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A comprehensive review of metal-organic framework based biosensors for detection of reactive oxygen species and hydrogen peroxide in biomedical applications

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Abstract

Metal-organic frameworks (MOFs) have emerged as revolutionary materials for developing advanced biosensors, especially for detecting reactive oxygen species (ROS) and hydrogen peroxide (H_2O_2) in biomedical applications. This comprehensive review explores the current state-of-the-art in MOF-based biosensors, covering fundamental principles, design strategies, performance features, and clinical uses. MOFs offer unique benefits, including exceptional porosity (up to 10,400 m^2/g), tunable structures, biocompatibility, and natural enzyme-mimicking properties, making them ideal platforms for sensitive and selective detection of ROS and H_2O_2. Recent advances have shown significant improvements in detection capabilities, with limits as low as 0.357 nM for H_2O_2 detection using ZIF-8-based SERS sensors and picomolar sensitivity for various ROS species. The review systematically examines different MOF structures, including pure MOFs, bimetallic systems, and composite materials, emphasizing their mechanisms through electrochemical, optical, and colorimetric methods. Key biomedical applications include cancer diagnosis, cardiovascular disease monitoring, inflammatory condition assessment, and point-of-care testing. Despite notable progress, challenges such as stability under physiological conditions, biocompatibility, manufacturing reproducibility, and regulatory approval remain for clinical translation. Future directions include developing AI-integrated systems, wearable devices, and theranostic platforms that combine sensing with therapeutic functions.

Keywords: Metal-Organic Framework; Reactive Oxygen Species; Hydrogen Peroxide; Biosensors

1. Introduction

Reactive oxygen species (ROS) and hydrogen peroxide (H_2O_2) play vital dual roles in biological systems, serving as important signaling molecules in normal processes while also acting as indicators of oxidative stress in disease conditions[1]. Under healthy conditions, ROS, including H_2O_2, are produced as byproducts of cellular respiration and enzymatic reactions, participating in immune responses, regulation of cell growth, and programmed cell death. However, high levels of these species are linked to various diseases, such as cancer, diabetes, cardiovascular disorders, neurodegenerative diseases, and inflammatory conditions[2]. Detecting ROS and H_2O_2 is clinically important not only for disease diagnosis but also for monitoring treatment and assessing drug effectiveness. Cancer cells often produce 2-10 times more H_2O_2 than normal cells, making H_2O_2 detection useful for early cancer diagnosis and treatment monitoring. Likewise, cardiovascular diseases involve increased oxidative stress, with H_2O_2 levels serving as biomarkers for myocardial infarction and other heart conditions[3]. Conventional methods for detecting ROS and H_2O_2 include colorimetry, titration, chromatography, spectrophotometry, and enzyme-based assays. However, these

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techniques frequently face limitations such as low sensitivity, poor selectivity, complicated sample preparation, and long analysis times. This has spurred the development of advanced biosensor technologies aimed at providing rapid, sensitive, and selective detection methods[4].

Metal-organic frameworks represent a revolutionary class of crystalline porous materials constructed through the self-assembly of metal ions or clusters (nodes) connected by organic ligands (linkers) via coordination bonds. This unique hybrid organic-inorganic architecture endows MOFs with exceptional properties that make them ideal candidates for biosensing applications[5, 6]. The most distinctive feature of MOFs is their ultrahigh porosity, with some materials achieving surface areas exceeding 10,400 m^2/g. This exceptional porosity, combined with tunable pore sizes ranging from microporous (<2 nm) to mesoporous (2-50 nm) dimensions, enables efficient molecular recognition and mass transport. The modular nature of MOF synthesis allows for precise control over pore geometry, surface chemistry, and functionality through judicious selection of metal nodes and organic linkers[6]. Biocompatibility represents another crucial advantage of MOFs for biomedical applications. Iron-based MOFs, particularly those of the MIL series (Materials of Institute Lavoisier), have demonstrated excellent biocompatibility due to the abundance and essential nature of iron in biological systems. Similarly, zinc-based MOFs such as ZIF-8 (Zeolitic Imidazolate Framework-8) exhibit low toxicity and good stability under physiological conditions[7, 8].

Despite the rapidly expanding field of MOF-based biosensors, a comprehensive and focused evaluation of their application for the detection of ROS and H_2O_2 in biomedical environments remains limited. This review aims to bridge that gap by systematically analyzing the fundamental principles of MOF design, the mechanisms and technologies that underpin their exceptional performance in ROS and H_2O_2 detection, and the specific biomedical scenarios where these platforms offer transformative advantages. Special emphasis is placed on recent innovations in MOF architectures, including bimetallic, composite, and nanozyme systems, which have pushed the boundaries of sensitivity, selectivity, and functional integration. Unlike previous reviews that often treat MOF-based biosensing in general terms, this article provides a detailed comparative assessment of methodologies, discusses translational challenges, and highlights emerging trends such as artificial intelligence integration and wearable diagnostics. By dissecting both technological advances and practical deployment barriers, this review offers valuable perspectives for researchers and clinicians aiming to harness the unique potential of MOF-based biosensors for precision medical diagnostics and real-time oxidative stress monitoring.

2. Detection Principles and Mechanisms

2.1. Electrochemical Detection Mechanisms

Electrochemical detection represents one of the most widely employed transduction methods for MOF-based H_2O_2 and ROS biosensors due to its high sensitivity, rapid response, and compatibility with miniaturized devices. The electrochemical behavior of MOFs in biosensing applications primarily relies on the redox activity of metal centers and the electronic properties of the framework structure[9]. In direct electrochemical sensing, MOFs facilitate electron transfer between the analyte and the electrode surface without requiring additional mediators. Conductive MOFs, particularly those containing π-conjugated organic linkers or multiple metal nodes, enable efficient charge transport through the framework. Two-dimensional (2D) MOFs have shown exceptional promise in this regard, with some materials achieving conductivities exceeding 1 S cm^{-1}[10]. Many MOFs exhibit intrinsic peroxidase-like activity, functioning as artificial enzymes (nanozymes) that catalyze the reduction of H_2O_2. This enzymatic behavior is particularly pronounced in MOFs containing transition metals such as iron, copper, manganese, and cerium, which can undergo reversible redox cycling. Iron-based MOFs, especially those of the MIL series, demonstrate exceptional peroxidase activity through Fe^{3+}/Fe^{2+} redox cycling[11].

Dou et al.[12] innovatively integrated chemically modified DNAzyme probes with UiO MOFs to fabricate an electrochemical sensor capable of binary detection of H_2O_2 and hypochlorous acid (HClO)(Fig. 1A). The DNAzymes undergo cleavage upon interaction with the ROS targets, triggering the controlled release of electrochemical signal molecules (doxorubicin and methylene blue) encapsulated within the MOF matrix. This yields two distinct voltammetric peaks correlating to ROS identity and concentration. Their sensor demonstrated sub-nanomolar detection limits for both analytes in living cancer cells, offering high sensitivity and selectivity. This dual detection addresses the complexity of ROS interplay in biological systems and represents a significant advance in multifunctional electrochemical biosensing.

Jiang et al. [13] performed a thorough study on the development and application of a bimetallic Fe/Co-MIL-88(NH_2) metal-organic framework (MOF) as a superior peroxidase-mimicking nanozyme for sensitive biomedical biosensing (Fig. 1B). By employing a 1:1 ratio of Fe(III) and Co(II) ions during the solvothermal synthesis with 2-aminoterephthalic

acid as the ligand, they achieved a stable hexagonal rod-like MOF architecture, as validated by PXRD, TEM, EDS, and DLS analyses. The inclusion of cobalt notably enhanced the catalytic properties of MIL-88, producing a nanozyme with Michaelis constants (Km) for H_2O_2 and TMB that were 3–5 times lower and catalytic turnover (kcat) 5–10 times higher than natural horseradish peroxidase (HRP) and most previously reported HRP-mimicking MOFs. Kinetic studies confirmed that this bimetallic MOF's highly exposed, unsaturated Fe and Co sites provided excellent affinity and rapid signal generation for peroxidase reactions, outperforming monometallic analogues. Jiang's team further demonstrated the clinical potential of this nanozyme by coupling it with glucose oxidase (GOx) in a cascade reaction format. Here, the Fe/Co-MIL-88(NH_2) was functionalized with an anti-CD63 aptamer to specifically capture extracellular vesicles (EVs) from cell cultures or serum; these vesicles were then labeled with antibody-conjugated GOx, enabling on-bead generation of H_2O_2 from glucose, which the MOF subsequently converted together with oxidizing TMB for straightforward colorimetric readout. The resulting assay achieved a detection limit of 7.8×10^4 EV particles/mL, which is at least two orders of magnitude more sensitive than standard ELISA or nanoparticle tracking analysis.

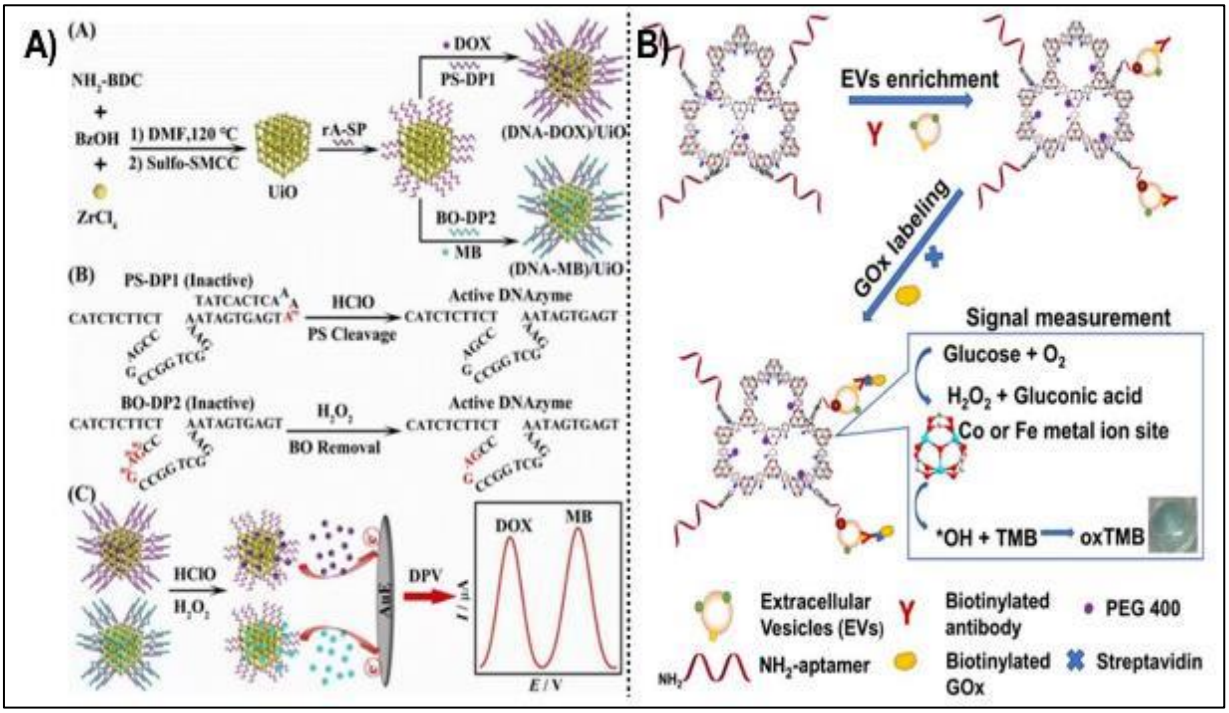

Figure 1.A) The schematic illustration showing (A) the preparation of (DNA–MB)/UiO and (DNA–DOX)/UiO, (B) the activation mechanism of DNAzyme cleavage by HClO and H2O2, and (C) the simultaneous electrochemical detection of HClO and H2O2. B) A schematic illustration of EVs enrichment and GOx labeling

Zhang et al.[14] conducted an in-depth investigation into how nanostructure engineering of the well-known copper-based MOF, HKUST-1, influences its performance as an electrochemical sensor for hydrogen peroxide (H_2O_2) detection (Fig. 2). Through a controlled room-temperature synthesis strategy, they fabricated both two-dimensional (2D) nanosheet and three-dimensional (3D) octahedral morphologies of HKUST-1. Comprehensive morphological and structural analyses using SEM, TEM, and PXRD confirmed the successful preparation of distinct geometric forms, with the 3D octahedral variant exposing a higher density of catalytically active Cu^{2+} sites on its well-developed facets. When these MOFs were drop-cast onto glassy carbon electrodes, the 3D HKUST-1-modified electrodes demonstrated markedly improved electrocatalytic activity for H_2O_2 reduction compared to their 2D counterparts, as evidenced by cyclic voltammetry (CV) and electrochemical impedance spectroscopy (EIS) results that showed lower charge-transfer resistance and higher faradaic currents. The sensor based on 3D HKUST-1 achieved an impressively wide linear detection range (2 μM to 3 mM and 3 to 25 mM) and a low detection limit of 0.68 μM for H_2O_2, outperforming many previously reported MOF-based sensors. Importantly, the platform exhibited strong anti-interference capability, excellent reproducibility, and stability in the electrochemical detection of H_2O_2 even within complex matrices such as milk samples. This practical application validated the sensor's robustness and selectivity, demonstrating its potential utility for food safety and biomedical diagnostics.

