF@SalmpYZU47 nanozyme; and c) schematic of colorimetric detection of multiple *S. enterica* strains in food using the developed Fe-MOF@SalmpYZU47 platform. Copyright 2024 Springer Nature [72].

To further demonstrate point-of-care applicability, a portable and cost-effective visual biosensor was developed by integrating MOFs with a pregnancy test strip (PTS) platform for the detection of *E. coli* O157:H7 [73]. The design incorporated a hybridization chain reaction (HCR) amplification mechanism. Magnetic beads (MBs) functionalized with a single-stranded capture probe (CP) hybridized with an aptamer (AP) specific to *E.*

coli. Upon target binding, the aptamer was released, allowing the CP strands to trigger HCR with biotin-labeled DNA polymers. Streptavidin-modified MOFs encapsulating human chorionic gonadotropin (hCG) were subsequently recruited to the polymers. The hCG acted as a signal generator on the commercial PTS, allowing visual detection with a LOD of 530 CFU/mL.

In another study focused on respiratory pathogens, a dual-channel electrochemical immunosensor was constructed using a nanocomposite of graphene oxide and Cu-MOFs for the simultaneous detection of *Mycoplasma pneumoniae* and *Legionella pneumophila* [74]. The platform employed pyrene linkers for antibody immobilization via EDC-NHS chemistry and exhibited a broad dynamic range (1 pg/mL to 100 ng/mL). The dual-sensor format was successfully validated in spiked water samples, emphasizing its real-world applicability.

The detection of foodborne pathogens in dairy matrices has also advanced significantly. A polydopamine/CoFe-MOFs@Nafion-based electrochemical immunosensor was developed for *Salmonella* detection in milk [75]. CoFe-MOFs provided structural stability and high antibody immobilization efficiency, while Nafion prevented detachment from the electrode. Electrodeposited polydopamine facilitated covalent bonding with anti-*Salmonella* antibodies via Michael addition and Schiff base reactions. The sensor exhibited a detection range of 1.38×10^2 to 1.38×10^8 CFU/mL, with an LOD of 1.38×10^2 CFU/mL.

A similar label-free electrochemical immunosensor was fabricated by incorporating CoFe-MOFs with multi-walled carbon nanotubes (MWCNTs), followed by gold nanoparticle (AuNP) electrodeposition [76]. This hybrid enhanced conductivity and surface area for antibody anchoring, yielding a detection range of 1.04×10^4 to 1.04×10^8 CFU/mL and an LOD of 2.89×10^3 CFU/mL.

Beyond electrochemical platforms, dual-mode optical biosensors have been developed to improve accuracy and redundancy. A colorimetric/fluorescent biosensor for *Salmonella typhimurium* utilized magnetic covalent organic frameworks (MCOFs), gold nanoparticles, and aggregation-induced emission luminogens (AIEgens) [77]. The aptamer-mediated system prevented nanoparticle-MCOF aggregation in the presence of target bacteria, altering the signal in both detection modes. The biosensor achieved LODs of 1000 CFU/mL (colorimetry) and 10 CFU/mL (fluorescence), with smartphone-based linear discriminant analysis enhancing field usability.

A dual-mode Cu-MOF-based aptasensor targeting C-reactive protein (CRP), a biomarker elevated in bacterial and viral infections (including COVID-19), combined fluorescence and colorimetric readouts [78]. The Cu-MOF acted both as a signal quencher and enzyme mimic. RNA aptamer binding to CRP released the quenched signal, enabling detection with LODs of 40 pg/mL (fluorescence) and 240 pg/mL (colorimetry), outperforming conventional assays. Moreover, though not directly microbial, a fluorometric Zn-MOF biosensor was reported for HER2 a cancer biomarker demonstrating high selectivity and a low detection limit of 1.38 pM [79]. Similarly, UiO-66-NH₂ MOFs loaded with methylene blue and TMB enabled simultaneous electrochemical detection of tumor-related microRNAs (let-7a and miRNA-21) with detection limits of 3.6 fM and 8.2 fM, respectively (Figure 4) [80]. These findings reveal that MOF-based biosensors designed for oncology can be readily repurposed for pathogen related biomarkers such as CRP and miRNA.

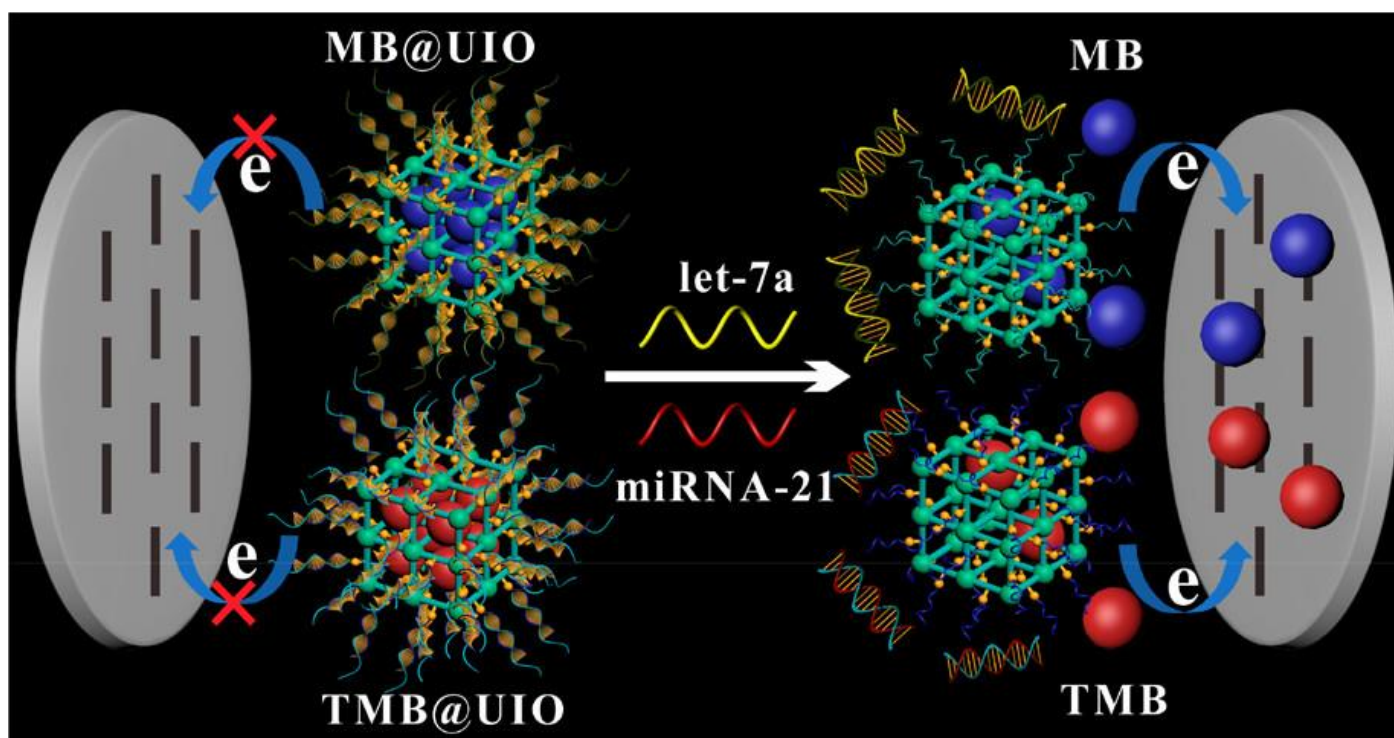


Figure 4. Schematic illustration of a homogeneous electrochemical biosensing platform based on functionalized UiO-66-NH₂ MOFs for simultaneous detection of multiple microRNAs (let-7a and miRNA-21). Electroactive dyes (MB and TMB) are encapsulated within the MOFs and gated by duplex DNA. Copyright 2019 ACS [80].

Finally, a study utilizing porphyrinic covalent organic frameworks (p-COFs) though not strictly a MOF demonstrated promising photoelectrochemical detection of CRP using silver nanoparticle enhanced aptamer platforms [81]. The p-COF system showed reduced electron transfer upon CRP binding, resulting in photocurrent suppression. The material's high photostability and conductivity provide insights into the broader applicability of crystalline porous frameworks for microbial biosensing.

3.2. Detection platforms (label-free vs. labeled)

MOFs are highly versatile scaffolds capable of supporting diverse detection strategies [82]. In biosensing, MOFs can be tailored to operate through either label-free or labeled detection platforms, depending on whether external signal reporters are used. Label-free platforms offer simplicity and faster readout by directly converting target recognition events into measurable signals, while labeled platforms employ fluorescent tags, enzymes, nanozymes, or amplification reactions to boost signal sensitivity and specificity [83–85].

3.2.1. Label-Free Detection Platforms

Label-free biosensors are increasingly favored in point-of-care diagnostics and real-time monitoring due to their inherent simplicity, cost-effectiveness, and minimal sample preparation requirements. These platforms exploit direct interactions between the MOF sensor surface and the target pathogen, which result in detectable optical or electrochemical changes without the need for additional signal labels.

In the electrochemical arena, MOFs have also proven to be robust platforms for nucleic acid sensing. A polyaniline@nickel-MOF (Ni-MOF) nanocomposite was developed into a highly sensitive, label-free biosensor for detecting hepatitis C virus (HCV) RNA

without the need for amplification [86]. The nanocomposite was assembled layer-by-layer onto a glassy carbon electrode functionalized with a DNA probe. Hybridization with target RNA altered the electrochemical impedance, allowing for detection across an exceptionally wide concentration range (1 fM to 100 nM) with a detection limit as low as 0.75 fM. This performance rivals the sensitivity of RT-PCR, illustrating the power of MOF-based materials in nucleic acid diagnostics.

Similarly, MOFs have shown strong promise for exosome detection, which is relevant in both infectious and non-infectious diseases. A label-free biosensor based on Zr-MOFs encapsulating methylene blue was employed for the detection of exosomes from glioblastoma multiforme (GBM) [87]. By utilizing a peptide that binds to EGFR and EGFRvIII markers overexpressed in GBM exosomes the MOF-electrode interface could directly transduce binding events into electrochemical signals. The biosensor achieved a detection limit of 7.83×10^3 particles/ μL with a wide detection range (9.5×10^3 to 1.9×10^7 particles/ μL), offering a non-invasive diagnostic tool for early disease detection.

Colorimetric detection systems have also benefited from MOF-based innovations. For instance, a visual dual-pathogen detection platform was developed using a positively charged Pt-COF nanozyme and a Chromotrope 2R-modified membrane to simultaneously identify *Listeria monocytogenes* and *Salmonella typhimurium* (**Figure 5**) [88]. The positively charged nanozyme facilitated electrostatic adsorption onto the pathogen-enriched membrane, enabling subsequent catalytic oxidation of TMB in the presence of H_2O_2 . The assay achieved dual detection limits of 1.31 and 1.61 CFU/mL, demonstrating the potential of label-free MOF nanozymes for multiplexed, field-deployable detection.