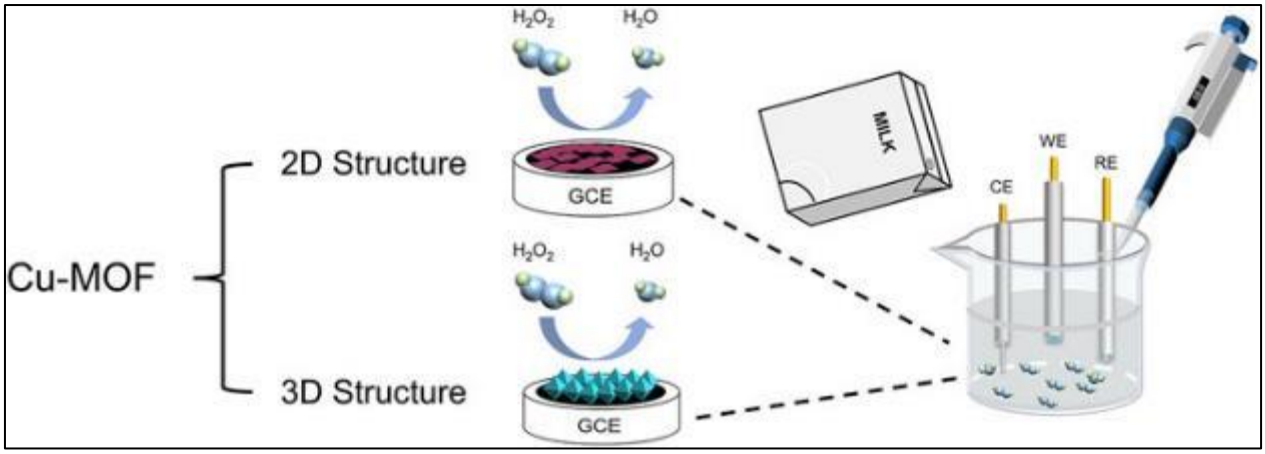

Figure 2 Schematic illustration of Cu-MOFs detecting H2O2 from the milk sample using the electrochemical method

2.2. Optical Detection Mechanisms

Optical detection methods offer advantages including non-invasive measurement, real-time monitoring capabilities, and compatibility with biological samples. MOF-based optical biosensors employ various mechanisms, including fluorescence modulation, colorimetric changes, and luminescence enhancement or quenching[15]. Fluorescence-based MOF biosensors operate through several mechanisms, including photoinduced electron transfer (PET), Förster resonance energy transfer (FRET), and inner filter effects. The inherent luminescent properties of many MOFs, particularly those containing lanthanide metals or π-conjugated organic ligands, provide excellent platforms for fluorescent sensing[16]. ZIF-8 has emerged as an exceptional fluorescence quencher, demonstrating 78.39% quenching efficiency for probe DNA molecules. The quenching mechanism involves π-π stacking interactions and electrostatic interactions between the MOF and fluorophore-labeled probes[17]. Colorimetric detection offers the advantage of visual observation without requiring sophisticated instrumentation, making it particularly suitable for point-of-care applications. MOF-based colorimetric sensors typically employ the nanozyme activity of the framework to catalyze chromogenic reactions. The most common approach involves the use of peroxidase-like MOFs to catalyze the oxidation of colorless substrates such as TMB in the presence of H_2O_2, producing blue-colored products with characteristic absorption at 652 nm[18].

Liu et al.[19] developed a ZIF-8@Au NPs hybrid SERS sensor for ultra-sensitive H_2O_2 detection (Fig. 3). The sensor utilizes the dual function of ZIF-8, serving as a nanoreactor for in situ growth of gold nanoparticles and as a selective filter to block interfering biomolecules, and enables real-time tracking of H_2O_2 released from living cells after drug stimulation. The luminescent and quenching abilities of ZIF-8 facilitated selective detection by shielding non-specific proteins, while SERS provided amplification of the detection signal. The sensor reached a low detection limit of 0.357 nM for H_2O_2 and allowed for visual differentiation of healthy versus cancerous cell behaviors.

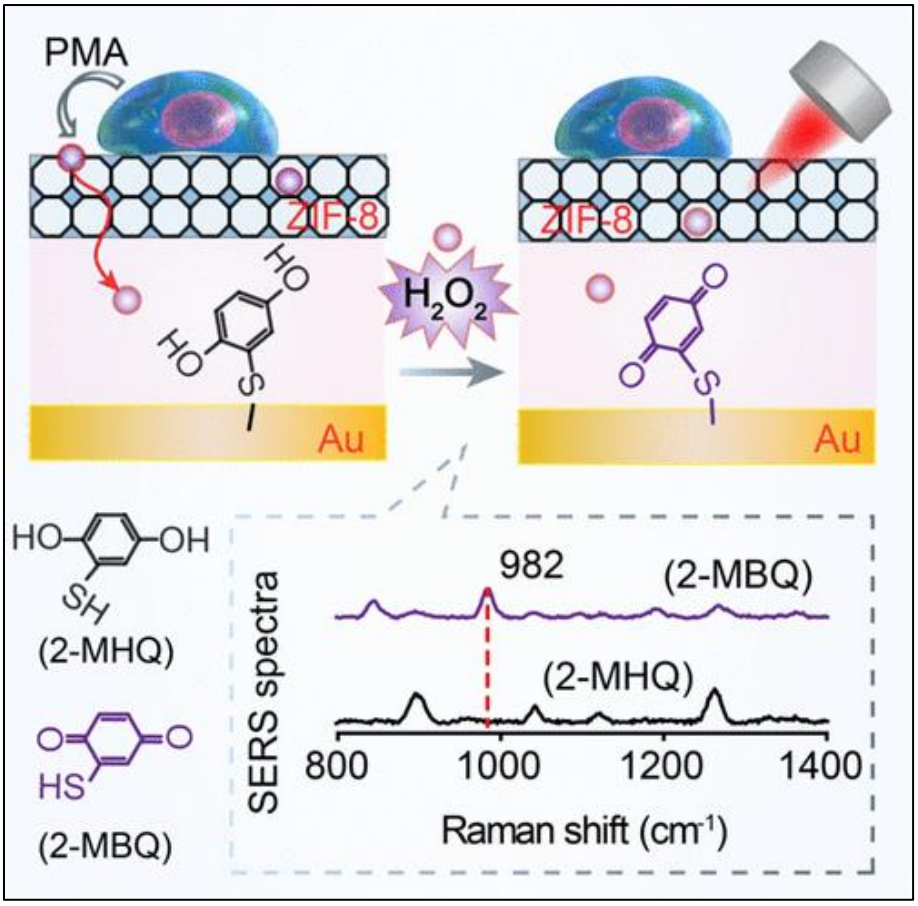

Figure 3 Schematic illustration of the "one-pot" synthesis of the ZIF-8@Au NPs SERS sensor and the detection concept for H_2O_2 released from living cells

Elgazar et al.[20] presented an innovative MOF-based biosensor that exploits the exceptional fluorescence quenching properties of ZIF-8 (Zeolitic Imidazolate Framework-8) for ultra-sensitive and selective detection of COVID-19 RNA sequences. The research highlights that ZIF-8, with its nanometer-scale porosity and large surface area, readily adsorbs FAM-labeled single-stranded DNA probes through strong π–π stacking and electrostatic interactions, resulting in up to 78.39% quenching efficiency. When the complementary COVID-19 RNA sequence is present, it hybridizes with the probe DNA, causing displacement from the ZIF-8 surface and thus restoring fluorescence, a highly specific and reversible mechanism. The biosensor demonstrated a remarkable detection limit of 6.24 pM, which is substantially lower than most previously reported nucleic acid biosensors, enabling early-stage viral detection and robust discrimination against single-base mismatches. The platform showed excellent selectivity and reliability even in complex samples such as clinical throat swab extracts, underscoring its real-world diagnostic utility. The study's (Fig. 4) provides a concise schematic diagram, visually describing the stepwise process: initial probe adsorption/quenching on ZIF-8, RNA-induced hybridization, and fluorescence "turn-on," making the workflow transparent and accessible for translation across other biosensing contexts.

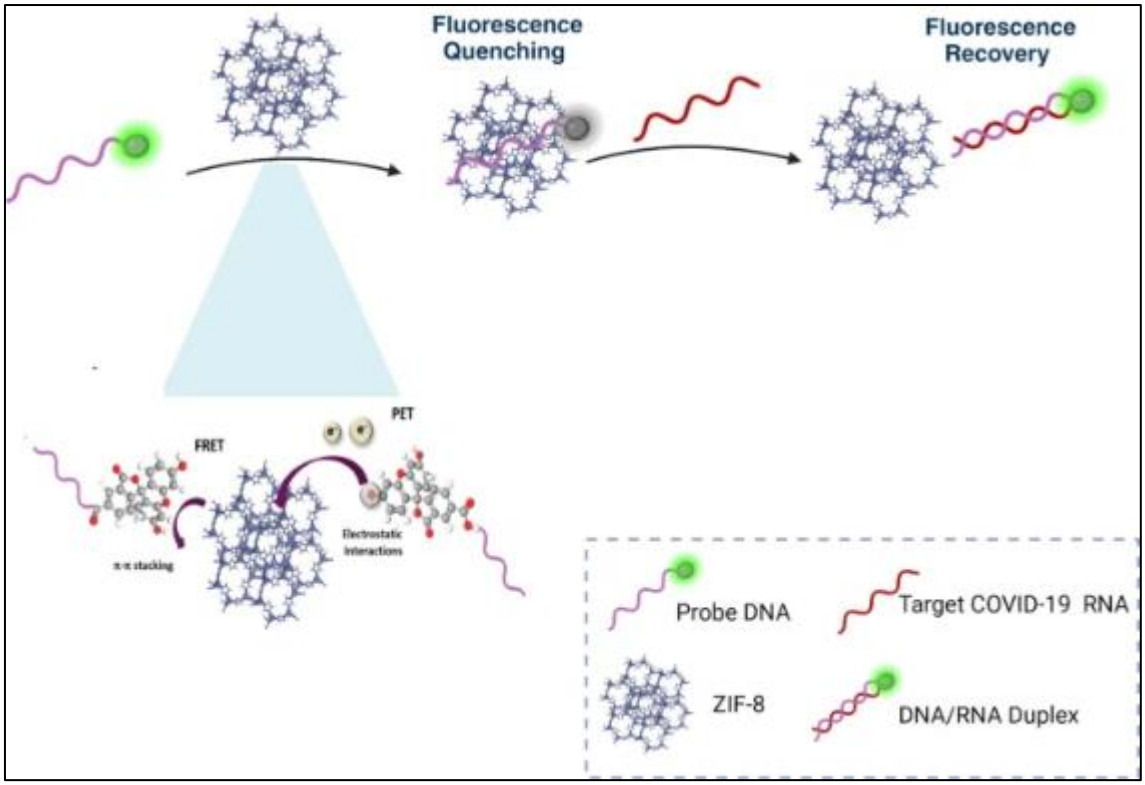

Figure 4 Detection Mechanism of ZIF-8-based Fluorescent Biosensor for the Target COVID-19 RNA

Zhou et al.[21] developed an innovative dual-mode biosensor by decorating an amino-functionalized UiO-67(Zr/Cu) metal–organic framework (MOF) with luminescent gold nanoclusters (AuNCs), enabling both colorimetric and fluorometric detection of hydrogen peroxide (H_2O_2) in biological environments. The NH_2-UiO-67(Zr/Cu) MOF features bimetallic nodes where the presence of copper not only imparts robust peroxidase-like nanozyme activity but also, in synergy with Zr, supports high structural stability and biocompatibility. The sensor's working principle leverages two complementary mechanisms: First, its peroxidase-mimicking function converts 3,3′,5,5′-tetramethylbenzidine (TMB) to a blue oxidized product upon contact with H_2O_2, yielding a strong and quantifiable colorimetric signal at 652 nm. Second, the emission intensity of the AuNCs (around 420 nm) is quenched proportionally in the presence of H_2O_2, producing a sensitive fluorescence turn-off readout. Zhou and colleagues demonstrated that these two signal outputs are both linear and highly sensitive to H_2O_2 levels, with low detection limits (down to 0.39 μM for colorimetric and even lower for fluorometric mode) and a wide dynamic range, making the system reliable for real bio-sample analyses such as serum and cell extracts. Importantly, their (Fig. 5) presents a clear schematic integrating both aspects: it visually explains how H_2O_2 exposure triggers the nanozyme-mediated TMB oxidation (bluing the solution for visual readout) while simultaneously quenching the MOF's inherent fluorescence (for spectrometric quantification).

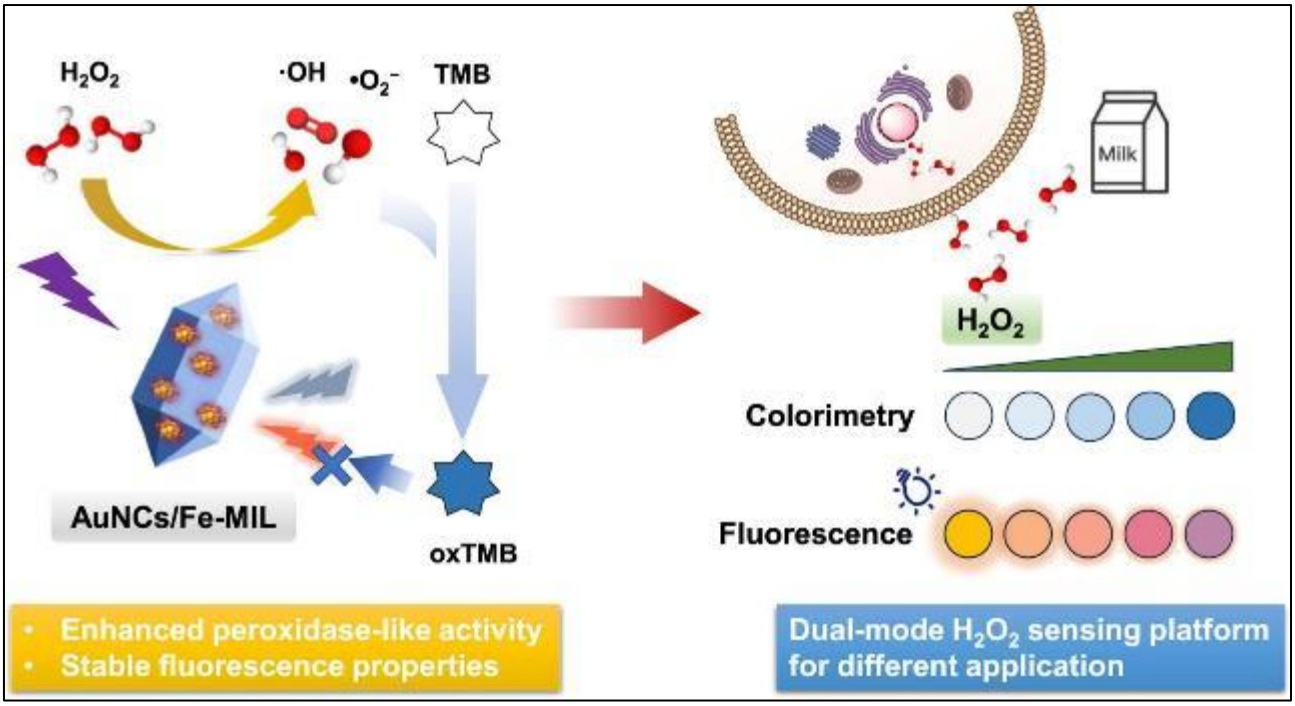

Figure 5 Schematic integrating both how H_2O_2 exposure triggers the nanozyme-mediated TMB oxidation (bluing the solution for visual readout) while simultaneously quenching the MOF's inherent fluorescence (for spectrometric quantification)

3. MOF-Based Biosensor Platforms

Metal-organic framework-based biosensor platforms represent a diverse and rapidly evolving field, with different architectural designs offering unique advantages for the detection of reactive oxygen species (ROS) and hydrogen peroxide (H_2O_2) in biomedical applications. This section provides a comprehensive overview of the major categories of MOF biosensor platforms, their synthesis methodologies, and performance characteristics.

Table 1 Classification of MOF biosensor performance

MOF Type	Detection Method	Target Analyte	Detection Limit	Linear Range	Application
ZIF-8 (SERS)	SERS	H2O2	0.357 nM	0.357 nM - 10 μM	Living cells
Cu@ZIF-8	Electrochemical	H2O2	0.46 mM	0.5-5 mM	Milk samples
UiO-66-NH2	Fluorescent	H2O2	0.002 μM	0-750 μM	Smartphone detection
MIL-53(Fe)	Colorimetric	H2O2	0.25 mM	0.25-20 mM	Glucose sensing
MIL-101(Fe/Co)	Colorimetric	H2O2	0.26 μM	1-80 μM	Tetracycline detection
PCN-222-Fe@PAA	Colorimetric	H2O2	0.06 mM	pH 4-8	Physiological pH
HKUST-1	Electrochemical	H2O2	1.2 μM	5-850 μM	Food analysis
Fe3Ni-MOF-Ar	Colorimetric	H2O2	0.15 μM	0.5-120 μM	Antioxidant capacity
Cu-MOF	Colorimetric	H2O2	5 μM	5-300 μM	Biosensing

Ag-Bi-BDC	Electrochemical	H2O2	0.0201 μM	0.01-10 μM	Cancer cells
Tb-MOF	Fluorescent	ROS	6.24 pM	0.1-1000 nM	Cell imaging
FeCo-MOF-H2	Colorimetric	H2O2	0.06 mM	0.1-10 mM	Glutathione detection
NH2-UiO-67(Zr/Cu)	Dual-mode	H2O2	0.0093 μM	0-750 μM	Point-of-care
Zr/Pr MOF	Dual-mode	miRNA	0.1 pM	0.1-100 pM	Cancer diagnosis
MOF-808@PEI	Electrochemical	H2O2	9-fold enhancement	pH 7.4	Enhanced activity

3.1. Structural Classifications and Platform Categories

3.1.1. Pristine MOF Platforms

Pristine MOFs represent the foundational biosensor platforms that rely solely on the inherent properties of the metal-organic framework structure for analyte detection. These single-component systems have demonstrated remarkable capabilities across various detection mechanisms.

Liu et al.[22] presented an innovative strategy utilizing ZIF-8 as both a nanoreactor and a molecular sieve in the fabrication of highly sensitive biosensors for hydrogen peroxide (H_2O_2) detection (Fig. 6). In their approach, ZIF-8's highly porous, crystalline framework served as a scaffold for the in situ growth of gold nanoparticles (AuNPs), resulting in a robust ZIF-8@Au hybrid. This design offered dual advantages: first, the uniform distribution of catalytically active AuNPs within the MOF's cavities significantly enhanced the sensor's signal strength by boosting the surface-enhanced Raman scattering (SERS) effect. Second, ZIF-8 functioned as a size- and charge-selective barrier, effectively shielding the embedded AuNPs from nonspecific adsorption of macromolecules, proteins, and other common interferents present in complex biological samples. Functionally, the ZIF-8@Au sensor exhibited an impressive limit of detection for H_2O_2 down to 0.357 nM, surpassing many traditional nanomaterial-based sensors. This exceptional sensitivity allowed for real-time monitoring of H_2O_2 released from living cells after drug stimulation, enabling differentiation between healthy and cancerous cells by tracking their oxidative burst signatures. Their work not only validated the protective and selective "molecular gating" effect of ZIF-8 but also demonstrated its feasibility as a multifunctional platform for SERS-based biosensing in vitro and in situ biomedical studies. The combination of sensitivity, anti-interference properties, and operational stability highlighted in this study establishes ZIF-8@Au hybrids as a powerful tool for ROS and H_2O_2 biosensing across biomedical diagnostics and cell biology research.

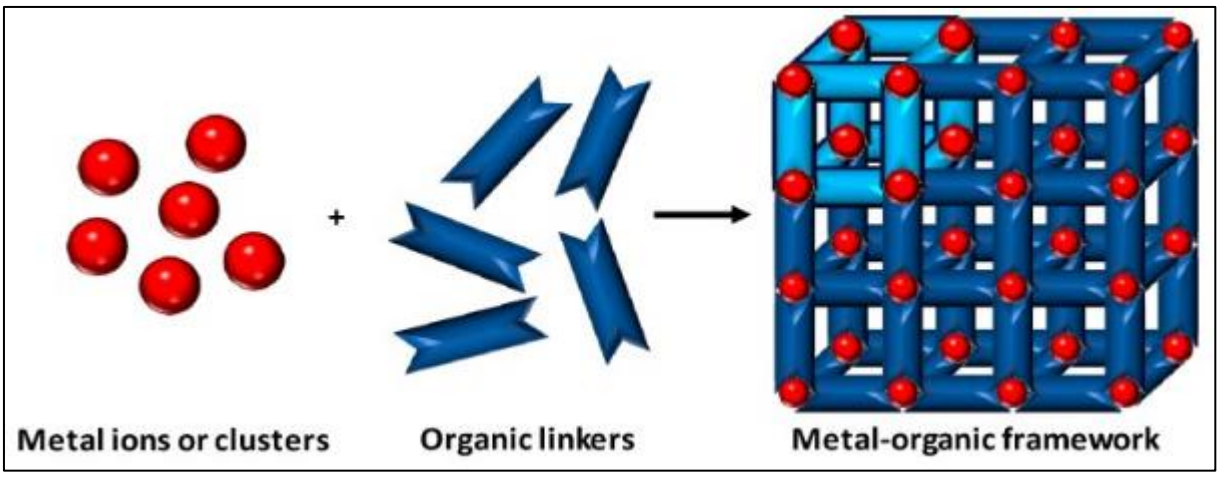

Figure 6 Scheme for the preparation of MOF

Peng et al.[23] conducted a systematic investigation into the synthesis, multifunctional reactivity, and biomedical application of pristine MIL-88A, an iron-based metal–organic framework prepared via a simple hydrothermal route using iron chloride and fumaric acid as precursors. The resulting MIL-88A nanoparticles exhibited well-defined rod-like morphology, high crystallinity, and abundant Fe(III) coordination sites confirmed by PXRD, TEM, and FTIR.

Functionally, the MOF showed robust peroxidase-like catalytic activity, efficiently catalyzing the oxidation of 3,3′,5,5′-tetramethylbenzidine (TMB) by hydrogen peroxide, producing a pronounced blue color for quantitative, colorimetric sensing. The detection platform displayed excellent sensitivity and operational stability for H_2O_2 in bioanalytical assays. Beyond biosensing, Peng et al. explored MIL-88A's therapeutic potential in osteoarthritis (OA): in vitro, MIL-88A treatment promoted chondrocyte survival (>80% viability at 10 μg/mL), significantly scavenged intracellular ROS, and decreased pro-inflammatory cytokine (IL-1β) expression, thus protecting cartilage cells from oxidative damage. In vivo, intra-articular injection of MIL-88A into OA-induced mice led to marked histological improvements in cartilage and subchondral bone, reduced Safranin O–fast green staining loss, and positively modulated key anabolic (Col2) and catabolic (MMP13) gene expression profiles.

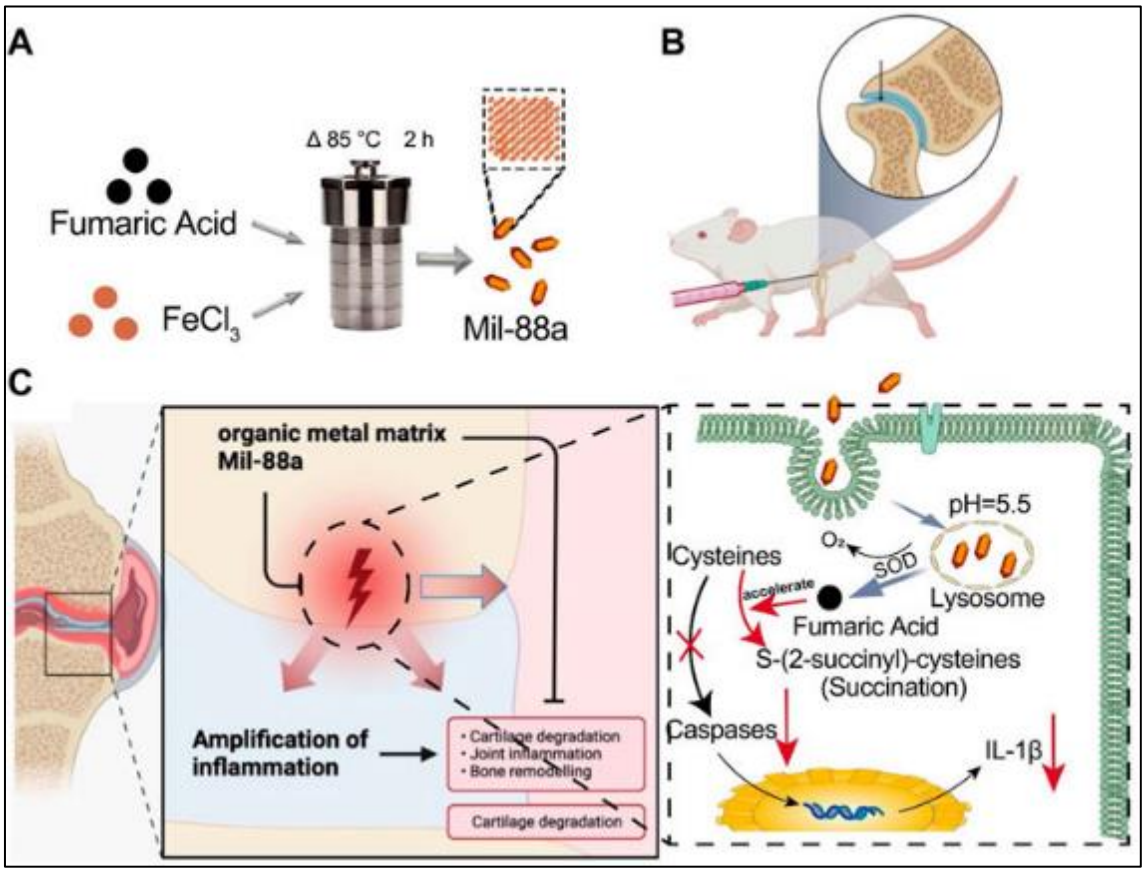

Figure 7 Schematic of how Mil-88a could improve OA in a mouse model. (A) Flow diagram of the prepared Mil-88a. (B) Illustration of the injected method of Mil-88a. (C) The treatment process for suppressing the expression of IL-1β and relief of inflammatory response

In another project, Wang et al.[24] introduced MOF-808 a zirconium-based metal–organic framework assembled from Zr_6-oxo clusters and 1,3,5-benzenetricarboxylate (BTC) linkers as a highly effective, enzyme-free peroxidase mimic for dual-mode biosensing of hydrogen peroxide (H_2O_2) in complex biological samples. The preparation of MOF-808 yielded uniform, microporous particles with a highly accessible, open structure, which, unlike traditional Zr-MOFs, provided exposed Zr_6 nodes acting as the catalytic centers. In this work, the catalytic oxidation of the chromogenic substrate TMB (3,3',5,5'-tetramethylbenzidine) in the presence of H_2O_2 led to a pronounced blue color, which was readily quantified via colorimetric analysis. Simultaneously, the product of the TMB oxidation exhibited strong fluorescence (with a characteristic emission at ~411 nm), allowing for a ratiometric fluorescence readout. Comprehensive kinetic studies confirmed that MOF-808 followed typical Michaelis–Menten catalytic behavior, with the apparent affinity and activity rivaling or exceeding those of many nanozymes and even natural horseradish peroxidase. The platform achieved remarkable analytical sensitivity, with detection limits as low as 0.12 μM (colorimetric) and 0.05 μM (fluorometric). The sensor's high selectivity was maintained in the presence of various biological interferents, and recovery studies demonstrated robust performance for H_2O_2 detection in real human serum samples. This research underscores the advantage of well-designed Zr-MOFs: their modular, open coordination environment and high chemical stability enable efficient multi-modal biosensing without the need for post-synthetic modification or bioconjugation.