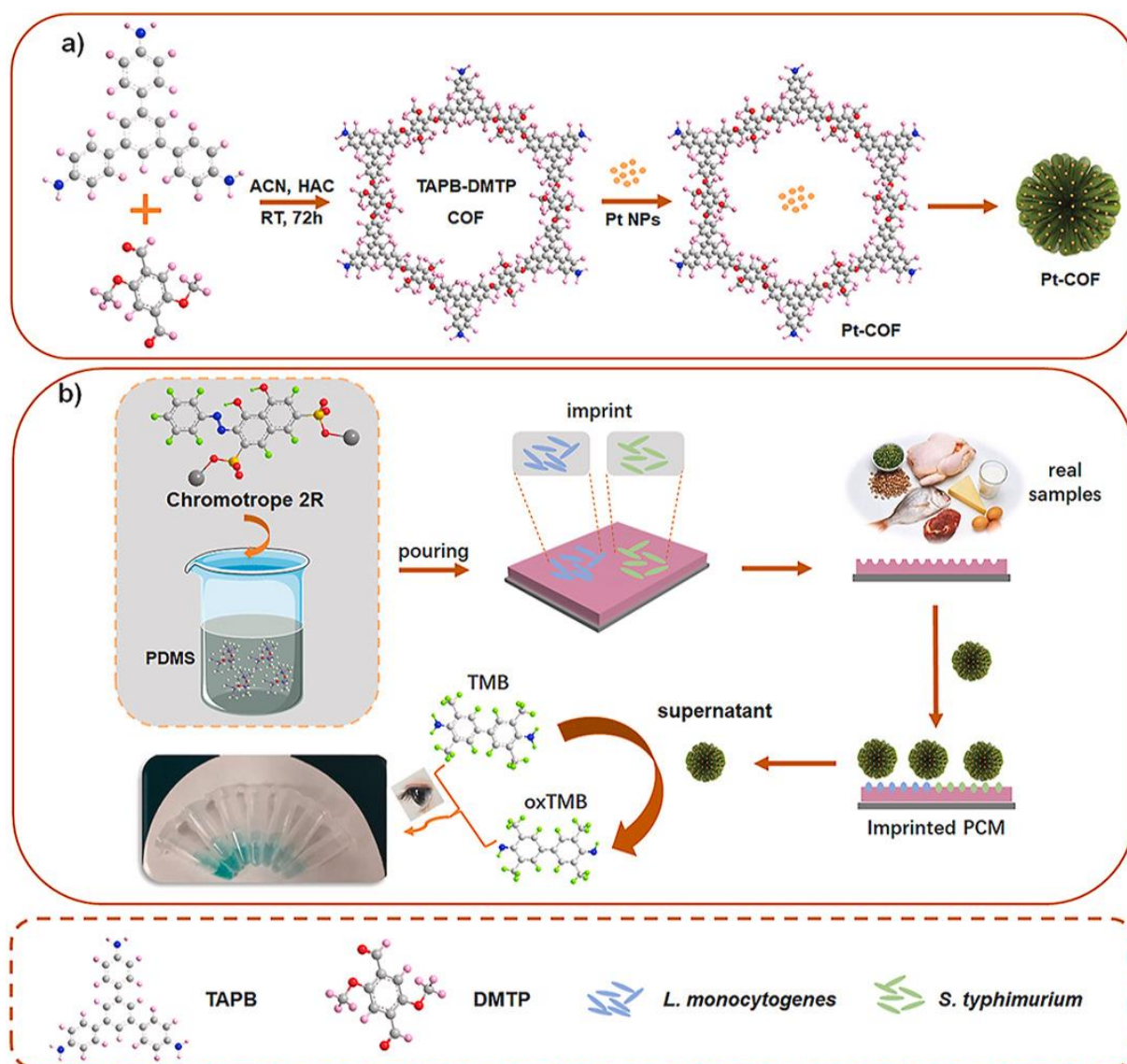


Figure 5. a) The synthesis procedure of the Pt-covalent organic framework (Pt-COF), b) Illustration of the imprinted PCM visual platform used for the rapid and sensitive detection of *Listeria monocytogenes* and *Salmonella typhimurium*. Copyright 2024 Elsevier [88].

In another application tailored for food safety, CoFe-MOFs hybridized with graphene were employed for label-free electrochemical detection of *Salmonella* in milk [89]. Incorporation of Au-NH₂ not only stabilized the antibody immobilization but also enhanced conductivity and surface area. The resulting sensor displayed an impressive linear range from 2.4×10^2 to 2.4×10^8 CFU/mL, with an LOD of 1.2×10^2 CFU/mL, confirming its suitability for complex sample matrices.

Going further into optical biosensing, a platform based on ultrathin MOF nanosheets (MOF-NSs) was designed for label-free, multiplexed DNA detection [90]. These nanosheets acted as highly selective adsorbents for dye-labeled ssDNA probes, which were released upon hybridization with target DNA from various pathogens. This release restored fluorescence, enabling simultaneous detection of *Salmonella enterica*, *Listeria monocytogenes*, and *Vibrio parahaemolyticus*, with detection limits as low as 15 pM. Taken together, these label-free approaches underscore the utility of MOFs in simplifying biosensor design while maintaining high sensitivity and specificity. Their adaptability across optical and electrochemical modalities makes them ideal candidates for rapid, on-site pathogen detection.

3.2.2. Labeled Detection Platforms

While label-free systems emphasize simplicity, labeled biosensors are designed to maximize signal output through strategic incorporation of external signal reporters. These platforms often yield superior sensitivity and specificity, and are particularly valuable in early-stage diagnostics where pathogen levels are extremely low.

One of the most compelling examples is a microfluidic immunosensor for *Salmonella* detection, which integrated Fe-MIL-88NH₂ MOF nanocubes loaded with platinum nanoparticles (PtNPs) as peroxidase-mimicking nanozymes [91]. The sensor used a sandwich immunoassay format where magnetic nanoparticles first captured the target bacteria, and the MOF-PtNP probes catalyzed H₂O₂ decomposition to generate oxygen. This oxygen was detected via a smartphone-based thermal imaging system, enabling visual, label-based detection with a sensitivity of 93 CFU/mL within one hour. This example demonstrates how labeled MOF platforms can be coupled with portable readouts to enable real-time pathogen detection.

Further extending this approach, a Cu-MOF/PEDOT:PSS composite platform was developed for the labeled electrochemical detection of *E. coli* O157:H7 [92]. Sulfonic acid groups were introduced into the MOF to facilitate antibody attachment, and the antigen–antibody interaction was transduced via enhanced electron transfer in the conductive composite. This system achieved a wide detection range (3×10^2 – 3×10^8 CFU/mL) with a detection limit of 7.4 CFU/mL, illustrating how labeled strategies can be adapted for robust electrochemical biosensing.

Visual biosensors have also benefitted from enzyme encapsulation in MOFs. A prominent example involved enzyme-loaded ZIF-8 particles for the detection of *E. coli* O157:H7 [93]. The stable, porous MOF matrix preserved enzyme activity, enabling colorimetric detection with a detection limit of just 1 CFU/mL, and visible detection by eye down to 10 CFU/mL in complex matrices such as milk, seawater, and cosmetics. This approach exemplifies how MOFs can enhance enzyme stability while allowing simple and effective visual detection.

Despite the sensitivity advantages of enzymatic labels, immobilization often reduces their catalytic efficiency. This limitation was addressed using MOF-encapsulated iron porphyrin nanozymes, such as MIL-88@TcP [94]. Upon ethanol mediated release, the TcP exhibited 1430-fold higher catalytic efficiency compared to traditional MIL-88. This nanozyme-linked immunosorbent assay (N-ELISA) format enabled sensitive detection of *Salmonella typhimurium* with a detection limit of 1.68×10^2 CFU/mL over 500 times more sensitive than conventional HRP-based ELISAs while maintaining excellent specificity.

Incorporating nucleic acid amplification into MOF-based labeled systems can further enhance sensitivity. One example is a fluorescence biosensor combining recombinase-aided amplification (RAA), CRISPR/Cas12a-based recognition, and ZIF-8 loaded with fluorescein sodium (FLS) [95]. In this system, ZIF-8 served both as a carrier and a pH-sensitive release vehicle for FLS. Upon target recognition, the MOF released the dye, producing intense fluorescence for sensitive detection of *Salmonella typhimurium* with a detection limit of 1.3×10^2 CFU/mL within two hours.

Other innovative formats include dual-aptamer sandwich immunoassays and magnetic separation strategies. A colorimetric sensor for *E. coli* used streptavidin-labeled Cu-MOFs as catalytic probes with peroxidase-like activity [96]. This system achieved a detection limit of 2 CFU/mL and a linear range from 16 to 1.6×10^6 CFU/mL. Similarly, a magnetic separation-enhanced colorimetric platform was developed using platinum-loaded ZIF-8 (Pt@ZIF-8) nanozymes for detecting *Salmonella typhimurium*, reaching a detection limit of 11 CFU/mL in poultry samples [97]. This biosensor achieved a low detection limit of 11 CFU/mL, with a linear range of 10^1 – 10^4 CFU/mL, and demonstrated high recovery (~109.8%) in spiked chicken carcass samples. The use of MOF-based nanozymes in a

labeled configuration, combined with efficient magnetic separation, highlights the potential of this platform for sensitive and scalable foodborne pathogen detection without the need for pre-enrichment steps.

For rapid point-of-care testing, a pipette tip-based biosensor was devised, incorporating immune-functionalized nickel meshes and fluorescent MOFs modified with boronic acid groups (MOFs@B(OH)₂) [98]. The platform enabled selective binding of *Salmonella* in a conical separation unit, followed by acid-triggered release of the fluorescent label. The detection limit reached 18.8 CFU/mL, and results were available in just 20 minutes, highlighting the translation of labeled MOF biosensors into practical diagnostic tools. Moreover, a labeled electrochemical immunosensor was developed for the sensitive and rapid detection of *Salmonella typhimurium* in milk. The sensor incorporated platinum nanoparticles and a Co/Zn-MOF supported on carboxylated multiwalled carbon nanotubes (MWCNTs), which synergistically improved both sensitivity and signal stability [99]. In the optimized system, antibodies specific to *S. typhimurium* were immobilized on the sensor, enabling selective recognition and signal generation. The immunosensor exhibited a wide linear detection range from 1.3×10^2 to 1.3×10^8 CFU/mL and a low detection limit of 94 CFU/mL. The platform also demonstrated strong specificity, reproducibility, and stability, showing strong promise for extension to other labeled detection strategies targeting foodborne pathogens.

Overall, labeled MOF-based detection platforms offer amplified signals and higher sensitivity than their label-free counterparts. These systems can be tailored for specific readouts (fluorescence, electrochemical, colorimetric) and integrated with microfluidics or portable devices, making them powerful tools for sensitive, real-world biosensing applications.

3.3. Performance metrics (sensitivity, selectivity, LOD)

The performance of MOF-based optical biosensors is primarily evaluated through sensitivity, selectivity, and limit of detection (LOD), all of which are critical for effective pathogen diagnostics. High surface area and adjustable pore structures enable MOFs to achieve low detection limits by increasing analyte capture and signal response. The performance of biosensors and therapeutic platforms is often gauged by their sensitivity, selectivity, and functional efficiency. In a recent study, self-fueled MOF-based micromotors were designed to combine autonomous motion with intrinsic antibacterial functionality, offering a highly integrated sensing-therapeutic approach. These micromotors spontaneously degrade in aqueous environments, releasing ionic species that not only fuel their self-propulsion via ionic diffusiophoresis but also act as antibacterial agents. The release of metal cations enhanced the selective killing of *Escherichia coli* (*E. coli*), with motion-assisted activity significantly improving antibacterial efficacy (Figure 6) [100]. In an in vivo wound model, this system led to accelerated wound healing, demonstrating both biological specificity and functional effectiveness. While traditional biosensing metrics such as detection limit (LOD) are not directly reported, the system's selective antibacterial action and self-powered delivery highlight its potential for future high-performance biosensing and theranostic applications, particularly where both biological targeting and therapeutic impact are required. A comprehensive summary of MOF-based biosensors, including sensor materials, target microorganisms, detection methods, detection limits, and linear ranges, is provided in Table 2.