3.1.2. Bimetallic MOF Systems

Bimetallic MOF systems represent a transformative development in the field of nanozyme-based biosensors, as the deliberate integration of two distinct metal ions into a single MOF framework can unlock synergistic catalytic phenomena that are unattainable with monometallic structures. The rational design of bimetallic MOFs not only capitalizes on metal synergism for superior biosensing but also provides a versatile scaffold for the development of next-generation biomedical sensors with broad applicability and enhanced performance in complex biological matrices [25].

Chen et al.[26] introduced a novel co-catalytic strategy to markedly enhance the peroxidase-like activity of MOF nanozymes, specifically for colorimetric cholesterol detection. The researchers synthesized a molybdenum-doped copper–2-methylimidazole MOF (MoCu-2MI) nanozyme, where the integration of Mo uniquely accelerated the crucial rate-limiting step in the Cu^{2+}/Cu^{+} redox cycle of the Cu–Fenton reaction. Using 3,3′,5,5′-tetramethylbenzidine (TMB) as a chromogenic substrate, they demonstrated that MoCu-2MI possessed significantly higher catalytic activity compared to undoped Cu-2MI. Detailed mechanistic studies revealed that Mo atoms acted as co-catalysts, boosting electron transfer within the system and thus facilitating faster cycling between Cu oxidation states. This, in turn, enhanced the generation of reactive oxygen species (ROS) from H_2O_2, fundamentally elevating the nanozyme's enzymatic efficiency. For practical application, the authors developed a biosensing platform combining MoCu-2MI with cholesterol oxidase, enabling rapid, one-step colorimetric detection of cholesterol across a broad linear range (2–140 μM) with a detection limit as low as 1.2 μM. This work not only clarifies the synergistic catalytic mechanism of Mo and Cu in MOF nanozymes but also provides a robust and generalizable framework for tailoring MOF activity via rational co-catalyst incorporation, which is highly significant for the future of biomedical sensing and diagnostics.

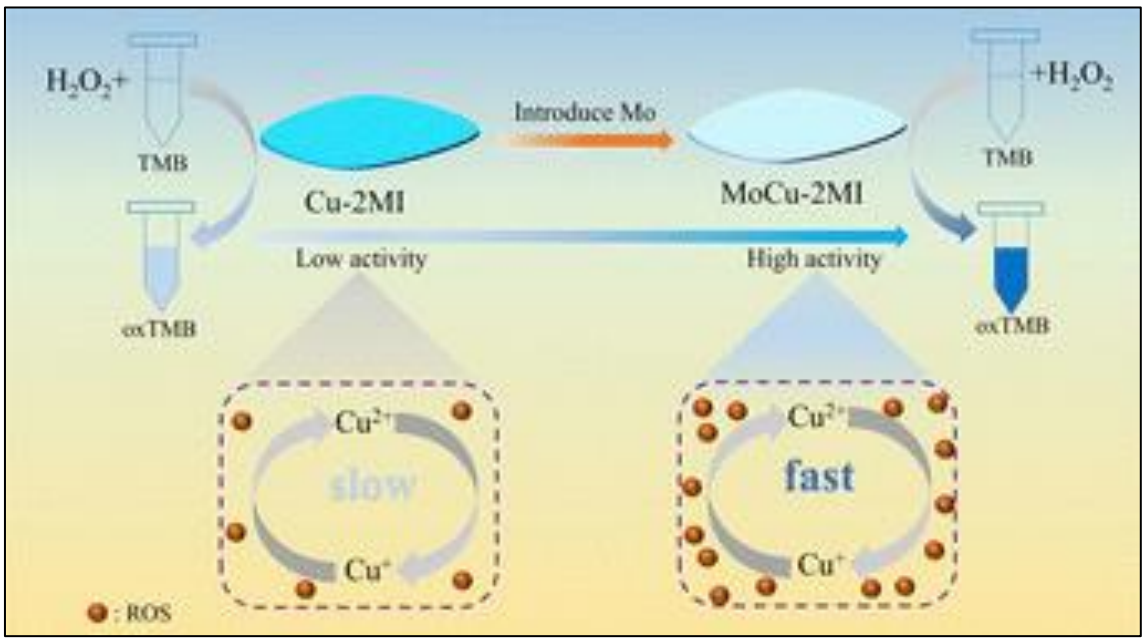

Figure 8 Schematic of the synthesis of a molybdenum-doped copper–2-methylimidazole MOF (MoCu-2MI) nanozyme

Gu et al.[27] engineered a bimetallic copper–cobalt metal–organic framework (Cu@Co-MOFs) via a hydrothermal synthesis using terephthalic acid (H_2BDC) as the bridging ligand to generate a highly efficient peroxidase-mimicking nanozyme (Fig. 9). Detailed characterization confirmed the formation of a well-defined bimetallic crystalline structure, where the synergistic interplay between Cu and Co active centers substantially enhanced peroxidase-like activity. In the presence of hydrogen peroxide, the Cu@Co-MOFs catalyzed the oxidation of 3,3′,5,5′-tetramethylbenzidine (TMB) through hydroxyl radical (- OH) generation, yielding a distinct blue color that enabled straightforward colorimetric detection. Leveraging this principle, the team developed a rapid and reliable method for detecting glutathione (GSH). When GSH was present, it inhibited the peroxidase-like reaction, resulting in a dramatic decrease in the blue color's intensity, allowing quantitative measurement. This sensor achieved a broad linear response range from 1 to 1,200 μM and a low detection limit of 0.72 μM for GSH, with strong reproducibility, operational stability, and minimal interference from common biological species. The work stands out for demonstrating that tuning the metal composition in MOFs can dramatically boost catalytic and analytical performance, making such bimetallic frameworks attractive and practical for enzyme replacement in biomedical sensors and point-of-care diagnostics.

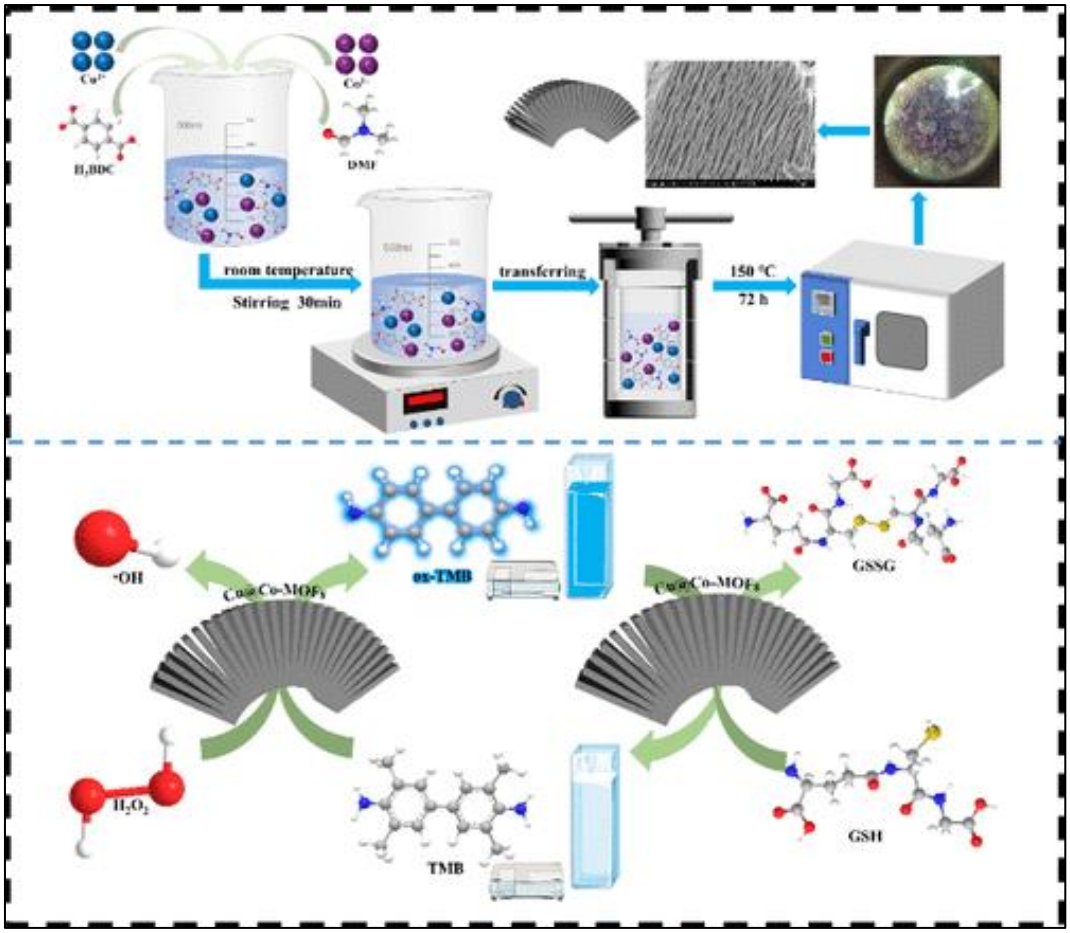

Figure 9 Schematic illustration of the synthesis of bimetallic Cu@Co-MOFs via a hydrothermal route, and their application as a peroxidase-mimicking nanozyme for the colorimetric detection of glutathione (GSH) based on TMB oxidation

In addition, Wang et al.[28] developed a hierarchical MOF composite with excellent structural integrity and tunable surface chemistry, which significantly enhanced catalytic activity compared to monometallic analogues (Fig. 10). The MOF displayed intrinsic peroxidase-like activity, efficiently catalyzing the oxidation of standard chromogenic substrates (such as TMB) in the presence of hydrogen peroxide (H_2O_2), producing a clear colorimetric response. To further improve biosensing performance for H_2O_2, the bimetallic MOF was employed as a host matrix for the immobilization of natural horseradish peroxidase (HRP) enzymes, leveraging the MOF's gentle encapsulation environment to preserve enzyme bioactivity and prevent leaching. This approach resulted in a dual-mode biosensor where the MOF nanozyme and immobilized HRP worked synergistically to amplify the detection signal. The sensor achieved high sensitivity, showing a low detection limit for H_2O_2, a broad linear response range, and robust anti-interference properties even in complex biological matrices. The work meticulously evaluated the stability, reusability, and catalytic kinetics of both the free and immobilized enzyme systems, demonstrating that the MOF platform enabled repeated, reliable measurements. Key innovations were the dual functionalization serving simultaneously as artificial and natural enzyme carrier, accompanied by detailed characterization (SEM, XRD, FTIR, and electrochemical tests) to confirm structural and functional integrity.

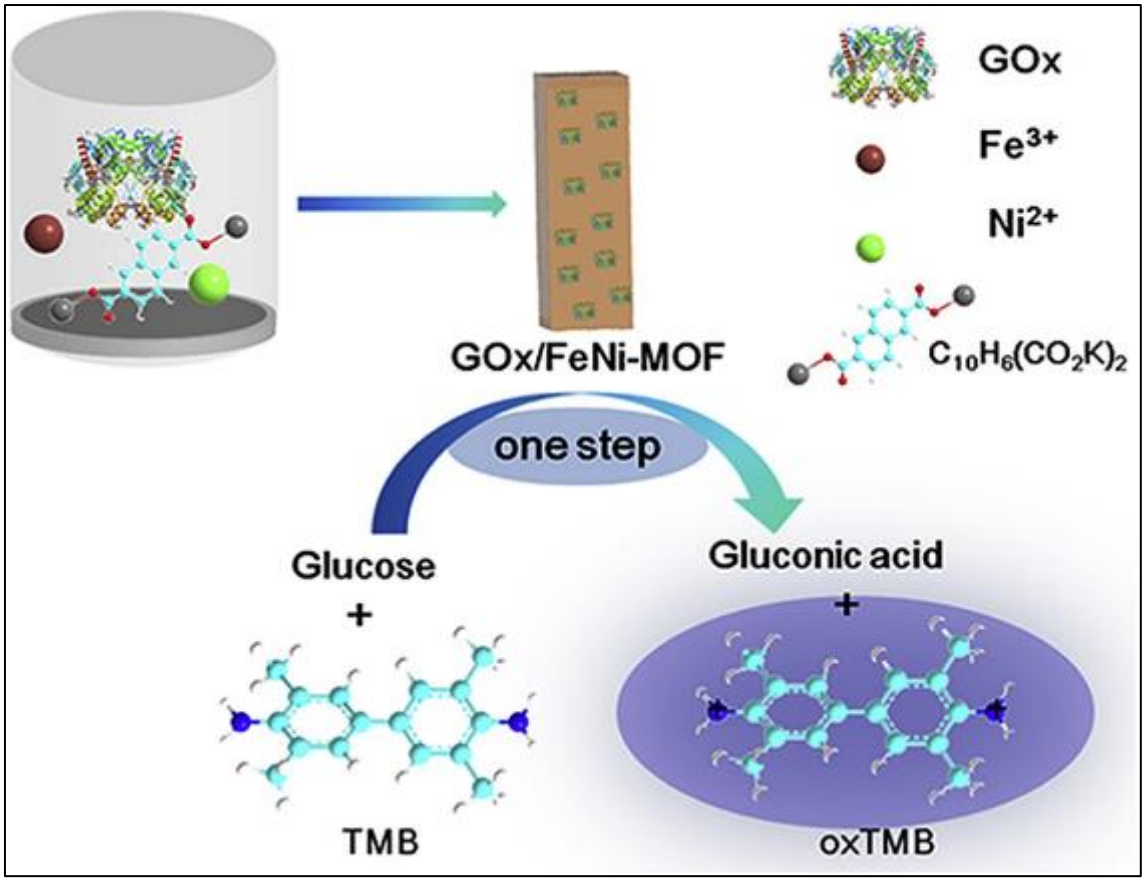

Figure 10 Schematic illustration of the bimetallic MOF synthesis and its dual role as both a peroxidase-like nanozyme and a support for horseradish peroxidase encapsulation

3.1.3. Composite MOF Systems

Composite MOF biosensors represent a significant advancement in the field by strategically integrating MOFs with additional functional materials such as carbon nanomaterials, metal nanoparticles, and conducting polymers to address the intrinsic limitations of pristine MOFs, especially their relatively low electrical conductivity and limited structural robustness in demanding environments. These hybrid structures synergistically combine the high surface area, molecular recognition capability, and tunable porosity of MOFs with the superior electron transport, mechanical flexibility, and catalytic activity of the guest materials, resulting in biosensors with markedly enhanced performance[29].