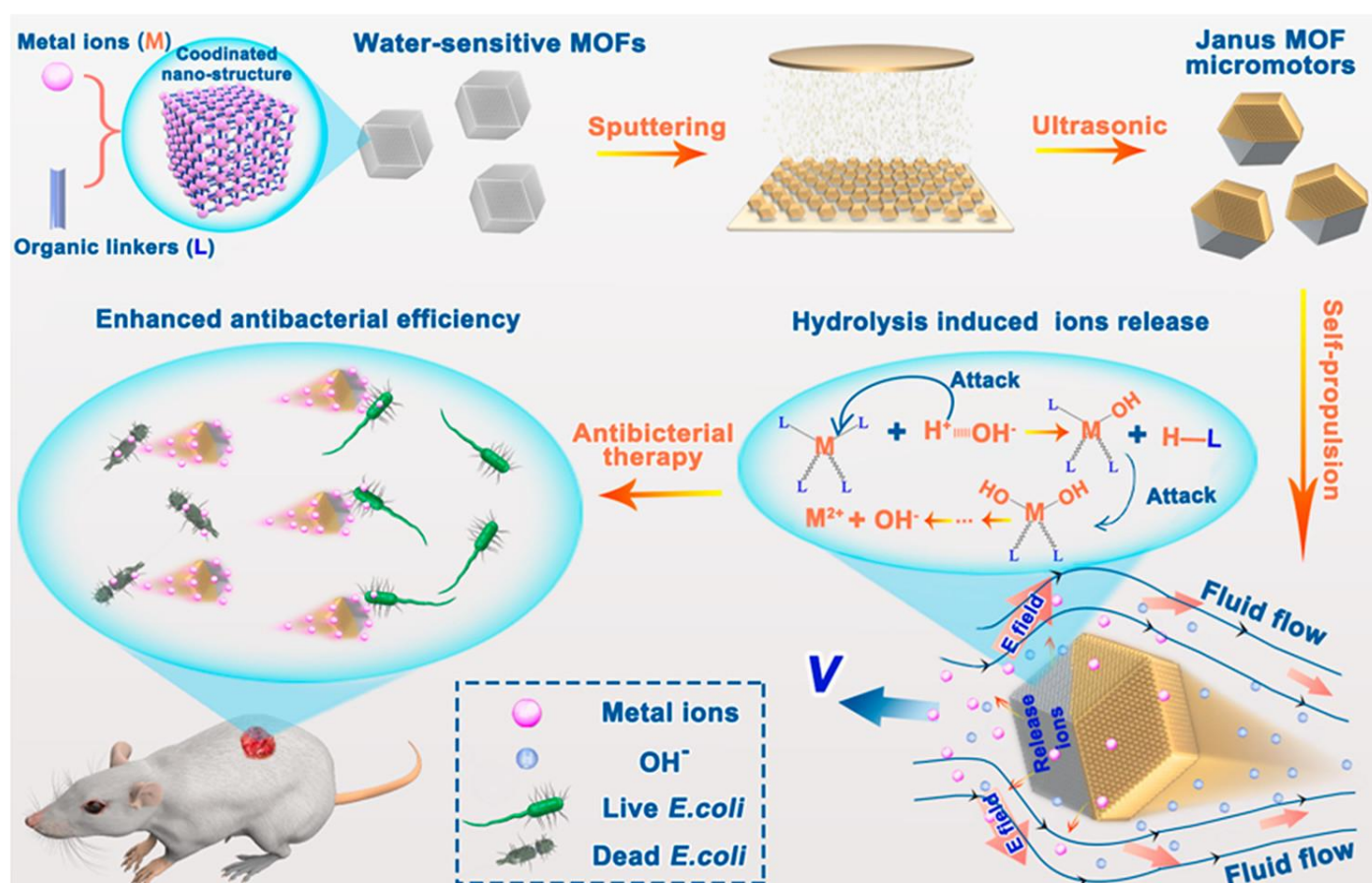


Figure 6. Schematic representation of the fabrication of MOF-based micromotors and their application in antibacterial wound treatment. Copyright 2022 ACS [100].

Table 2. Summary of MOF-Based Biosensors for Pathogen Detection.

Materials	Target Microorganisms	Method	LOD	Linear Range	Ref.
Zr-MOF + DNA aptamer	<i>E. coli</i> O157:H7	Fluorescence	—	—	[69]
Lanthanide-doped MOFs	<i>Staphylococcus aureus</i>	Fluorescence	—	—	[69]
MOFs + AuNPs + antibodies	SARS-CoV-2	Colorimetric	—	—	[70]
MOFs + lectins	<i>Candida albicans</i>	SERS	—	—	[71]
Fe-MOF@SalmpYZU47	<i>Salmonella enterica</i>	Colorimetric	11 CFU/mL	1.0×10^2 to 1.0×10^8 CFU/mL	[72]
MOF + PTS	<i>E. coli</i> O157:H7	Visual	530 CFU/mL	—	[73]
GO + Cu-MOF	<i>Mycoplasma pneumoniae</i> , <i>Legionella pneumophila</i>	Electrochemical	1 pg/mL	1 pg/mL to 100 ng/mL	[74]
CoFe-MOFs@Nafion	<i>Salmonella</i> in milk	Electrochemical	1.38×10^2 CFU/mL	1.38×10^2 to 1.38×10^8 CFU/mL	[75]

CoFe-MOFs + MWCNTs + AuNPs	Salmonella	Electrochemical	2.89×10^3 CFU/mL	1.04×10^4 to 1.04×10^8 CFU/mL	[76]
MCOF + AuNPs + AIEgens	Salmonella typhimurium	Colorimetric/fluorescent	1000 CFU/mL / 10 CFU/mL	–	[77]
Cu-MOF	CRP	Colorimetric/fluorescent	40 pg/mL / 240 pg/mL	–	[78]
Zn-MOF	HER2 (non-microbial)	Fluorescence	1.38 pM	–	[79]
UiO-66-NH ₂ MOF + MB + TMB	let-7a, miRNA-21	Electrochemical	3.6 fM, 8.2 fM	–	[80]
Porphyrinic COFs + AgNPs	CRP	Photoelectrochemical	–	–	[81]
Polyaniline@Ni-MOF	HCV RNA	Electrochemical	0.75 fM	1 fM to 100 nM	[86]
Zr-MOF + methylene blue	GBM exosomes	Electrochemical	7.83×10^3 particles/ μ L	9.5×10^3 to 1.9×10^7 particles/ μ L	[87]
Pt-COF nanozyme + Chromotrope 2R	Listeria monocytogenes, Salmonella typhimurium	Colorimetric	1.31, 1.61 CFU/mL	–	[88]
CoFe-MOFs + graphene + Au-NH ₂	Salmonella in milk	Electrochemical	1.2×10^2 CFU/mL	2.4×10^2 to 2.4×10^8 CFU/mL	[89]
Ultrathin MOF-NSs	Multiple bacterial DNAs	Fluorescence	15 pM	–	[90]
Fe-MIL-88NH ₂ + PtNPs	Salmonella	Colorimetric	93 CFU/mL	–	[91]
Cu-MOF/PEDOT:PSS	E. coli O157:H7	Electrochemical	7.4 CFU/mL	3×10^2 to 3×10^8 CFU/mL	[92]
Enzyme-loaded ZIF-8	E. coli O157:H7	Colorimetric	1 CFU/mL	–	[93]
MIL-88@TcP	Salmonella typhimurium	Colorimetric	1.68×10^2 CFU/mL	–	[94]
ZIF-8 + FLS + CRISPR/Cas12a + RAA	Salmonella typhimurium	Fluorescence	1.3×10^2 CFU/mL	–	[95]
Cu-MOF + streptavidin	E. coli	Colorimetric	2 CFU/mL	16 to 1.6×10^6 CFU/mL	[96]
Pt@ZIF-8	Salmonella typhimurium	Colorimetric	11 CFU/mL	10^1 – 10^4 CFU/mL	[97]
MOF@B(OH) ₂ + Ni mesh	Salmonella	Fluorescence	18.8 CFU/mL	–	[98]

PtNPs + Co/Zn-MOF + MWCNTs	Salmonella typhimurium	Electrochemical	94 CFU/mL	1.3×10^2 to 1.3×10^8 CFU/mL	[99]
MOF-based micromotors	E. coli	Theranostic	–	–	[100]

4. MOF-Based Optical Biosensors for Environmental Monitoring

MOF-based optical biosensors have emerged as promising tools for environmental monitoring due to their exceptional sensitivity, tunability, and adaptability. These materials offer unique advantages stemming from their highly porous architectures, large surface areas, and flexible chemical functionalities, which enable selective interaction with a wide range of environmental analytes. MOFs can be functionalized with luminescent ligands, chromophores, enzyme mimics, or responsive molecules to produce measurable optical responses such as fluorescence, colorimetric change, or photoluminescence upon interaction with specific contaminants. The integration of these responsive MOFs into platforms such as fiber optics, paper chips, or hybrid nanocomposites further enhances their usability in portable, field deployable formats. This makes MOF-based optical biosensors especially suitable for real-time, on-site analysis of environmental pollutants including heavy metals, pesticides, toxins, and microbial agents [101,102].

The accumulation of toxic heavy metals in the environment, particularly in water sources, poses a significant threat to public health and has been linked to neurodegenerative diseases like Alzheimer's [103]. Optical biosensors offer a powerful tool for environmental monitoring by enabling the rapid, selective, and ultra-sensitive detection of trace levels of heavy metals such as mercury, cadmium, lead, and arsenic, thereby supporting early warning and contamination control efforts [104].

4.1. Detection of pollutants (heavy metals, pesticides, toxins, etc.)

MOF-based optical biosensors enable rapid and sensitive detection of environmental pollutants such as heavy metals, pesticides, and toxins by translating molecular interactions into fluorescence or colorimetric signals [105,106]. Their customizable pore structures and surface chemistry allow selective recognition of target analytes, making them powerful tools for real-time environmental monitoring.

In the domain of heavy metal detection, an innovative zirconium-based MOF (dMOR-2), synthesized using a 2-picolylamine-modified terephthalate ligand, has been developed to simultaneously function as an optical sensor and an adsorbent [107]. Dispersed in water with polyvinylpyrrolidone, dMOR-2 demonstrated outstanding fluorescence sensing capabilities for Cu^{2+} , Pb^{2+} , and Hg^{2+} with detection limits below 2 parts per billion (ppb), even in complex aqueous matrices. Its sensing performance was attributed to chelation-induced fluorescence modulation by the picolylamine group. In parallel, dMOR-2 was also integrated into a calcium alginate composite and exhibited high adsorption capacities for these metal ions, thereby highlighting its multifunctional role in detection and remediation.

Moreover, Pu et al. reported an azobenzene-based luminescent probes were incorporated into a bio-MOF-1 matrix to create optical biosensors for the detection and adsorption of heavy metal ions, particularly Cu^{2+} [108]. These MOF-integrated sensors (P1@BMOF and P2@BMOF) exhibited high selectivity, low detection limits (as low as $0.20 \mu\text{M}$), and enhanced stability, demonstrating effective fluorescence quenching responses and strong adsorption capacities, making them promising tools for environmental monitoring of

toxic metal pollutants. A different approach involving defect engineering was employed to enhance the sensitivity of lanthanide-based luminescent MOFs. Specifically, Eu@UiO-MOFs were synthesized with modulator-induced missing-linker defects, which fine-tuned the photophysical properties of the framework [109]. The defect-rich Eu@UiO-MOFs, with an average of 0.53 missing linkers per Zr_6 node, exhibited significantly amplified fluorescence responses upon Cd^{2+} binding and enabled ultrasensitive detection at a limit of 114 ppb. These results emphasized the importance of structural defect modulation in improving MOF-based optical biosensor performance.

For chromium detection, a fiber-optic sensor platform was developed by coating a U-bent fiber optic probe with zeolitic imidazolate framework-67 (ZIF-67) via in situ deposition and subsequent thermal treatment [110]. The fabricated FOS/ZIF-67 sensor took advantage of the evanescent wave absorbance at 395 nm characteristic of Cr(VI), achieving a detection limit as low as 1 ppb. In addition to its wide linear detection range and rapid response, the sensor displayed high selectivity, operational stability in real water samples, and robust shelf life making it highly suitable for practical deployment in environmental monitoring. In a separate example, a manganese-based MOF (SM-1), formed from 2,5-furandicarboxylic acid and 4,7-phenanthroline, exhibited anionic framework characteristics with uncoordinated nitrogen sites that enhanced its stability and analyte interaction [111]. SM-1 functioned as a dual-mode fluorescent sensor, showing a “turn-on” response for Ag^+ and Cd^{2+} , and a “turn-off” signal for Hg^{2+} ions. The MOF achieved low detection limits in aqueous media and also demonstrated potential for environmental remediation through its reversible iodine adsorption capability.

To address the detection of spectroscopically silent ions, an optical biosensor targeting Pb^{2+} was designed by growing MOF-5 in situ on tannic acid-functionalized gold nanoparticles deposited on a U-bent fiber [112]. This plasmonic absorption-based sensor translated the refractive index shift upon Pb^{2+} binding into enhanced plasmonic signals, achieving a detection limit of 0.5 ppb. The sensor exhibited outstanding selectivity, stability, and operational effectiveness in complex sewage samples, illustrating its suitability for on-site water quality surveillance.

Furthermore, a fluorescence “turn-off” immunosensor was developed using amine-functionalized MIL-101(Fe) MOFs conjugated with monoclonal antibodies specific to Pb^{2+} ions [113]. The biosensor exhibited high aqueous stability and biocompatibility, enabling selective detection of Pb^{2+} at concentrations as low as 9.51 ppb in real water samples, meeting the safety limits set by the WHO and EPA. Complementing these optical platforms, a dual-mode biosensor combining photoelectrochemical (PEC) and electrochemical (EC) responses was constructed using a phthalocyanine-based covalent organic framework (CoPc-PT-COF) grown covalently onto a Cu-MOF substrate [114]. This hybrid structure combines the high photo- and electroactivity of phthalocyanine and bipyridine units with the porous and functional surface of the MOF. The enhanced photoelectric properties of CoPc-PT-COF@Cu-MOF, along with its favorable band structure, enable amplified signal output in both PEC and EC detection modes. DNA probes immobilized on the heterostructure selectively recognize Cr^{3+} ions through specific interactions, allowing for highly sensitive detection in aqueous environments. The biosensor achieved remarkably low detection limits 14.5 fM (PEC) and 22.9 fM (EC) across a wide concentration range (0.1 pM to 100 nM), with excellent selectivity, stability, and reproducibility. It also demonstrated successful detection of trace Cr^{3+} in real-world samples such as river and tap water. This work highlights the potential of MOF-based photoelectrochemical biosensors for advanced environmental monitoring, particularly in tracking ultra-trace levels of toxic heavy metals in complex water matrices.

Though not directly based on optical readout, a hybrid electrochemical sensor combining Bi_2CuO_4 , UiO-67, and Al-MOF achieved simultaneous detection of Cd^{2+} , Cu^{2+} , Pb^{2+} , and Hg^{2+} with remarkable detection limits down to the picomolar range (e.g., 0.02 pM for Cd^{2+}) [115]. This unique architecture not only provides superior electrocatalytic redox activity but also ensures high stability, reproducibility, and selectivity (Figure 7). Remarkably low detection limits were achieved for each metal ion, down to picomolar levels (e.g., 0.02 pM for Cd^{2+}). The detection mechanism involves both adsorption and electrochemical accumulation of metal ions on the MOF-modified electrode surface. Demonstrating real-world applicability, the sensor was successfully employed to detect heavy metals in various complex food matrices such as rice, milk, and tea, highlighting its potential for environmental and food safety monitoring.

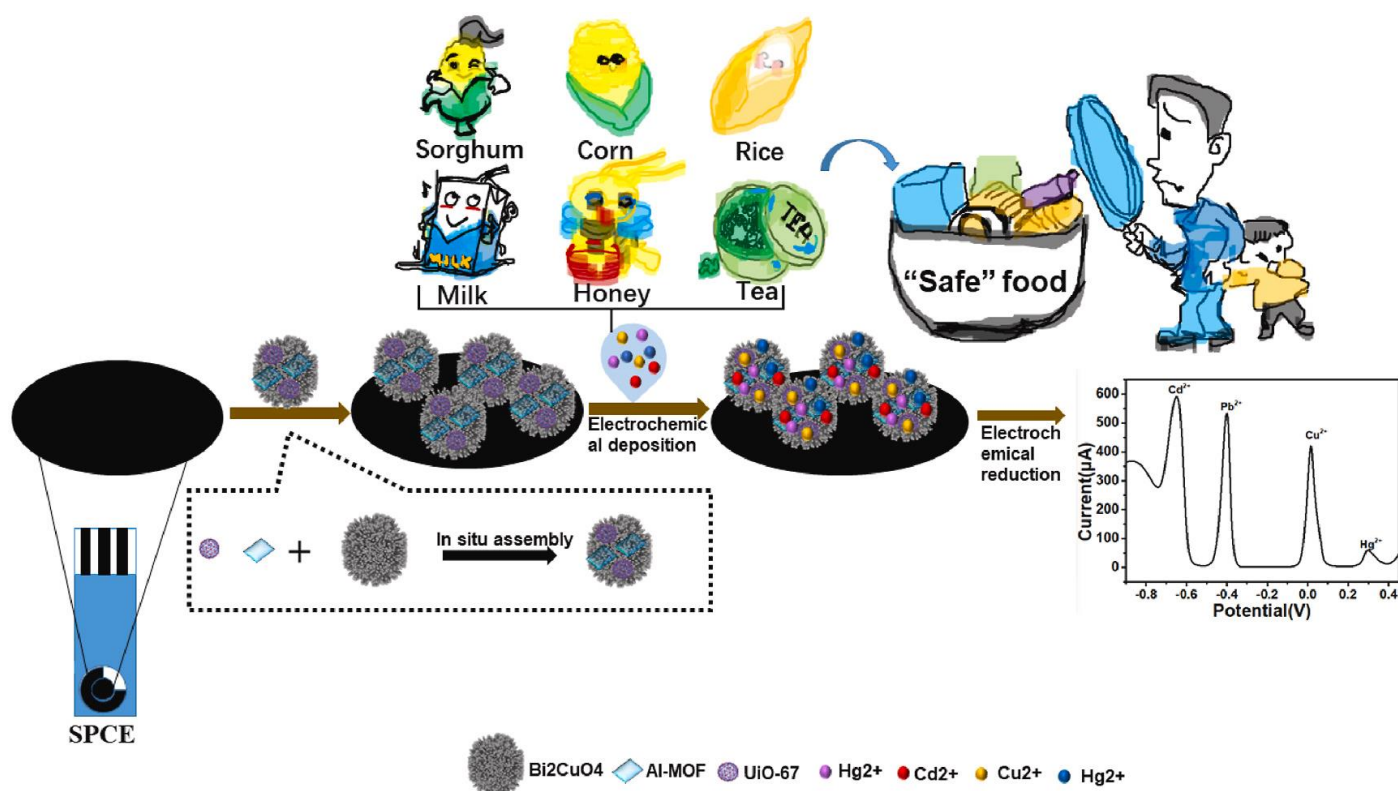


Figure 7. Illustration of the Bi_2CuO_4 @Al-MOF@UiO-67/SPCE sensor used for detecting Cd^{2+} , Cu^{2+} , Pb^{2+} , and Hg^{2+} ions in food samples. Copyright 2024 Elsevier [115].

4.2. Detection of Pesticides and Herbicides

The pervasive use of pesticides and herbicides in agriculture introduces toxic residues into ecosystems, necessitating robust detection methods. MOF-based optical biosensors offer field-friendly alternatives to chromatographic techniques through their rapid response and visual readouts.

One such example is a Cu-MOF nanoprobe developed using a one-pot reaction among Cu^{2+} , 5-aminoisophthalic acid (AIA), and trimesic acid (H_3BTC) [116]. The MOF exhibited strong quenching behavior due to ligand-to-metal charge transfer (LMCT) and photoinduced electron transfer (PET). Upon glyphosate exposure, competitive binding disrupted the framework, releasing the AIA ligand and triggering fluorescence recovery. The sensor achieved a detection limit as low as 33 nM, significantly below the U.S. EPA maximum contaminant level. In addition to environmental sensing, the probe enabled real-time imaging of glyphosate in plant tissues and screening of agricultural samples.

Another effective platform is a paper-based biosensor composed of acetylcholinesterase (AChE) immobilized on a ZIF-8-modified cellulose matrix [117]. The MOF encapsulation enhanced enzyme stability under variable pH, temperature, and storage conditions, while the peroxidase-like activity of ATCI allowed for efficient signal generation. The sensor achieved a low detection limit of 0.29 µg/L and a linear range of 0.5–50 µg/L for dichlorvos within 20 minutes. Integration with a 3D-printed holder and smartphone readout enabled portable, instrument-free point-of-care testing. This work demonstrates the potential of MOF-enabled colorimetric biosensors as reliable, field-deployable tools for environmental and agricultural monitoring, particularly in ensuring food safety and pesticide regulation.

4.3. Detection of Microbial Pathogens

MOF-based optical biosensors have also made considerable progress in detecting pathogenic microorganisms, offering a non-invasive and highly specific alternative to culture-based methods. By integrating biological recognition elements such as antibodies and aptamers, MOFs can detect bacteria through fluorescence quenching or enzymatic signal recovery. A notable development in this domain is a terbium-based MOF constructed with 1,3,5-benzenetricarboxylic acid (Tb-BTC), functionalized with anti-E. coli antibodies [118]. coli antibodies to enable selective bio-recognition. The optical response, based on changes in fluorescence intensity, allows for the detection of E. coli across a wide concentration range (1.3×10^2 to 1.3×10^8 CFU/mL), with an exceptionally low detection limit of 3 CFU/mL and a rapid response time of just 5 minutes. This work highlights the significant potential of MOF-based fluorescent platforms for optical biosensing applications. Due to its high sensitivity, selectivity, fast response, and successful demonstration in complex matrices such as fruit juice, the Tb-BTC system holds promise for real-time environmental monitoring of microbial contamination in water or food sources.

In a similar approach, a zirconium–praseodymium-based MOF nanozyme (ZrPr-MOF) was combined with aptamer-based recognition to develop a colorimetric sensor for Salmonella Typhimurium [119]. The presence of S. Typhimurium disrupts the aptamer–nanozyme interaction, restoring catalytic activity and enhancing the colorimetric response. The biosensor showed excellent sensitivity under optimized conditions, with a linear detection range of 10^2 – 10^8 CFU/mL and a low detection limit of 37 CFU/mL. Additionally, a paper-based format of the biosensor was demonstrated for portable, point-of-care detection, successfully identifying S. Typhimurium in spiked milk samples. This study highlights the promise of MOF-based nanozyme optical biosensors for rapid, selective, and on-site microbial monitoring in food safety and environmental surveillance applications.

4.4. Detection of Biochemical and Volatile Environmental Contaminants

Beyond heavy metals, pesticides, and pathogens, environmental pollutants encompass a broad category of volatile and biochemical substances, including quorum sensing molecules, plant stress markers, volatile organic compounds (VOCs), biochemical waste, and gaseous pollutants. MOFs, owing to their high porosity, structural tunability, and optical versatility, have been successfully employed to detect these diverse targets with excellent sensitivity and selectivity using a variety of optical modalities.

For instance, quorum sensing molecules such as N-(3-oxodecanoyl)-L-homoserine lactone (3-O-C10-HL), which mediate microbial communication and contribute to biofilm formation, have been detected using a sophisticated optoelectronic biosensor system [120]. This system integrated a Z-scheme heterojunction comprising CAU-17 MOF and

Bi₂S₃ nanostructures, configured into an organic photoelectrochemical transistor (OPECT). Functionalized with self-screening aptamers, the sensor enabled highly selective detection of 3-O-C10-HL down to 0.441 pM, presenting a promising platform for marine biofouling monitoring and early-stage microbial activity surveillance.