Wanqing Zhang et al.[30] provide a comprehensive review of metal–organic framework (MOF) composites in electrochemical sensors, emphasizing how integrating MOFs with carbon-based materials, metal nanoparticles, metal oxides, and biomolecules substantially overcomes the inherent limitations of pristine MOFs, particularly their low conductivity and moderate stability (Fig. 11). The review highlights the advantages of MOF/carbon composites (such as MOF/carbon nanotubes and MOF/graphene hybrids), which offer synergistic improvements in surface area, electron transfer rates, and catalytic efficiency, making them highly suitable for use in sensitive electrochemical biosensors. A key highlight is the reported Sn-MOF@CNT composite developed via solvothermal synthesis: the Sn-MOF's porous structure provides abundant active sites, while CNTs enable rapid electron transfer pathways. When used in electrochemical sensors, this composite demonstrated remarkable selectivity and sensitivity for H_2O_2 detection, with minimal interference from common analytes and robust current responses even at low concentrations, thanks to the highly interconnected hybrid network. The review also discusses other influential MOF/carbon systems for detecting drugs, neurotransmitters, and environmental toxins, demonstrating how composite design can be universally applied to various biomedical and environmental monitoring targets.

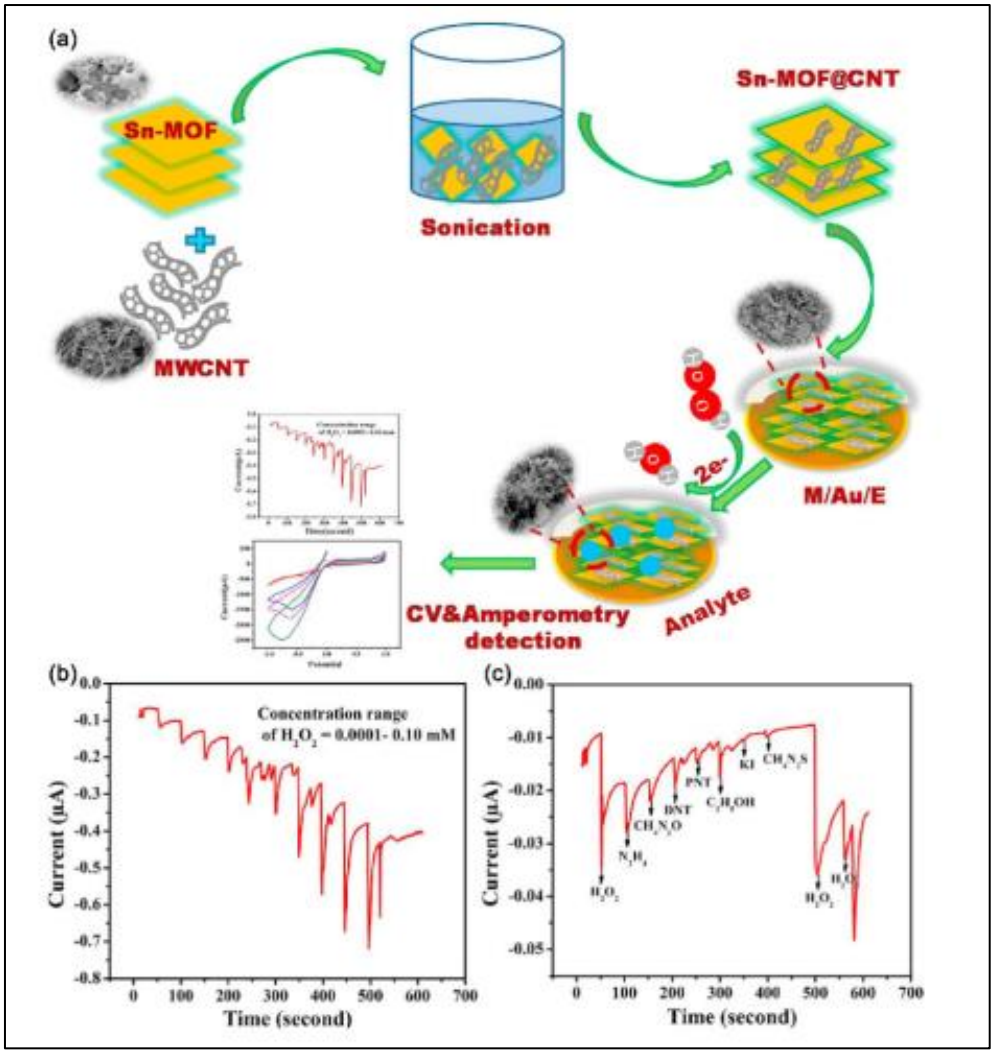

Figure 11) (a) Detection of H2O2 by the electrochemical sensor based on the Sn-MOF@CNT composite; (b) i–t curves obtained by adding H2O2 solution with different concentrations to the Sn-MOF@CNT/Au sensor every 50 s; (c) specificity of the Sn-MOF@CNT/Au sensor toward H2O2

3.2. Synthesis and Fabrication Methods

3.2.1. Conventional Synthesis Approaches

Hydrothermal and solvothermal synthesis remain the most widely employed methods for MOF preparation due to their versatility and ability to produce high-quality crystalline materials. These methods involve the reaction of metal precursors and organic linkers in solvent media under controlled temperature and pressure conditions[31].

Yari et al.[32] have presented a highly innovative approach to enhancing the biosensing capabilities of MIL-101(Fe) by employing hydrothermal synthesis to obtain highly crystalline frameworks, subsequently functionalized with silver nanoparticles (AgNPs) and amino-rich adenosine triphosphate (ATP) (Fig. 12). The MIL-101(Fe) was synthesized from iron chloride and terephthalic acid under controlled hydrothermal conditions, ensuring optimal phase purity and robust nanoporous structure characteristics confirmed by PXRD, SEM, and BET analyses. The post-synthetic integration of AgNPs provided a substantial increase in the composite's electrical conductivity and catalytic activity for electrochemical sensing, while ATP functionalization endowed the surface with abundant amino groups, enhancing biomolecule affinity, charge transfer, and electrochemical signal amplification. These structural advantages translated into outstanding biosensor performance: the composite material, used as an electrode modifier, exhibited highly sensitive and selective detection of trace-level biomolecules, such as dopamine and other small molecular targets, with a wide linear range, low detection limits, and strong resistance to biological interferents. The sensor also demonstrated good long-term operational stability and repeatability.

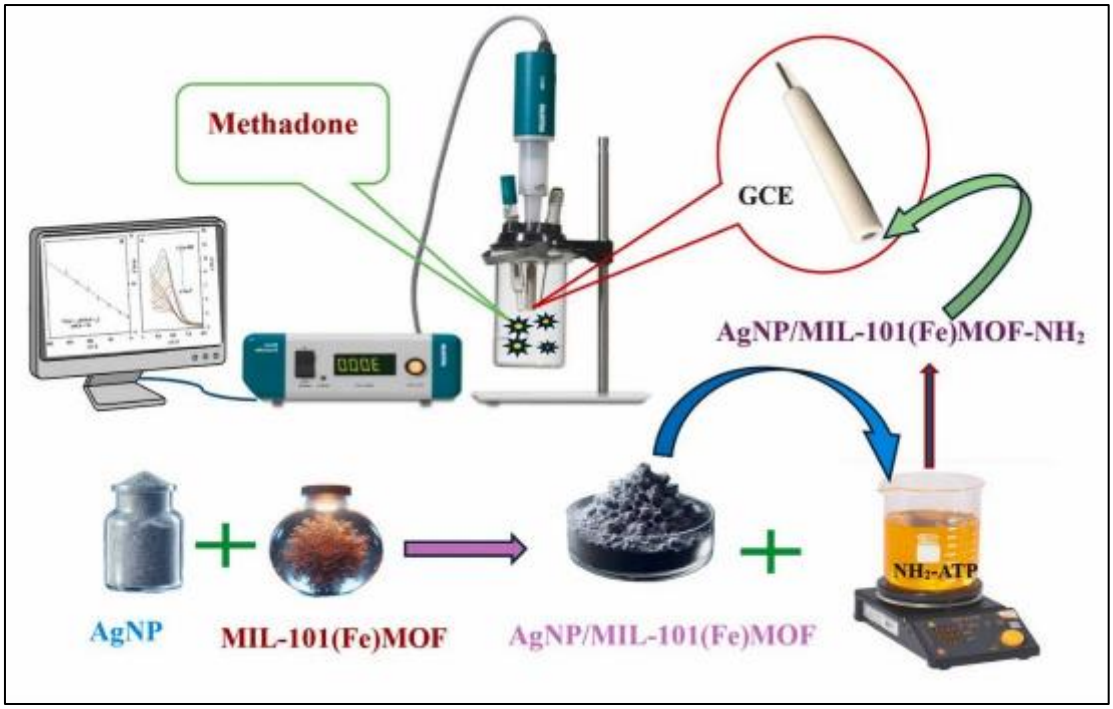

Figure 12 Schematic illustration of the hydrothermal synthesis of MIL-101(Fe), its post-synthetic functionalization with silver nanoparticles (AgNPs) for enhanced conductivity, and ATP for biomolecule affinity

Moreover, Morsey et al.[33] have presented a methodical one-pot solvothermal synthesis of MIL-88B(Fe), employing iron(III) chloride and 1,4-benzenedicarboxylic acid (H_2BDC) as starting materials, with dimethylformamide (DMF) as the solvent. By systematically varying synthesis parameters—most notably the reaction temperature (optimized at 120°C) and time (ranging from 6 to 24 hours) they achieved precise control over the morphology and crystalline quality of the resulting nanoparticle rods. X-ray diffraction (XRD) confirmed the high phase purity and crystallinity of the optimized conditions, while BET surface area analysis and electron microscopy revealed that rod-shaped MIL-88B(Fe) was produced with a substantial surface area and porosity, features crucial for analyte accessibility and high biosensor sensitivity. Functionally, these engineered MOFs exhibited strong intrinsic peroxidase-like activity: they rapidly catalyzed the oxidation of TMB (a standard chromogenic substrate) by H_2O_2, resulting in a pronounced colorimetric signal proportional to H_2O_2 concentration. The Michaelis–Menten kinetic analysis revealed a low Km and high Vmax, evidencing outstanding substrate affinity and catalytic efficiency often surpassing that of natural enzymes or conventionally prepared MOFs. The tailored MIL-88B(Fe) also demonstrated remarkable operational stability over multiple assay cycles and was resistant to interference from common biomolecules found in real sample matrices. Finally, the porous framework effectively supported further enzyme immobilization, enabling the construction of hybrid or cascade biosensors for more complex biomarker detection schemes.

3.2.2. Green and Sustainable Synthesis

Environmental awareness and biocompatibility standards have spurred the development of green synthesis techniques for MOF biosensors. Aqueous synthesis methods remove the need for toxic organic solvents, while microwave-assisted synthesis shortens reaction times and cuts energy use. Synthesis at room temperature in water has been successfully achieved for several MOF types, including biocompatible versions of ZIF-8 and UiO-66. These approaches often use natural modulators and eco-friendly solvents, resulting in materials that are more biocompatible and have a smaller environmental footprint[34, 35].

In this case, Zhang et al.[36] introduced a genuinely green and bioinspired method for synthesizing porous zirconium-based MOFs specifically, UiO-66 by utilizing natural amino acids (such as glycine and alanine) as modulators and water as the reaction solvent, thereby eliminating the need for traditional toxic amines like triethylamine or organic solvents like DMF(Fig. 13). Through systematic variation of amino acid type and concentration, they achieved precise control over crystal nucleation, growth, and defect formation, resulting in highly crystalline MOF structures with increased porosity and greater surface exposure of catalytically active Zr_6 nodes. Structural characterization with XRD, nitrogen adsorption, and TEM confirmed the maintenance of UiO-66's signature framework, while also revealing that the mild, biofriendly conditions led to improved particle uniformity and dispersion. Functionally, these "green" Zr-MOFs

displayed outstanding peroxidase-like (nanozyme) activity, effectively catalyzing the colorimetric oxidation of TMB by H_2O_2 in a highly sensitive and enzyme-free manner, delivering a rapid visual response even in the presence of potentially interfering species found in human serum and physiological fluids. Importantly, biosensing experiments established a wide linear detection range and low limit of detection for H_2O_2, with minimal background signal and excellent reusability attributes directly traced to the enhanced accessibility of active sites and greater biocompatibility conferred by the amino acid modulation. The avoidance of hazardous chemicals not only reduces environmental impact and enhances user/clinical safety but also makes scale-up and implementation for real-world diagnostics more feasible.

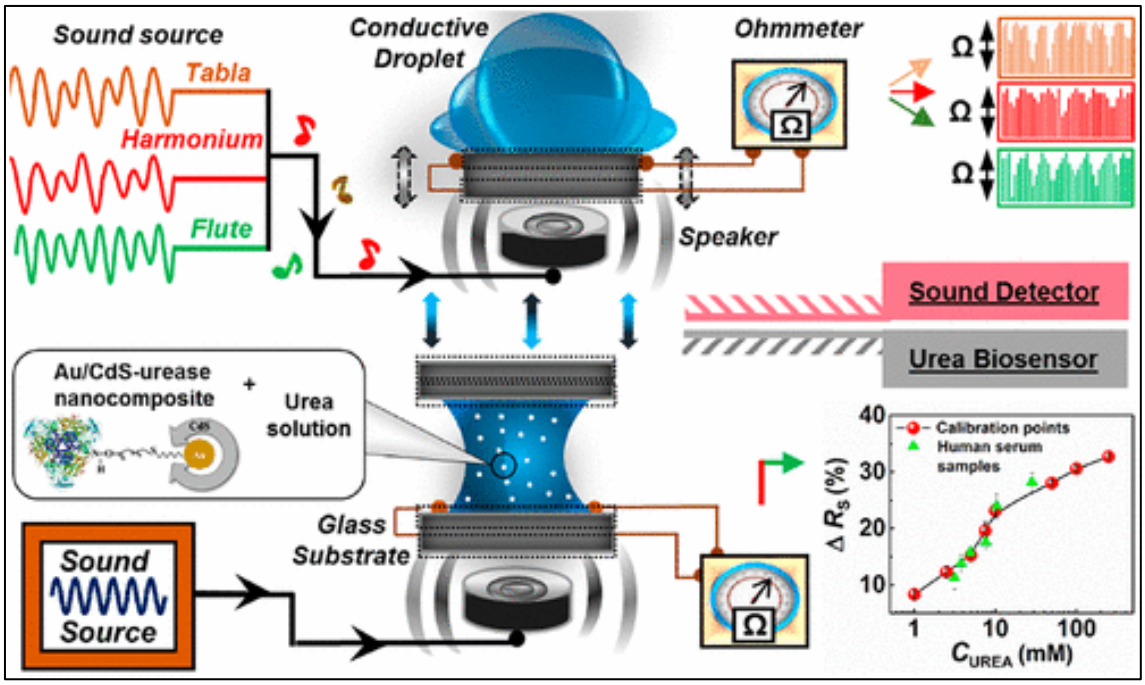

Figure 13 Schematic illustration of the bioinspired green synthesis of porous Zr-MOF (UiO-66) using natural amino acids as modulators in aqueous solution

4. Biomedical Applications

4.1. Cancer Diagnostics and Monitoring

MOF-based ROS and H_2O_2 biosensors have garnered substantial attention in cancer diagnostics and monitoring because aberrant oxidative stress particularly elevated hydrogen peroxide (H_2O_2) production is a biochemical hallmark of malignant transformation and tumor progresion[37]. Cancer cells generate approximately 2–10 times more H_2O_2 than normal cells, a consequence of both heightened metabolic flux and dysregulated redox homeostasis. This elevated intracellular H_2O_2 not only facilitates cancer cell survival, proliferation, and metastasis but also provides a unique, non-invasive biomarker that can be harnessed for early diagnosis, real-time monitoring of therapeutic response, and even prediction of drug resistance. Recent studies have shown that MOF-based biosensors are uniquely suited to exploit this differential[38].

In addition, Yang et al.[39] developed a highly sensitive and biocompatible ZIF-8-based nanozyme platform for the colorimetric quantification of hydrogen peroxide (H_2O_2) produced by live breast cancer cells a biomarker closely linked to tumor aggressiveness and oxidative metabolic remodeling (Fig. 14). The authors synthesized ultrasmall ZIF-8 nanocrystals using a facile room-temperature method, confirming their uniform rhombic dodecahedral morphology and high porosity by SEM, TEM, and BET analyses. The unique structural features provide a high density of accessible zinc active sites that grant the MOF robust peroxidase-like (nanozyme) catalytic activity. In the presence of H_2O_2, ZIF-8 catalyzes the oxidation of 3,3′,5,5′-tetramethylbenzidine (TMB) to a blue-colored product, which is quantified by absorbance at 652 nm. The method demonstrated a low detection limit of 18 nM for H_2O_2 with a wide linear dynamic range, enabling sensitive analysis both in buffer and complex biological media. Crucially, the team applied the sensor to live breast cancer cell cultures, distinguishing between metastatic (MDA-MB-231) and non-tumorigenic (MCF-10A) cells based on the differential H_2O_2 secretion rates, thus illustrating direct, label-free discrimination of cancer

phenotypes. The authors validated the cytocompatibility of ZIF-8 through cell viability assays and showed robust selectivity and reproducibility even in the presence of common interferents.

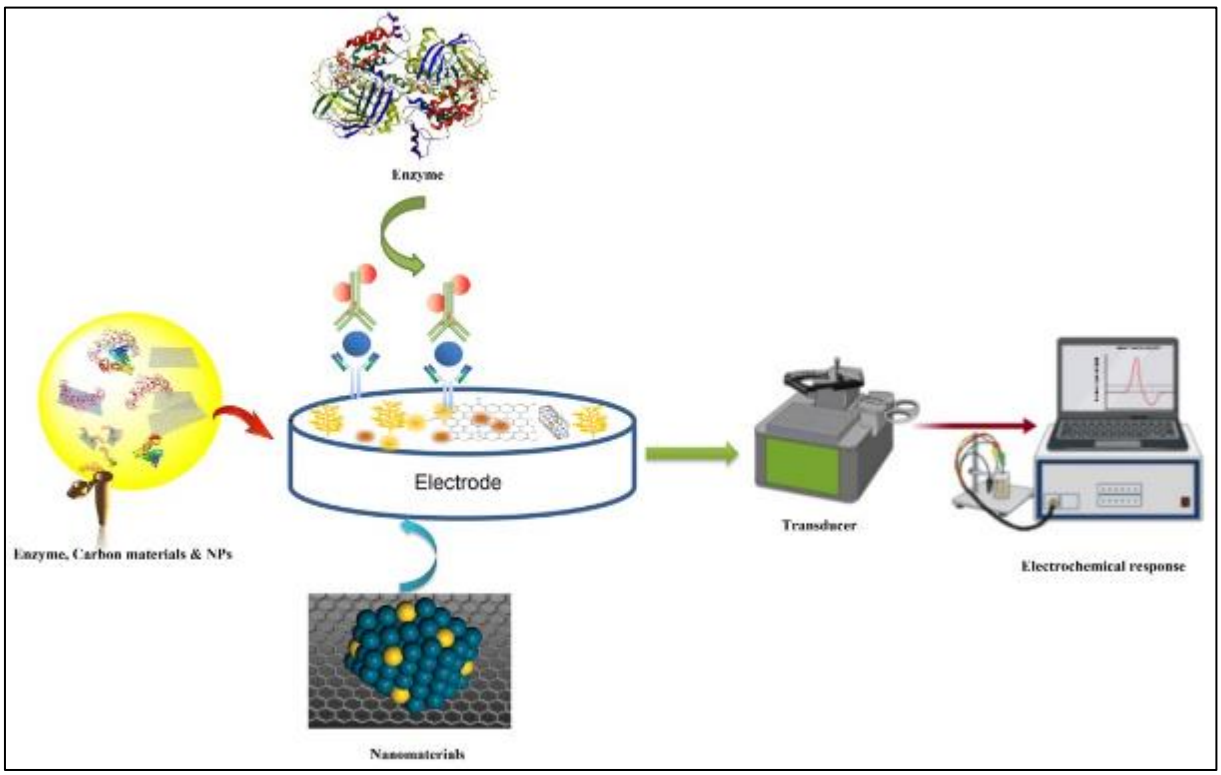

Figure 14 Schematic illustration of the ZIF-8 nanozyme-based biosensing strategy for real-time, colorimetric detection of hydrogen peroxide secreted by live breast cancer cells

In another research paper, Dong et al.[40] have fabricated a composite nanostructure integrating Fe_3O_4 nanoparticles, CaO_2 nanoparticles, and Prussian Blue into a single biomaterial (Fig. 15). This architecture enables localized and controllable production of H_2O_2 under the acidic tumor microenvironment, significantly enhancing the Fenton reaction yield of cytotoxic hydroxyl (●OH) radicals without relying on the inherently low tumor H_2O_2 levels that typically limit catalytic cancer therapies. Upon exposure to an alternating magnetic field, the Fe_3O_4 nanoparticles induce hyperthermia, which not only promotes tumor killing directly but also accelerates the catalytic Fenton process by increasing reaction rates and H_2O_2 decomposition. The platform demonstrates robust magnetic responsiveness, precise tumor targeting via magnetic guidance, high efficiency in ROS generation, and outstanding antitumor performance both in vitro and in vivo. Key factors of this reaserch include: the use of MOF composites for synergistic, multi-modal therapeutic and biosensing tasks; engineering of intelligent nanomaterials that combine endogenous substrate supply (H_2O_2 generation), catalytic site amplification (PB/Fe_3O_4), and external modulation (hyperthermia); and proof that MOF-based catalytic platforms can successfully overcome physiological bottlenecks (like low H_2O_2 in tumors) for advanced biomedical applications.

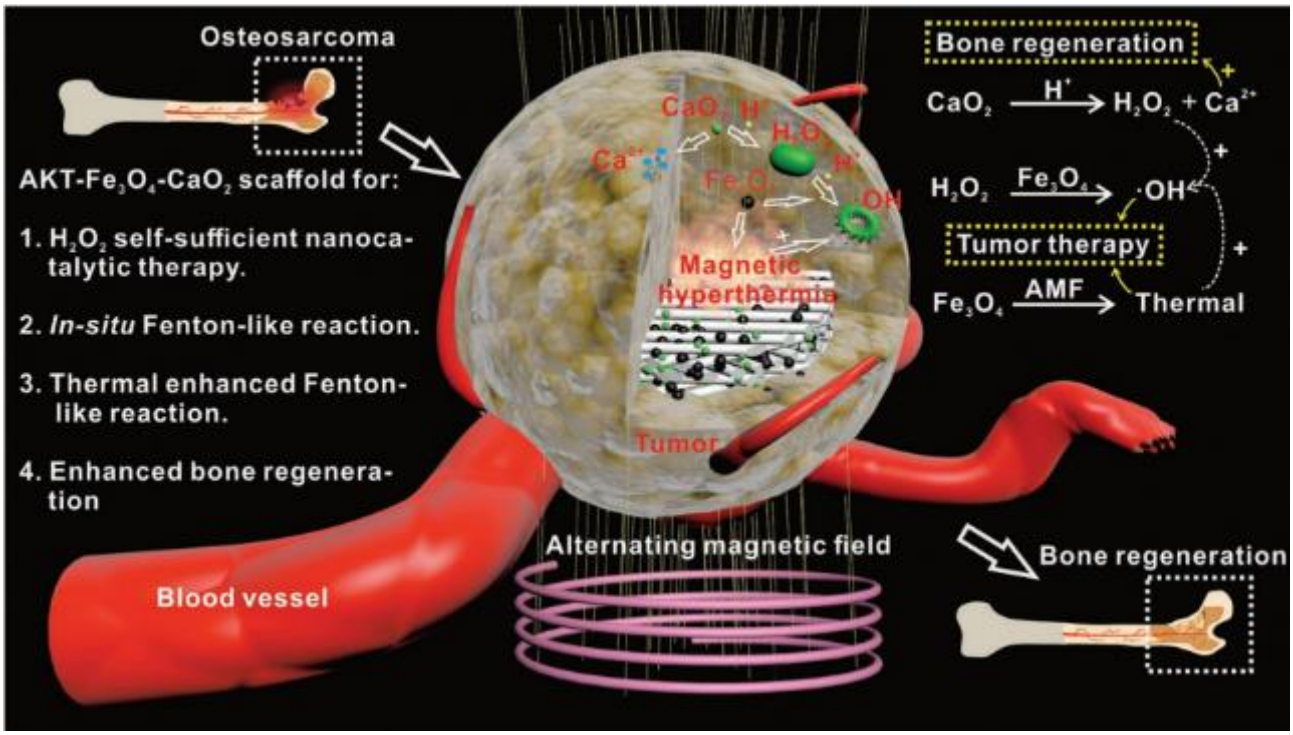

Figure 15 Schematic illustration of the cancer-therapeutic performance and bone-regeneration bioactivity of 3D-printing scaffolds coloading with Fe3O4 and CaO2 NPs (AKT-Fe3O4-CaO2)

4.2. Cardiovascular Disease Applications

Oxidative stress plays a decisive role in the onset and progression of cardiovascular diseases (CVDs). Clinically relevant concentrations of hydrogen peroxide rise sharply during myocardial infarction (MI), ischemia/reperfusion (I/R) injury, atherosclerotic plaque growth and heart-failure-related remodeling, making H_2O_2 an attractive early-stage biomarker and therapeutic target. Recent research demonstrates that metal–organic-framework (MOF) nanozymes and MOF-derived composites combine high catalytic activity with excellent biocompatibility, enabling real-time, sensitive and even wearable H_2O_2 monitoring in cardiac settings[41, 42].