In the realm of plant health diagnostics, hydrogen peroxide (H₂O₂) serves as a key signaling molecule indicating biotic or abiotic stress. Traditional methods for H₂O₂ detection typically involve destructive sample processing, which can further stress the plant and are labor-intensive. To overcome these limitations, the authors developed a ZIF-8-based color-to-thermal biosensor formed directly on plant tissues (roots, petioles, or leaves) by spraying a mixture of horseradish peroxidase (HRP), ABTS, and ZIF-8 precursors [121]. Upon exposure to near-infrared (NIR) light, the oxidized product (ABTS•⁺) produced heat, allowing thermal signal detection of sub-micromolar concentrations of H₂O₂ (Figure 8). Because plant tissues have minimal absorption in the NIR region, the biosensor enabled remote optical readout with a high signal-to-noise ratio, without damaging the plant. This work demonstrates the utility of MOF-based optical biosensing platforms for noninvasive, real-time monitoring of plant stress responses, offering significant promise for applications in precision agriculture, environmental monitoring, and plant physiology research.

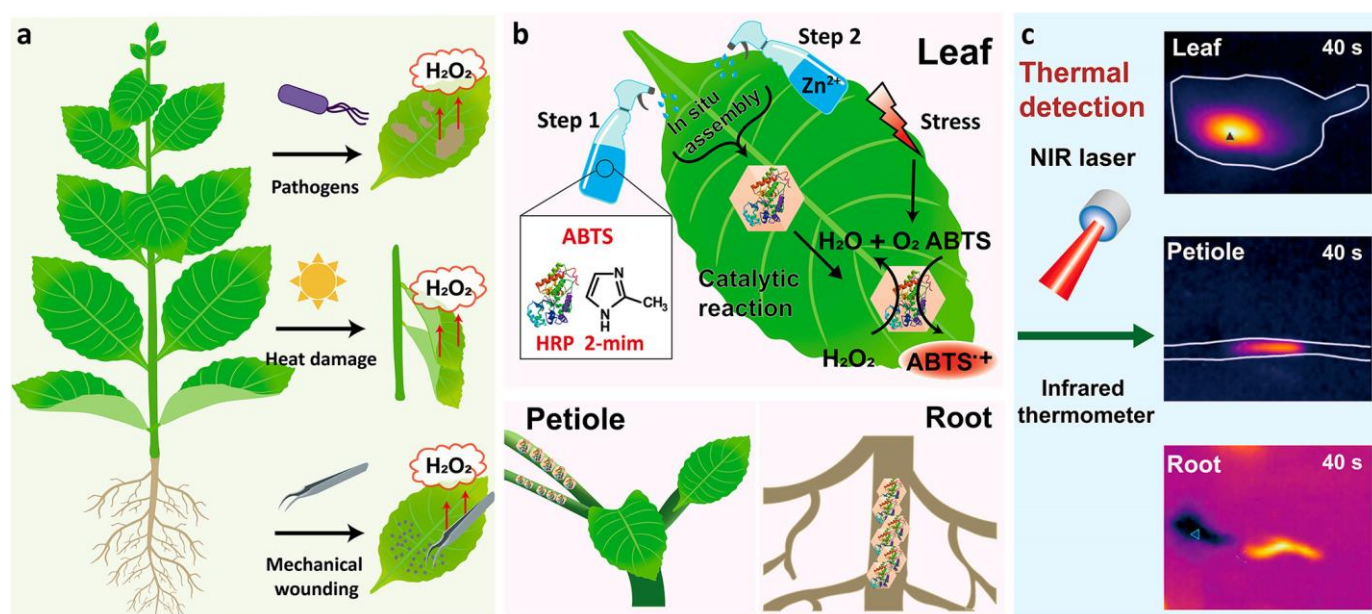


Figure 8. Illustration of ZIF-8-Based Plant H₂O₂ Biosensor (a) *Nicotiana benthamiana* under stress (e.g., pathogens, heat, wounding) produces H₂O₂. (b) A mixture of HRP, ABTS, and 2-methylimidazole is sprayed onto plant tissues, followed by Zn²⁺ to form ZIF-8 encapsulating the sensing components in situ. (c) H₂O₂ oxidizes ABTS to ABTS•⁺, which generates a thermal signal under NIR light, enabling remote detection via a thermometer [121].

Volatile organic compounds (VOCs), which include industrial solvents such as ethanol, acetone, and methanol, are significant air pollutants due to their toxicity and flammability. A localized surface plasmon resonance (LSPR)-based optical fiber sensor was developed using a layer-by-layer deposition of gold nanoparticles and HKUST-1 on a fiber tip [122]. Varying the number of MOF coating cycles (40, 80, 120) allowed tuning of the sensor's sensitivity, with significant optical responses observed only at higher coating thicknesses. The sensor exhibited a measurable redshift in resonance wavelength upon VOC exposure due to refractive index changes from VOC adsorption into the MOF layer,

with high sensitivity and low detection limits for acetone, ethanol, and methanol. The sensor also demonstrated reversible behavior, rapid response and recovery times, and minimal interference from humidity and temperature, highlighting its promise as a reliable MOF-based optical platform for real-time environmental VOC monitoring.

In addition to air and plant stress analytes, MOF-based biosensors have addressed biochemical pollutants such as urea and morphine. A tapered single-mode-coreless-single-mode (SCS) optical fiber, functionalized with urease-loaded ZIF-8, allowed urea detection via enzyme-mediated changes in local refractive index [123]. The detection mechanism relies on the binding of urea to urease, which induces changes in the local refractive index, leading to measurable resonance wavelength shifts in the fiber's transmission spectrum. The biosensor demonstrated a linear optical response to urea concentrations ranging from 1 to 10 mM, with a detection limit of 0.1 mM and sensitivity of 0.8 mM/RIU when operated over a broadband light source (1525–1590 nm). Performance evaluation using real samples confirmed the sensor's high selectivity and sensitivity, establishing its suitability for optical biosensing applications. This work underscores the potential of MOF-enzyme hybrid systems, particularly ZIF-8/urease, for environmental monitoring of biochemical contaminants like urea in water, offering a robust and precise sensing platform for real-world applications.

Complementing this approach, a hydrogel-confined dual-enzyme cascade system (UFD-DEC), comprising Fe-cdDNA nanozymes and urease, produced a visible color change upon urea decomposition [124]. By precisely tuning the catalytic activity of Fe-cdDNA nanozymes using DNA control, the cascade reaction is significantly accelerated while maintaining high structural stability. Encapsulated within a hydrogel matrix, the system forms a portable “lab-in-a-tube” device capable of on-site urea detection. The readout is facilitated via a smartphone-based image analysis algorithm, enabling real-time, colorimetric signal interpretation with a detection limit of 0.12 mmol/L. This work showcases a customizable, low-cost, and miniaturized biosensor platform with strong potential for point-of-care diagnostics and environmental monitoring, particularly for urea profiling in agricultural or clinical contexts.

Wearable and physiological biosensing was also demonstrated using a MOF-based colorimetric sensor for transcutaneous CO₂ detection [125]. It offers high sensitivity and selectivity, detecting CO₂ levels as low as 26 ppm across a wide range (0–2% CO₂) while resisting interference from skin gases. Human trials confirm its clinical potential, and its compact, responsive design suits applications in sports and exercise for respiratory monitoring. Overall, this MOF-CMOS sensor's affordability, reversibility, and sensitivity make it ideal for wearable remote health tracking devices.

Additionally, a Cr(III)-based MOF nanoparticle fluorescent sensor was engineered for the optical detection of morphine (**Figure 9**) [126]. The Cr(III)-MOF-NPs displayed a characteristic emission at 593 nm, which shifted to 566 nm with enhanced intensity upon MOR addition, accompanied by a visible color change from brown to yellow, enabling rapid and selective optical detection. The developed PL sensor showed high sensitivity with a detection limit of 0.167 nM and strong selectivity for MOR across a concentration range of 0.1 to 350 nM. It was successfully applied for ultrasensitive morphine quantification in spiked serum and urine samples, demonstrating practical utility in complex biological matrices.

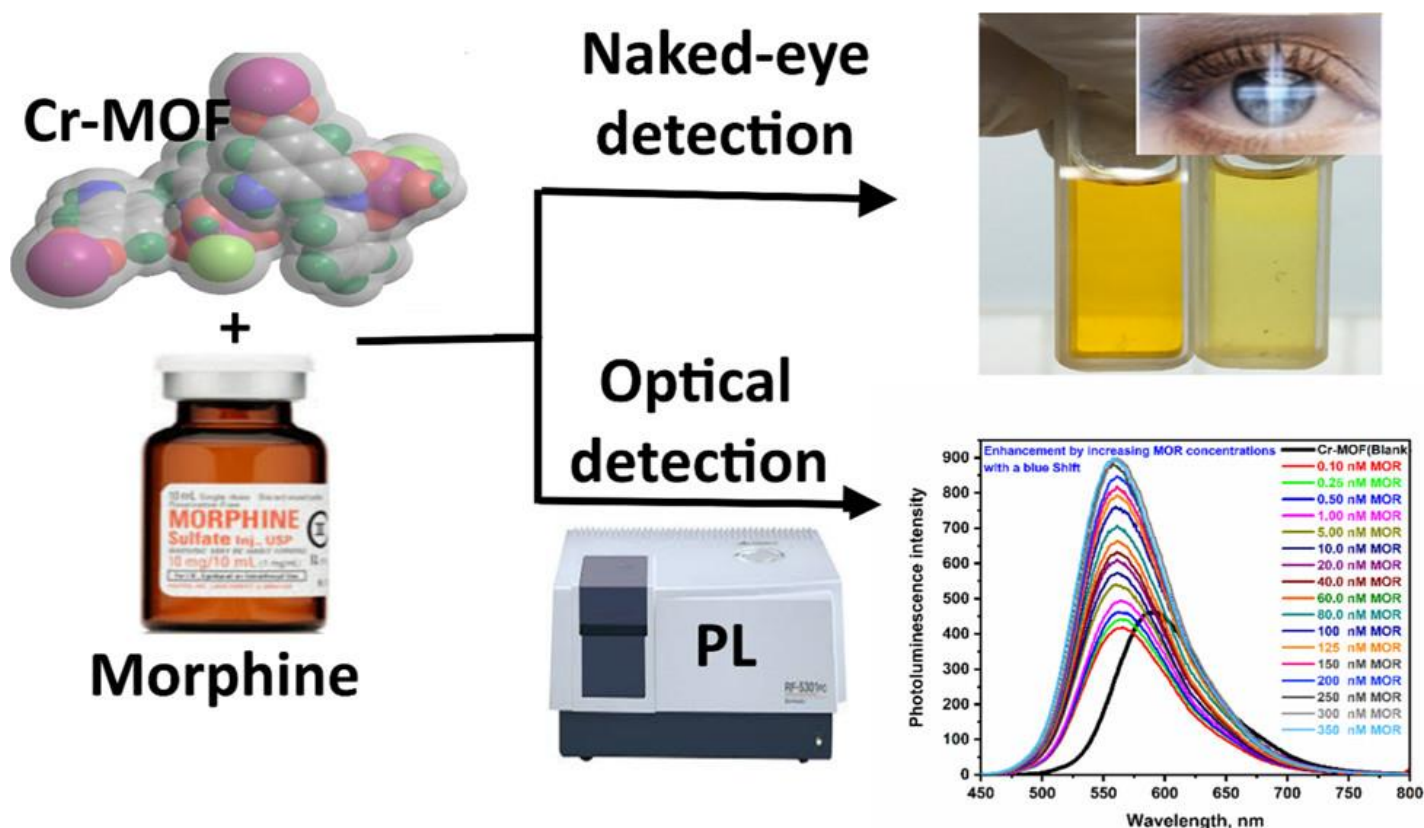


Figure 9. Illustration of the MOF assembly and applications for optical based bio-sensing. Copyright 2020 ACS [126].

Additionally, enhancing plasmonic optical biosensors with MXene-MOF hybrids has improved sensitivity in biochemical detection [127]. Furthermore, combining Ti_3C_2 with a terbium-based metal–organic framework (Tb-BTC) enabled the fabrication of a selective optical biosensor for haemoglobin. The Tb-BTC MOF selectively binds to the iron center in haemoglobin, enhancing the sensor's specificity. The sensor demonstrated reliable detection of haemoglobin in the range of 100 to 500 $\mu\text{g}/\text{mL}$ and maintained selectivity even in the presence of interfering biomolecules such as immunoglobulin, glucose, uric acid, and bovine serum albumin. This hybrid MXene-MOF platform showcases significant potential for sensitive and selective optical biosensing in both environmental and clinical monitoring contexts. A summary of the key MOF-based optical biosensors discussed in this section, including their materials, target analytes, detection methods, performance metrics, and references, is provided in **Table 3** for easy comparison and overview.

Table 3. Summary of MOF-Based Optical Biosensors for Environmental Monitoring.

Materials	Target Analytes	Methods	LOD	Linear Range	Ref.
Zr-based MOF	Cu^{2+} , Pb^{2+} , Hg^{2+}	Fluorescence	< 2 ppb	-	[107]
P1@BMOF, P2@BMOF	Cu^{2+}	Fluorescence	0.20 μM	-	[108]
Defect-rich Eu@UiO-MOFs	Cd^{2+}	Fluorescence	114 ppb	-	[109]
ZIF-67 on fiber optic probe	Cr(VI)	Evanescent	1 ppb	-	[110]
SM-1	Ag^+ , Cd^{2+} , Hg^{2+}	Fluorescence	-	-	[111]
MOF-5	Pb^{2+}	Plasmonic	0.5 ppb	-	[112]
$\text{NH}_2\text{-MIL-101(Fe)-mAb}$	Pb^{2+}	Fluorescence	9.51 ppb	-	[113]

CoPc-PT-COF@Cu-MOF	Cr ³⁺	PEC + EC	14.5 fM (PEC), 22.9 fM (EC)	0.1 pM – 100 nM	[114]
Bi ₂ CuO ₄ + UiO-67 + Al-MOF	Cd ²⁺ , Cu ²⁺ , Pb ²⁺ , Hg ²⁺	Electrochemical	0.02 pM (e.g., Cd ²⁺)	-	[115]
Cu-MOF	Glyphosate	Fluorescence	33 nM	-	[116]
ZIF-8@Cellulose	Dichlorvos	Colorimetric	0.29 µg/L	0.5–50 µg/L	[117]
Tb-BTC MOF	E. coli	Fluorescence	3 CFU/mL	1.3×10 ² – 1.3×10 ⁸ CFU/mL	[118]
ZrPr-MOF	Salmonella Typhimurium	Colorimetric	37 CFU/mL	10 ² –10 ⁸ CFU/mL	[119]
CAU-17/Bi ₂ S ₃	3-O-C10-HL	Optoelectronic	0.441 pM	-	[120]
ZIF-8 + HRP	H ₂ O ₂	NIR-induced	Sub-µM	-	[121]
AuNPs/HKUST-1	VOCs	LSPR	-	-	[122]
Urease@ZIF-8	Urea	Refractive index	0.1 mM	1–10 mM	[123]
UFD-DEC	Urea	Colorimetric	0.12 mmol/L	-	[124]
MOF-CMOS	CO ₂	Colorimetric	26 ppm	0–2% CO ₂	[125]
Cr(III)-MOF-NPs	Morphine	Fluorescence	0.167 nM	0.1–350 nM	[126]
Ti ₃ C ₂ + Tb-BTC MOF	Hemoglobin	Optical	-	100–500 µg/mL	[127]

5. Integration with Advanced Technologies

The integration of MOF-based optical biosensors with advanced technologies such as microfluidics, portable electronics, artificial intelligence (AI), and the Internet of Things (IoT) is driving a new generation of smart sensing platforms for real-time pathogen and environmental monitoring. These synergistic advancements significantly expand the practical applicability of MOF-based optical biosensors in diverse settings, from clinical diagnostics to environmental safety.

5.1. portable-based sensing

Smartphone-based sensing offers a powerful platform for portable, user-friendly detection using MOF-based optical biosensors [128]. With built-in cameras, advanced processors, and connectivity, smartphones can capture and analyze optical signals such as fluorescence or colorimetric changes generated by MOF sensors. This approach enables rapid, on-site detection of pathogens or pollutants without the need for complex instrumentation. Moreover, smartphone apps can process data in real time, display results, and upload information to cloud platforms for remote monitoring [129–131]. The widespread availability and versatility of smartphones make them ideal tools for expanding the accessibility and scalability of MOF-based biosensing technologies.

A smartphone-integrated electrochemical biosensing platform was developed for on-site toxicity evaluation of heavy metal ions, specifically Cd²⁺, Pb²⁺, and Hg²⁺, using a Hep G2 cell response model [132]. The system employs a reduced graphene oxide (RGO)/molybdenum disulfide (MoS₂) composite electrode for enhanced biocompatibility and signal amplification, with differential pulse voltammetry (DPV) capturing electrochemical

changes linked to cytotoxicity. This compact sensor interfaces with a smartphone for data acquisition and visualization, enabling accurate real-time monitoring (IC_{50} values: $Cd^{2+} = 49.83 \mu M$, $Hg^{2+} = 36.94 \mu M$, $Pb^{2+} = 733.90 \mu M$). Its integration supports food and environmental safety assessment, confirmed by MTT assay, microscopy, and flow cytometry.

Another portable point-of-care testing (POCT) platform was designed for rapid detection of multiple heavy metal ions (HMIs) in milk. The system uses a disposable disk with six screen-printed electrodes (SPEs) and MOFs to amplify the electrochemical signal of methylene blue [133]. Differential pulse voltammetry (DPV) enabled highly sensitive detection of Cd^{2+} , Hg^{2+} , Pb^{2+} , and As^{3+} , with detection limits as low as 0.022–0.073 ppb, all within four minutes. Successfully applied to milk samples, this flexible and efficient MOF-assisted platform offers a practical solution for on-site environmental and food safety monitoring.

Li et al. introduced a 3D-printed, smartphone-based optical sensing device as a portable, low-cost substitute for conventional UV–vis spectrometers in detecting heavy metals [134]. The device enables sensitive and accurate measurement without the need for bulky equipment or trained personnel. Its performance was validated through the successful detection of four common heavy metal ions in real water samples, showing strong correlation with results from standard UV–vis instruments. This approach highlights the potential of smartphone-based sensors for on-site environmental monitoring, offering high sensitivity, ease of use, and cost-effectiveness.

A cost-effective, smartphone-based POCT system was developed for simultaneous detection of multiple metal ions, including Cd^{2+} , Cu^{2+} , Hg^{2+} , and Pb^{2+} [135]. It integrates custom electrodes with a lightweight handheld electrochemical analyzer, allowing real-time data acquisition via a dedicated mobile app (DHMI). DPV enabled sensitive, broad-range detection, and the system demonstrated performance comparable to ICP-MS in real water samples, offering a user-friendly and reliable tool for environmental surveillance.

A smartphone-integrated chemiresistive sensor was engineered for label-free detection of Pb^{2+} in water. Using micro-interdigitated electrodes ($\mu IDEs$) functionalized with graphene oxide and β -cyclodextrin, the device achieved a detection limit as low as 100 pM [136]. The readout system was compact and energy-efficient, and the integration of machine learning enhanced classification accuracy in complex matrices.

Another portable, smartphone-based colorimetric sensing platform was developed for detecting heavy metal ion pollution in industrial wastewater. The sensor array used plasmonic nanocolorants and chromophores to detect 13 HMIs (e.g., Hg^{2+} , Cd^{2+} , Pb^{2+} , Cr^{6+}) at ppm levels within 15 seconds [137]. Optical fibers transmit sensor images to the smartphone's CMOS imager, generating distinct RGB fingerprints analyzed via multivariate pattern recognition techniques (**Figure 10**). The system effectively identifies both individual ions and complex wastewater sources (e.g., electroplating, battery, metallurgical, pesticide) with high reproducibility. Integrated with edge computing and IoT cloud capabilities, this smartphone-based platform offers a low-cost, fast, and intelligent solution for environmental monitoring, water quality assessment, and pollution source tracing.

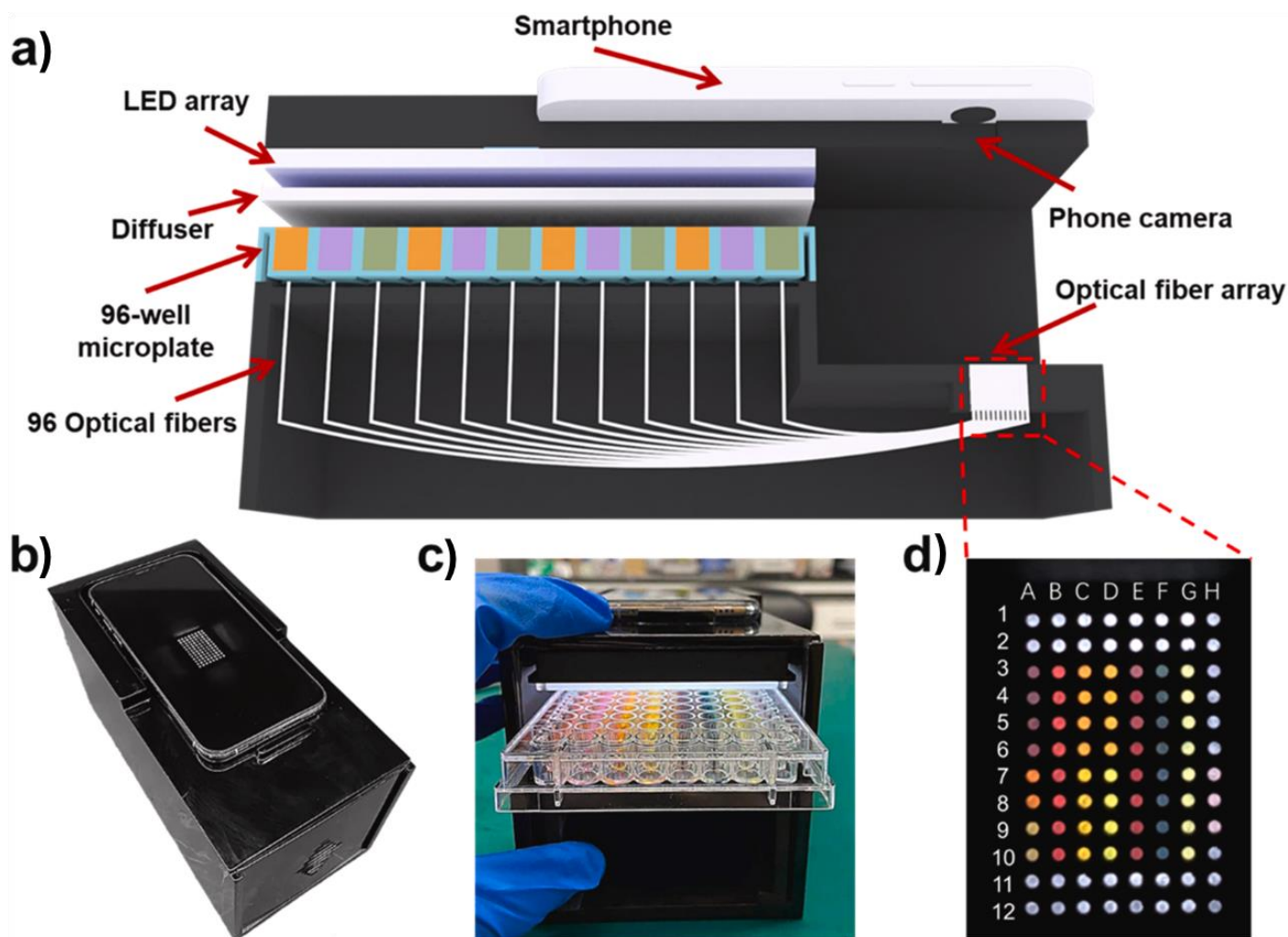


Figure 10. Overview of the compact smartphone-based CSA analysis system. (a) Diagram showing the device setup, which includes a smartphone, LED array, light diffuser, optical fiber bundle, and the CSA component. (b) Real-life image of the complete device. (c) Close-up view of the device's front panel. (d) Captured image of the CSA, reduced in scale, using the portable platform. Copyright 2022 Elsevier [137].