For instance, Xu et al.[43] developed an innovative electrochemical biosensor utilizing a HRP/Ti_3C_2/Nafion film-modified glassy carbon electrode (GCE) for the sensitive determination of hydrogen peroxide (H_2O_2) in serum samples of patients with acute myocardial infarction (AMI)(Fig. 16). The biosensor leveraged Ti_3C_2 MXene nanosheets as carriers for horseradish peroxidase (HRP) due to their exceptional conductivity and high specific surface area, which significantly enhanced the electrochemical performance and enzyme immobilization efficiency. The biosensor demonstrated excellent analytical performance with a broad linear detection range of 5–8,000 μM and a low detection limit of 1 μM (S/N = 3), enabling quantitative H_2O_2 measurement through peak current differences. In clinical validation, the researchers tested serum samples from normal controls and AMI patients both before and after percutaneous coronary intervention (PCI), revealing statistically significant differences: H_2O_2 levels were markedly elevated in AMI patients compared to healthy controls ($P < 0.05$), and showed a significant decrease following PCI treatment ($P < 0.01$), with post-operative levels returning to values comparable to normal controls.

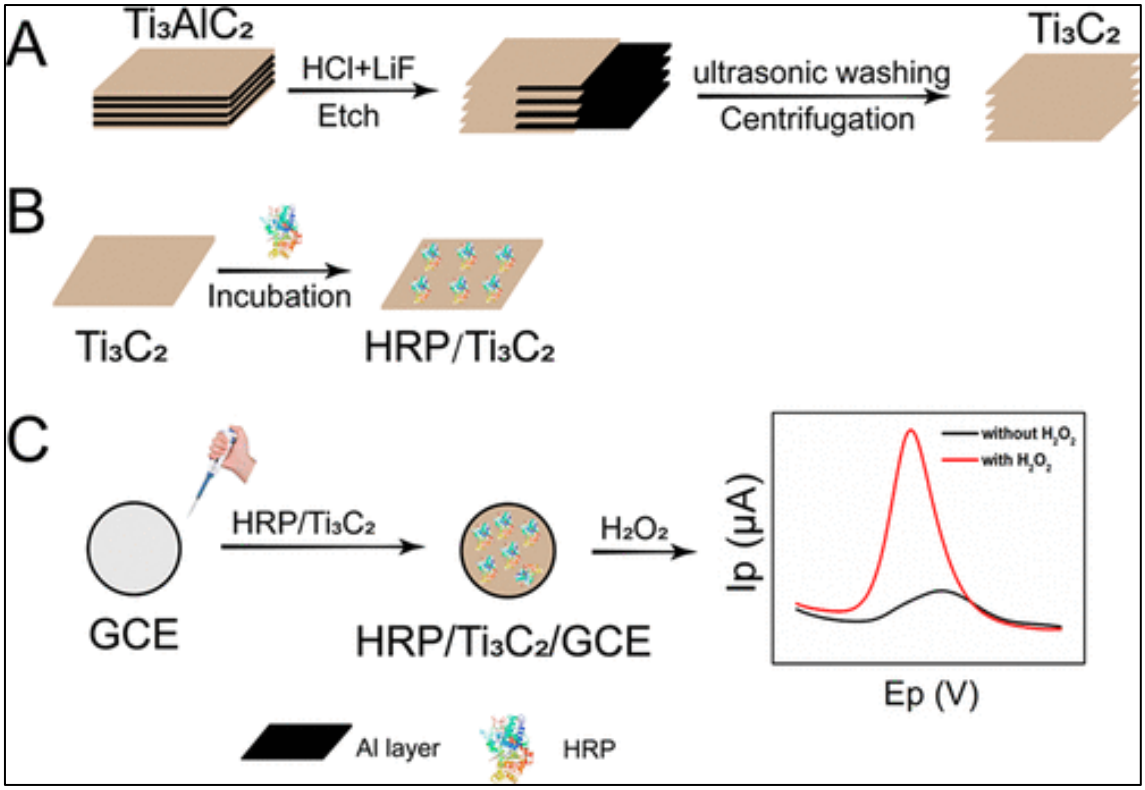

Figure 16 Schematic illustration of Construction of HRP/Ti3C2 Biosensor and the Determination of H_2O_2

Moreover, Li et al.[44] presented a groundbreaking study on the development of size-controlled MIL-53(Fe) metal–organic frameworks for dual-mode cancer therapy combining chemodynamic therapy (CDT) and chemotherapy (Fig. 17). The authors introduced an innovative synthetic approach using polyvinylpyrrolidone (PVP) as a non-ionic surfactant to precisely control the size of MIL-53(Fe) nanocrystals during hydrothermal synthesis. By systematically varying PVP concentrations (10, 50, 100, and 200 mg), they achieved remarkable size control: without PVP, large microcrystals (2.2 μm length × 0.49 μm width) were formed, while with increasing PVP amounts, crystal sizes progressively decreased to 600 nm, 380 nm, and finally 190 nm in length with corresponding widths of 140 nm, 240 nm, and 100 nm, respectively. The PVP acted as a nano-reactor controlling crystal nucleation and growth, with higher concentrations promoting more nucleation sites and smaller final particle sizes. The optimized MIL-53(Fe)-200 nanocrystals demonstrated exceptional drug-loading capacity for doxorubicin (DOX) via physisorption, achieving 45% loading efficiency, and exhibited pH-responsive drug release behavior (80.25% DOX released at pH 5.2 vs. 32.77% at pH 7.4 over 72 hours), making them ideal for targeted cancer therapy. Crucially, the iron-based MOF possessed intrinsic Fenton-like catalytic activity, converting endogenous H_2O_2 into highly cytotoxic hydroxyl radicals (- OH) for chemodynamic therapy, with significantly enhanced ROS generation at acidic tumor pH (5.2) compared to physiological pH (7.4). In vitro studies using 4T1 breast cancer cells confirmed successful cellular uptake, time-dependent DOX release, substantial ROS generation, and superior cytotoxicity of the MIL-53(Fe)-200-DOX system (44.7% cell viability) compared to individual treatments, demonstrating the synergistic effect of combined chemotherapy and chemodynamic therapy.

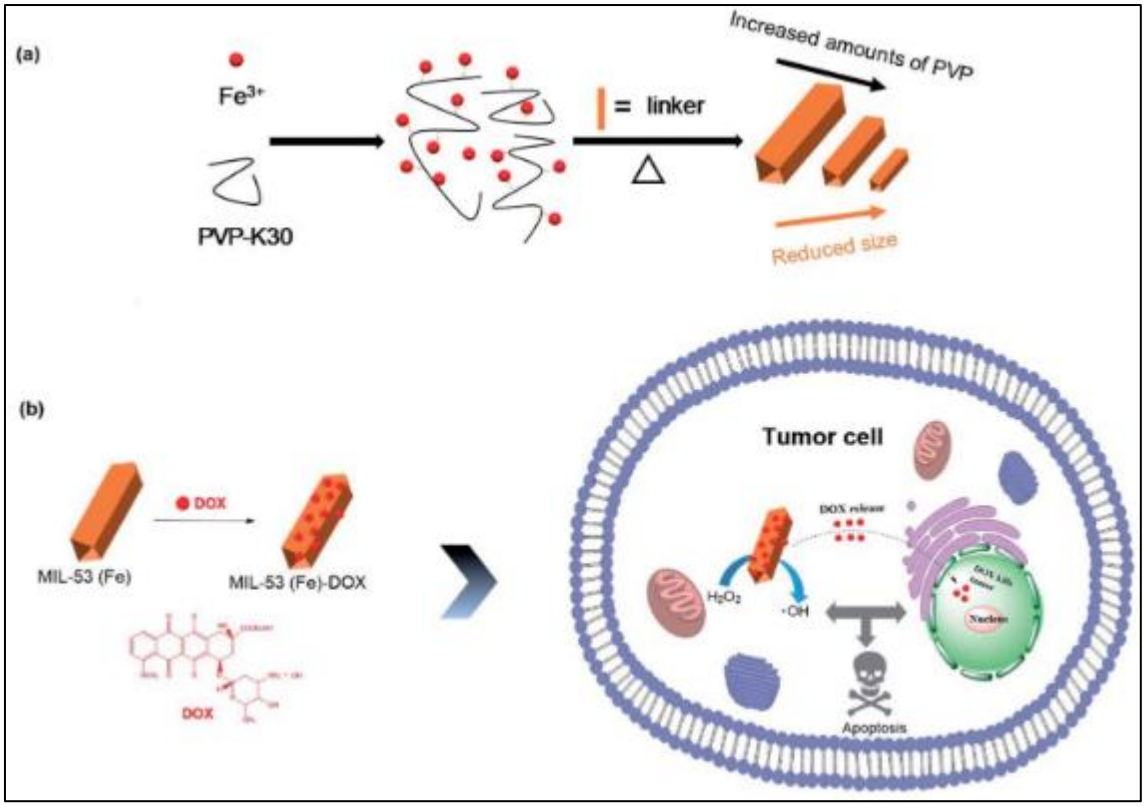

Figure 17 Schematic illustration of the size-controlled fabrication of MIL-53(Fe) and enhancing antitumor effects. (a) Preparation of MIL-53(Fe) nanocrystals. (b) Preparation of MIL-53(Fe)-200-DOX and chemodynamic therapy and chemotherapy

4.3. Inflammatory Disease Monitoring

Inflammatory conditions are characterized by increased reactive oxygen species (ROS) production and elevated hydrogen peroxide (H_2O_2) levels, making these species valuable biomarkers for disease assessment and treatment monitoring. MOF-based sensors provide sensitive tools for tracking inflammatory responses in real-time, enabling early diagnosis, therapeutic intervention monitoring, and improved patient outcomes across a broad spectrum of inflammatory diseases including rheumatoid arthritis, osteoarthritis, inflammatory bowel disease, sepsis, and chronic wound healing disorders[45]. The pathophysiology of inflammatory diseases involves complex cascades of immune responses, wherein excessive ROS generation leads to oxidative stress, tissue damage, and sustained inflammatory states[46]. Studies demonstrate that inflammatory markers such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and other cytokines directly correlate with elevated H_2O_2 levels in affected tissues and biological fluids. This relationship provides a mechanistic foundation for using MOF-based H_2O_2 sensors as reliable indicators of inflammatory disease activity and progression[47].

In this case, the ZMTP (Zn-MnTCPP-PVP) nanosheets developed by Zhang et al.[48] represent a groundbreaking advancement in 2D metal-organic framework technology for rheumatoid arthritis treatment, combining sophisticated structural engineering with dual enzymatic functionality (Fig.18). These ultrathin nanosheets (~2.34 nm thickness) are constructed through a strategic coordination reaction between the benzoyloxy groups of manganese(III) meso-tetrakis(4-carboxyphenyl)porphyrin ($MnTCPP^+$) and zinc ions, forming an ordered crystalline structure with periodically assembled active Mn^{3+} sites distributed in an AB packing pattern. The key innovation lies in the zinc atoms' dual role: they serve as catalytically inactive secondary building units ($Zn_2(COO)_4$ paddlewheel nodes) that structurally stabilize the framework while simultaneously regulating the metal-centered redox potential of the coordinated manganese porphyrin ligands by counteracting the negative charge of peripheral benzoyloxy groups, thereby elevating the redox potential and facilitating ROS-scavenging reactions. This electronic modulation enables the ZMTP nanosheets to exhibit exceptional dual nanozyme activity—mimicking both superoxide dismutase (SOD) and catalase functions with catalytic efficiency surpassing natural SOD and demonstrating substantial H_2O_2 decomposition capability, albeit lower than natural catalase. In rheumatoid arthritis pathology, the nanosheets effectively scavenge intracellular reactive oxygen species ($O_2^{\cdot-}$ and H_2O_2) in inflamed synovial tissue, promoting the critical transition of pro-inflammatory M1 macrophages toward anti-inflammatory M2 phenotype, thereby reducing inflammation-related cytokine production

(IL-6, IL-1β, TNF-α) and preventing apoptosis of bone mesenchymal stem cells (BMSCs). Additionally, the controlled release of Zn^{2+} ions from degrading nanosheets provides a secondary therapeutic benefit by upregulating alkaline phosphatase (ALP) expression in BMSCs, facilitating biomineralization and bone repair processes.