Xiao et al. developed a paper-based microarray platform with smartphone-based fluorescence detection using carbon nanodots (CDs) for simultaneous detection of Hg^{2+} , Pb^{2+} , and Cu^{2+} in Pearl River water [138]. With no need for complex preparation or instrumentation, the system used a custom app (SBR-App) and detected all analytes within five minutes, underscoring its viability for use in resource-limited settings. Additionally, MOF-based sensing has shown strong potential in wearable formats. A screen-printed electrochemical platform using a flexible Silk-polyurethane (Silk-PU) composite film was reported for the detection of *E. coli* [139]. Gold nanoparticle-modified electrodes enabled detection as low as 0.12 CFU/mL, and the platform retained performance after repeated bending. This system shows strong applicability for flexible, wearable diagnostic devices.

A wearable, biocompatible fluorescent cotton fabric (FCF) functionalized with nano-silver/europium aggregates and sodium alginate was developed for dual-mode detection of bacteria (*E. coli*, *S. aureus*) and heavy metals via fluorescence quenching [140]. The material demonstrates good biocompatibility in NIH3T3 cell tests and combines wearability, antibacterial properties, and rapid dual-mode detection, making it a promising platform for on-the-go sensing in environmental and health applications.

5.2. Data processing with AI/ML for signal interpretation

The integration of artificial intelligence (AI) and machine learning (ML) into biosensing platforms significantly enhances signal interpretation, enabling more accurate, rapid, and autonomous analysis of complex sensing data [141]. In smartphone-based and wearable biosensors, AI/ML algorithms process optical, electrochemical, or fluorescence data to filter noise, recognize patterns, and quantify analytes with high precision [142]. Techniques such as principal component analysis (PCA), support vector machines (SVM), and neural networks are frequently used to classify targets, deconvolute overlapping signals, and manage multiplex data from sensor arrays [143]. This data-driven approach improves detection reliability, especially in real-world matrices where environmental variability and user inconsistencies are common. Advanced optical and electrochemical biosensors produce complex datasets that demand intelligent interpretation. AI and ML enable real-time signal analysis, reduce false positives, and improve specificity by learning from large datasets [144,145]. These tools are transforming raw signals into actionable insights for environmental and food safety applications.

From 2019 to 2024, advances in nanobiosensors and AI-enabled systems have driven improvements in pathogen detection and multidrug resistance profiling [146]. These systems combine diverse modalities electrochemical, photothermal, acoustic with deep learning algorithms to enable real-time classification and therapeutic decision-making. In one study, AI was integrated with photonic biosensors to classify bacterial species based on sensor-generated wavelength data. A decision tree classifier was employed to classify bacterial species based on wavelength data generated from photonic sensor simulations [147]. Preprocessing steps included univariate analysis, kernel density estimation, box plot evaluation, feature selection, and outlier removal. The optimized model achieved a classification accuracy of 70.27%, with performance validated via a confusion matrix. These findings highlight the potential of AI-driven signal interpretation to enhance the precision and efficiency of photonic biosensing for bacterial infections.

An AI-powered biosensing framework was developed for pathogen detection in complex food and water environments. An AI-powered biosensing framework was developed for rapid and automated identification of bacteria in food and agricultural water [148]. A deep learning model was trained on augmented images of bacteriophage-tagged bacterial patterns and fine-tuned on mixed cultures. Despite being trained only on lab-cultured samples, the model achieved 80–100% accuracy when applied to real-world water samples with unseen environmental noise, enabling pathogen prediction in under 5.5 hours. This demonstrates the strong generalization capability of AI for interpreting complex biosensing data and its potential for real-time microbial water quality monitoring.

Moreover, a novel AI-assisted biosensing strategy, SMART (Sensing Method using Artificial Intelligence Transcoding), was developed for rapid and multiplex detection of viable foodborne pathogens. This method uses programmable polystyrene microspheres to visually encode different bacteria, generating distinct optical signals detectable under standard microscopy [149]. A customized computer vision algorithm, trained via machine learning, interprets these signals to accurately identify pathogen type and count. The system enables amplification-free detection below 10^2 CFU/mL and distinguishes live from dead bacteria using phage-guided targeting, offering a fast, sensitive, and specific tool for food safety monitoring.

Another study emphasized AI integration for comprehensive food quality assessment. Integrating artificial intelligence with biosensors offers a promising solution for objective, rapid, and comprehensive food quality evaluation [150]. This approach aggregates diverse food quality data and applies AI-driven models to enhance detection accuracy, minimize human error, and enable real-time monitoring. The study underscores the

transformative role of AI-assisted biosensing in food safety while discussing future opportunities and challenges for its practical implementation.

To detect ochratoxin A (OTA) in food, a four-modal MXene-based nano-biosensor system was developed using V₂C nanosheets and a fully connected artificial neural network (FCANN) trained on RGB signal data. The system uses V₂C MXene nanosheets with high surface area and peroxidase-like activity for sensitive OTA detection, achieving limits of detection as low as 6.77 pg/mL [151]. A fully connected artificial neural network (FCANN) was trained on RGB data from the biosensor's outputs, enabling on-site or remote prediction of OTA concentrations within seconds (**Figure 11**). This AI-assisted approach enhanced detection accuracy and speed, with strong agreement across sensing modes and recovery rates between 95.33% and 105.79%, demonstrating high reliability for real-sample analysis.

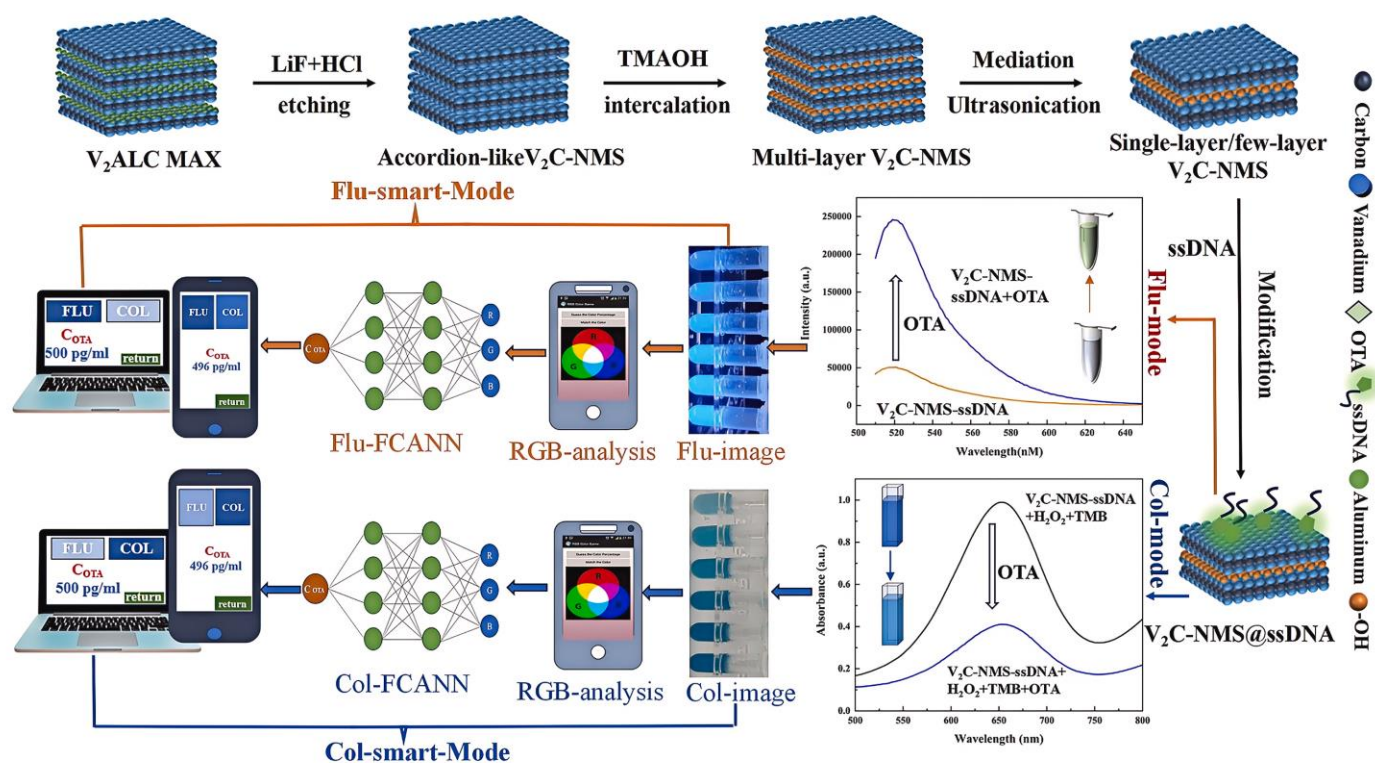


Figure 11. Fabrication strategy of a four-mode nanobiosensor utilizing V₂C-NMS enables dual-mode OTA detection via fluorescence recovery and colorimetric signal reduction upon ssDNA displacement. Signal changes were quantified and used to train a fully connected artificial neural network (FCANN) for rapid OTA concentration analysis. Copyright 2025 Elsevier [151].

Moreover, Wu et al. reported a rapid and accurate detection of multiple pathogens is vital for food safety, disease control, and environmental monitoring, yet traditional methods are limited by complexity and equipment requirements. Optical biosensors offer a promising alternative due to their portability, speed, and multiplexing capabilities. This work reviews recent progress in optical biosensing for multi-pathogen detection, covering core techniques such as colorimetry, fluorescence, SERS, and SPR [152]. It also highlights advancements enabled by microfluidics, nucleic acid amplification, and nanomaterials. While current systems show strong potential, integrating AI and machine learning for signal interpretation remains a key future direction to enhance accuracy, automation, and real-time decision-making in complex detection environments. AI and ML are also being used for nanosensor design and environmental health monitoring. ML models improve

cancer diagnostics and enable rapid, scalable data interpretation for food contaminant analysis, pathogen identification, and nanomaterial toxicity assessment [153].

6. Challenges and Opportunities

6.1. Stability, reusability, cost-effectiveness

Despite the remarkable optical performance of MOF-based biosensors, their practical utility remains hindered by challenges related to long-term stability, limited reusability, and production costs. Many MOFs are prone to structural degradation under ambient or aqueous conditions, which limits their operational lifespan, especially in complex real-world matrices. Stability remains a critical issue, particularly because many MOF-based sensors rely on delicate biorecognition elements like enzymes or antibodies, which require controlled environmental conditions to maintain functionality over time [154]. MOF-based wearable sensors face significant challenges related to stability and cost-effectiveness that hinder their broader adoption. Exposure to moisture, temperature fluctuations, and mechanical stress during wear can lead to degradation or loss of sensing performance, especially in long-term or real-world applications [155]. Additionally, achieving consistent performance across multiple uses or after prolonged storage remains difficult.

Biosensors designed for one-time use increase material waste and cost, underscoring the need for reusable platforms without compromising sensitivity. On the other hand, cost-effectiveness remains a barrier to scalability and commercialization. The synthesis of MOFs particularly those incorporating rare metals or requiring complex functionalization can be expensive and time consuming. Integrating these materials into wearable platforms with reliable, affordable fabrication methods for mass production is a major challenge [156]. To move toward practical deployment, future research must focus on developing more robust, chemically and mechanically stable MOF structures, as well as low-cost, scalable fabrication techniques without compromising sensitivity or selectivity. Achieving functional integrity, reproducibility, and affordability is essential for broad adoption in resource-constrained environments [157].

6.2. Bridging lab-scale and real-world application

While numerous MOF-based optical biosensors have demonstrated excellent sensitivity and selectivity in laboratory conditions, translating these systems to real-world applications remains a major hurdle [158]. Complex sample matrices, varying environmental conditions, and the need for minimal sample preparation often reduce sensor performance outside controlled settings. Furthermore, challenges such as sensor integration with portable devices, user-friendly interfaces, and field-deployable formats must be addressed to move from proof-of-concept to practical implementation. Bridging this gap requires interdisciplinary strategies encompassing engineering, material science, and systems-level design.

Scalability remains a significant limitation in the commercialization of MOF-based wearable sensors, particularly due to the high production costs and uncertainty around consumer acceptance. For successful market integration, products must not only be cost-effective but also user-friendly, safe, and require minimal effort to operate [159]. However, many current sensor designs still demand complex preparation steps, such as pre-use calibration and incubation in conditioning solutions, which are impractical for wearable applications. Additionally, sensor signal drift over time can lead to inaccurate analyte readings, necessitating frequent recalibration further complicating widespread use [160]. These challenges hinder scalability and adoption, though ongoing research into

calibration-free and more robust sensor designs offers promising opportunities to overcome these barriers and enable large-scale deployment.

Translating MOF-based optical biosensors from laboratory research to real-world applications presents both significant opportunities and notable challenges [161]. On one hand, the growing demand for rapid, sensitive, and user-friendly diagnostics particularly in the wake of pandemics like COVID-19 creates a favorable landscape for portable, point-of-care (POC) devices. Optical biosensors leveraging MOFs offer unique advantages, including high surface area, tunable structures, and versatile functionalization, making them well-suited for detecting pathogens with high sensitivity and specificity.

Techniques such as fluorescence sensing, surface-enhanced Raman spectroscopy (SERS), and plasmonic approaches further enhance their analytical performance. However, moving beyond proof-of-concept systems requires overcoming key challenges: ensuring sensor stability under variable environmental conditions, simplifying sample processing for non-specialist use, reducing fabrication costs, and validating performance with complex real-world samples like bodily fluids or environmental matrices. Moreover, regulatory approval, reproducibility across batches, and user acceptability remain critical hurdles. Nonetheless, with continued advances in materials science, miniaturization, and AI-assisted data interpretation, MOF-based optical biosensors hold strong potential to transition into practical tools for public health surveillance, food safety, and environmental monitoring.

6.3. Opportunities in multimodal sensing and MOF-hybrids

The future of MOF-based biosensing lies in the development of advanced platforms that integrate multiple detection modalities and functional hybrid materials. Combining optical sensing with electrochemical, magnetic, or thermal responses can enhance detection accuracy, enable cross-validation, and facilitate multiplexed analysis [162]. Moreover, hybridizing MOFs with nanomaterials such as quantum dots, plasmonic nanoparticles, or 2D materials can significantly improve signal transduction, stability, and biocompatibility. Such innovations open new avenues for real-time, point-of-care diagnostics, and environmental surveillance with enhanced robustness and adaptability [163].

The future of MOF-based biosensing lies in the development of advanced platforms that integrate multiple detection modalities and functional hybrid materials. Combining optical sensing with electrochemical, magnetic, or thermal responses can enhance detection accuracy, enable cross-validation, and facilitate multiplexed analysis [164]. Moreover, hybridizing MOFs with nanomaterials such as quantum dots, plasmonic nanoparticles, or 2D materials can significantly improve signal transduction, stability, and biocompatibility. Such innovations open new avenues for real-time, point-of-care diagnostics and environmental surveillance with enhanced robustness and adaptability.

Although this subheading focuses on hybrid sensing and multimodality, it is worth noting that one of the key future opportunities is designing MOF-based wearable sensors with improved morphology, biocompatibility, and biodegradability, particularly for in vivo health diagnostics [165]. For these sensors to function effectively on the human body particularly on sensitive areas like the skin they must exhibit not only biocompatibility, but also mechanical flexibility and chemical stability, without interfering with diagnostic results or causing harm.

Additionally, safe removal after use is essential to prevent potential side effects, especially if any component remains in the body or malfunctions during in vivo applications [166]. These requirements pose design and engineering challenges, such as ensuring durability against mechanical stress and chemical changes within biological environments. Despite these hurdles, next-generation MOF-based materials with enhanced

biocompatibility, self-degradability, or smart release mechanisms offer a future direction for developing safe, efficient, and disposable wearable biosensors tailored for real-time health monitoring.

7. Conclusion and Future perspective

Metal–organic frameworks (MOFs) have emerged as highly promising materials for the development of advanced optical biosensors, owing to their exceptional tunability, large surface areas, and versatile chemical functionalities. This review has showcased the remarkable progress in employing MOFs across various optical sensing modalities such as fluorescence, luminescence, and colorimetry for sensitive, selective, and rapid detection of pathogens and environmental contaminants. Innovations including MOF hybridization with nanomaterials, integration into microfluidic and wearable devices, and the advent of label-free and smartphone-compatible platforms underscore their potential to transform decentralized diagnostics and environmental monitoring. Despite these advances, several challenges must be addressed to facilitate real-world application. The stability of MOFs under physiological and environmental conditions, reproducibility in large-scale manufacturing, and cost-effectiveness remain significant hurdles. Additionally, regulatory frameworks and standardized validation protocols need to evolve to support the translation of these technologies from the laboratory to commercial markets. Overcoming these obstacles will be critical for broad adoption and impact.

Looking forward, the future of MOF-based optical biosensors lies in multidisciplinary efforts to enhance material robustness, biocompatibility, and functional diversity. Opportunities abound in developing multimodal sensing platforms that combine multiple optical transduction methods, enabling improved accuracy and reliability. Furthermore, coupling MOF sensors with digital technologies such as artificial intelligence and real-time data analytics offers exciting prospects for smart, autonomous monitoring systems. By addressing current limitations and leveraging emerging trends, MOF-based biosensors are poised to play a vital role in advancing global health, food safety, and environmental sustainability.

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Abbreviation:

2D	Two-Dimensional
3-O-C10-HL	N-(3-oxodecanoyl)-L-homoserine lactone
AAS	Atomic Absorption Spectroscopy
ABTS	2,2'-Azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)
ABTS ⁺	Oxidized Form of ABTS
AChE	Acetylcholinesterase
AFB1	Aflatoxin B1
AI	Artificial Intelligence
AIA	2-Aminoisonicotinic Acid
AI_Egen	Aggregation-Induced Emission Luminogen
ALP	Alkaline Phosphatase
AP	Aptamer
ATCI	Acetylthiocholine Iodide
ATP	Adenosine Triphosphate
Au NPs	Gold Nanoparticles
BSA	Bovine Serum Albumin
CD	Carbon Nanodot
cdDNA	Catalytic DNA
CFU	Colony Forming Unit
CFU/mL	Colony Forming Units per Milliliter
CMOS	Complementary Metal–Oxide–Semiconductor
COF	Covalent Organic Framework
CP	Capture Probe
Cr ⁶⁺	Hexavalent Chromium
Cu-MOF	Copper-Based Metal–Organic Framework
DNA	Deoxyribonucleic Acid
DPV	Differential Pulse Voltammetry
dsDNA	Double-Stranded Deoxyribonucleic Acid
E. coli	Escherichia coli
EC	Electrochemical
EDC–NHS	1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide–N-hydroxysuccinimide
EGFR	Epidermal Growth Factor Receptor
ELISA	Enzyme-Linked Immunosorbent Assay
Fc	Ferrocene
FcMBL	Fragment Crystallizable Mannose-Binding Lectin
FCF	Fluorescent Cotton Fabric
FLS	Fluorescein Sodium
FOS	Fiber Optic Sensor
FRET	Fluorescence Resonance Energy Transfer
GBM	Glioblastoma Multiforme
GO	Graphene Oxide
H ₃ BTC	1,3,5-Benzene Tricarboxylic Acid
HCR	Hybridization Chain Reaction

HER2	Human Epidermal Growth Factor Receptor 2
hCG	Human Chorionic Gonadotropin
HPLC	High-Performance Liquid Chromatography
HRP	Horseradish Peroxidase
ICP-MS	Inductively Coupled Plasma Mass Spectrometry
IFE	Inner Filter Effect
IoT	Internet of Things
LOD	Limit of Detection
LMCT	Ligand-to-Metal Charge Transfer
LFIA	Lateral Flow Immunoassay
LSPR	Localized Surface Plasmon Resonance
MB	Methylene Blue
miRNA	MicroRNA
MIL	Materials of Institute Lavoisier (e.g., MIL-53(Al))
ML	Machine Learning
MoS ₂	Molybdenum Disulfide
MOF	Metal–Organic Framework
MXene	Transition Metal Carbide/Nitride 2D Material (e.g., Ti ₃ C ₂)
MWCN	Multi-Walled Carbon Nanotube
N-ELISA	Nanozyme-Linked Immunosorbent Assay
NC	Nanocoral
NB	Nanobiosensor
Ni-MOF	Nickel-Based Metal–Organic Framework
NIR	Near-Infrared
NMOF	Nanoscale Metal–Organic Framework
NS	Nanosheet
OPECT	Organic Photoelectrochemical Transistor
OTA	Ochratoxin A
PCA	Principal Component Analysis
PCR	Polymerase Chain Reaction
PDMS	Polydimethylsiloxane
PEC	Photoelectrochemical
PEDOT:PSS	Poly(3,4-ethylenedioxythiophene):poly(styrenesulfonate)
PET	Photoinduced Electron Transfer
POCT	Point-of-Care Testing
PSA	Prostate-Specific Antigen
PtNP	Platinum Nanoparticle
PTS	Pregnancy Test Strip
RAA	Recombinase-Aided Amplification
RGO	Reduced Graphene Oxide
RNA	Ribonucleic Acid
Ru(bpy) ₃ ²⁺	Tris(2,2'-bipyridyl)ruthenium(II) Complex
S. aureus	Staphylococcus aureus
S. typhimurium	Salmonella typhimurium

SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SBR	Smartphone-Based Reader
SCS	Single-mode–Coreless–Single-mode (fiber)
SERS	Surface-Enhanced Raman Scattering
SGI	SYBR Green I
SMART	Sensing Method using Artificial Intelligence Transcoding
SOS	Second-Order Scattering
SPE	Screen-Printed Electrode
SPR	Surface Plasmon Resonance
SVM	Support Vector Machine
TcP	Tetraphenylporphyrin
TMB	3,3',5,5'-Tetramethylbenzidine
UFD-DEC	Urease–Fe-cdDNA Dual-Enzyme Cascade
UV-vis	Ultraviolet–Visible Spectroscopy
VOC	Volatile Organic Compound
ZIF	Zeolitic Imidazolate Framework
ZIF-8	Zeolitic Imidazolate Framework-8
Zn-MOF	Zinc-Based Metal–Organic Framework
μIDE	Micro-Interdigitated Electrode
μm	Micrometer

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