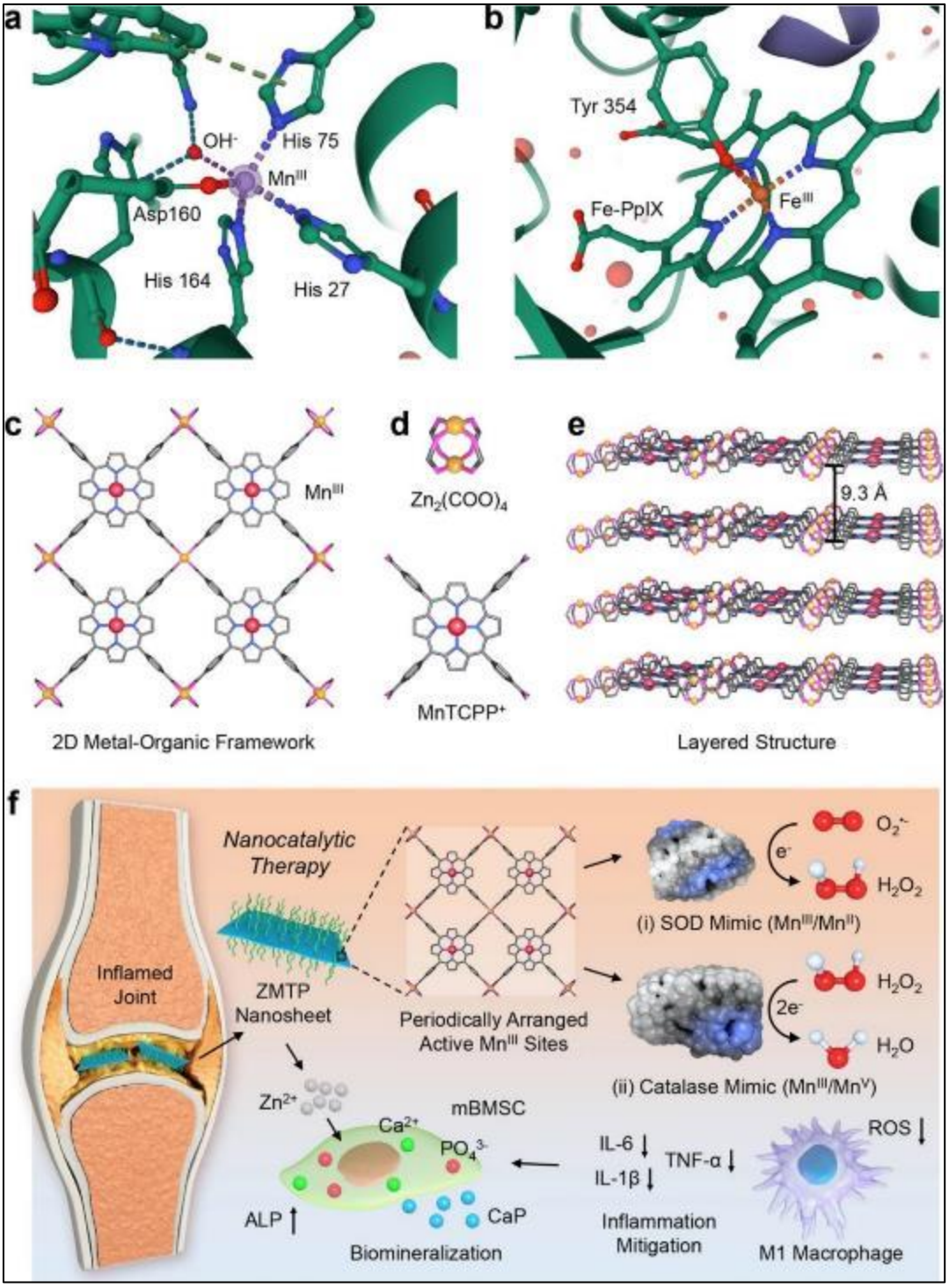

Figure 18) a Coordination geometry around the MnIII center of human mitochondrial Mn-SOD (PDB: 1N0J). **b** Coordination geometry around the FeIII center in the heme group of human erythrocyte catalase (PDB: 1DGF). **c** Chemical structure of the 2D MOF ZMTP nanosheet. **d** Building units of ZMTP nanosheets, Zn(COO)4 paddlewheel metal nodes and MnTCPP+ ligand. **e** Layered structure of ZMTP nanosheet. f Therapeutic mechanism of ZMTP nanosheet for nanocatalytic rheumatoid arthritis treatment

Furthermore, Pan et al.[49] developed an innovative multifunctional nanoplatform, Pt-MOF@Au@QDs/PDA, which represents a sophisticated combination of metal-organic framework engineering with advanced nanomedicine for rheumatoid arthritis treatment through synergistic hydrogenothermal therapy (Fig. 19). The platform consists of a zirconium-based MOF (synthesized from $ZrCl_4$ and terephthalic acid) embedded with platinum nanoparticles for H_2 catalytic generation, gold nanoparticles that provide surface plasmon resonance (SPR) enhancement, perovskite quantum dots (QDs) for fluorescence imaging and positioning, and a polydopamine (PDA) coating that enables efficient photothermal conversion. The key innovation lies in the creation of a Schottky junction between the Pt-MOF semiconductor and Au plasmonic nanoparticles, which dramatically enhances photocatalytic hydrogen production under visible light irradiation while simultaneously enabling NIR-responsive photothermal therapy through the PDA coating. The platform exploits the "ELVIS" effect (extravasation through leaky vasculature and subsequent inflammatory cell-mediated sequestration) to achieve passive targeting of inflamed synovial tissue, with fluorescence imaging confirming accumulation and retention in joint synovium sites reaching peak signals at 24 hours post-injection. Mechanistically, the generated hydrogen selectively neutralizes cytotoxic hydroxyl radicals (·OH) without affecting beneficial ROS involved in normal cellular functions, while the photothermal component (achieving 64.8% conversion efficiency) provides localized hyperthermia to eliminate proliferating synovial fibroblasts. In the collagen-induced arthritis (CIA) mouse model, the combined NIR-visible light treatment protocol demonstrated remarkable therapeutic efficacy: significant reduction in paw swelling and clinical arthritis scores, dramatic suppression of pro-inflammatory cytokines (IL-6 and TNF-α), restoration of smooth articular surfaces between cartilage and bone, and prevention of synovial hyperplasia and bone/cartilage erosion all while maintaining excellent biocompatibility with no observable organ toxicity, thus establishing the platform's potential for clinical translation in RA therapy.

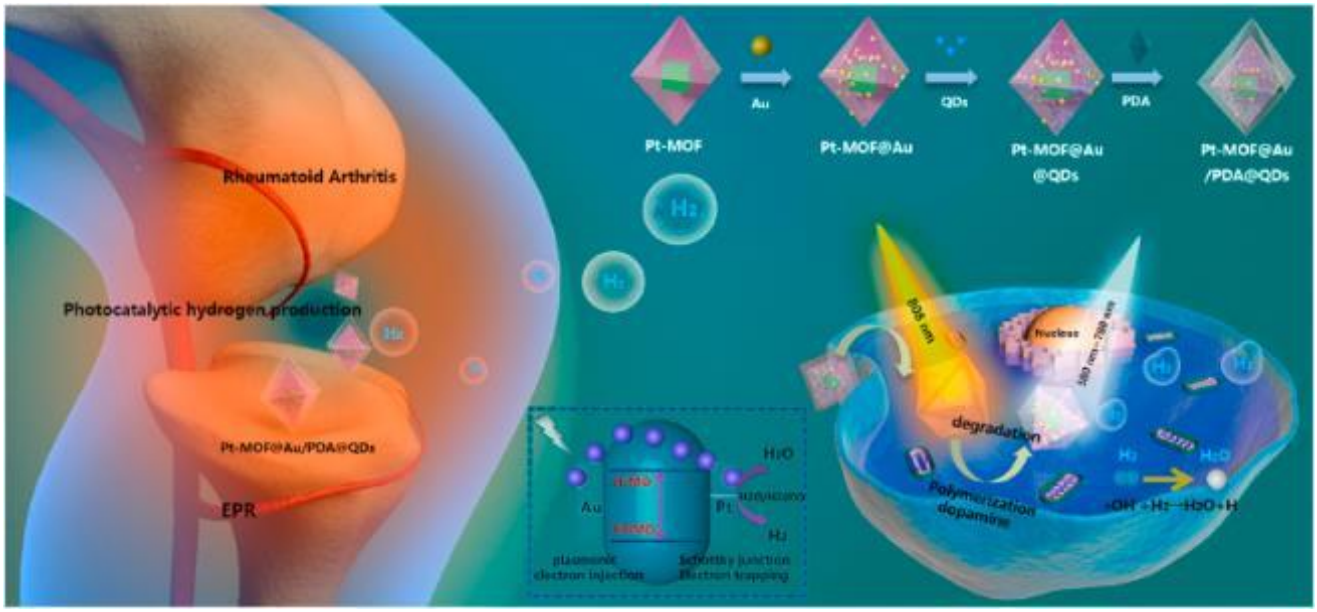

Figure 19 Schematic illustration of the synthesis route and the hydrogen-photothermal treatment therapeutic mechanism based on the Pt-MOF@Au@QDs/PDA

4.4. Point-of-Care Testing Applications

Point-of-care (PoC) diagnostics demand sensors that are disposable, inexpensive, and operable without benchtop instrumentation; MOF-based nanozyme platforms are now meeting these criteria through ingenious integration with microneedles, paper strips, and smartphone read-outs[50].

Yang et al.[11] developed a groundbreaking portable hydrogen peroxide detection system integrating a NH_2-UiO-67(Zr/Cu) nanozyme (Fig. 20) with advanced smartphone-based colorimetric analysis, representing a significant advancement in point-of-care testing for food safety and biomedical applications. The bimetallic MOF nanozyme was synthesized through a green aqueous route, combining the exceptional structural stability of zirconium-based UiO-67 framework with copper incorporation to achieve dual-mode detection capabilities—both colorimetric (LOD: 0.0057 μM) and fluorescence (LOD: 0.0020 μM)—significantly outperforming conventional detection methods. The platform's innovation lies in its comprehensive integration: the NH_2-UiO-67(Zr/Cu) nanozyme exhibits robust peroxidase-like activity, catalyzing the oxidation of TMB substrate in the presence of H_2O_2 to generate a distinct blue coloration, while the amino-functionalization provides inherent fluorescence properties for dual-signal confirmation. To enable field

deployment, the researchers engineered a sophisticated 3D-printed portable device housing that precisely positions paper strips coated with the nanozyme, coupled with a custom smartphone application featuring advanced RGB color analysis algorithms capable of converting color intensity changes into quantitative H_2O_2 concentrations. The smartphone app employs machine learning-enhanced image processing to compensate for ambient lighting variations and provides real-time quantitative readouts with detection ranges spanning 0–750 μM (colorimetric) and 0–1000 μM (fluorescence), making it suitable for diverse applications from wound fluid analysis to food preservation monitoring. Crucially, the system maintains exceptional stability and reproducibility: the nanozyme-coated strips retain full activity for over one month at room temperature, the detection process requires less than 90 seconds from sample application to result display, and the platform demonstrates excellent selectivity with minimal interference from common biological and food matrix components.

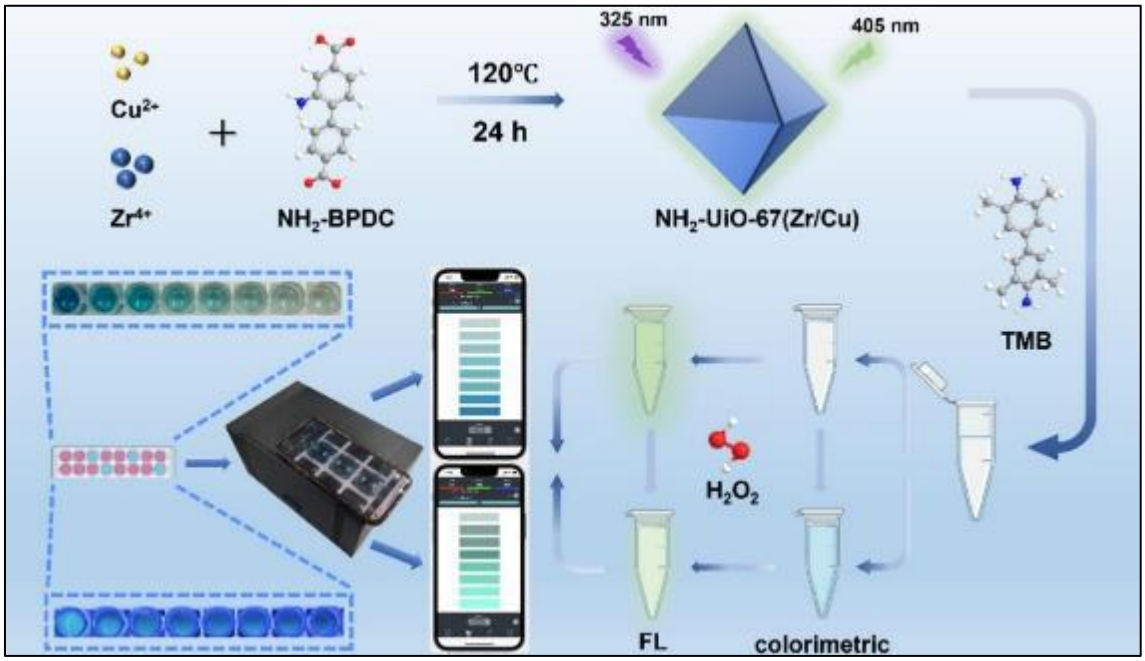

Figure 20 Schematic showing aqueous synthesis of NH_2-UiO-67(Zr/Cu) nanozyme and 3D-printed device assembly

5. Challenges and Limitations

The translation of MOF-based biosensors from laboratory research to clinical applications faces multifaceted challenges that collectively represent significant barriers to commercialization and widespread adoption in healthcare settings. Stability and degradation issues constitute the most critical impediment, as many MOFs exhibit limited structural integrity in aqueous physiological environments due to the kinetically labile nature of coordination bonds, which can be easily disrupted by endogenous proteins, biological anions, varying pH conditions, and competing ions in biological fluids, leading to framework collapse and complete loss of sensing functionality[51, 52]. While water-stable MOFs such as UiO-66 and ZIF-8 have demonstrated improved performance under physiological conditions, maintaining structural integrity for extended periods, chemical degradation through hydrolysis, oxidation of organic linkers, and ion exchange processes remains problematic in harsh biological environments containing enzymes, reducing agents, and reactive oxygen species[53, 54]. Biocompatibility and toxicity concerns present equally significant challenges, as comprehensive safety assessment reveals that MOFs containing heavy metals or potentially toxic organic linkers may exhibit cytotoxicity at concentrations required for effective sensing, with metal ion release during framework degradation causing cellular damage and inflammatory responses[55]. Although iron-based MOFs generally demonstrate superior biocompatibility due to iron's essential biological role, even biocompatible metals can cause toxicity when released in excessive amounts, while limited long-term toxicological data regarding tissue accumulation and chronic effects necessitates extensive animal model studies before human application[56, 57]. Reproducibility and quality control issues further complicate translation, as MOF synthesis sensitivity to temperature, pH, reaction time, and reagent purity parameters leads to significant batch-to-batch variability in crystal size, morphology, defect concentration, and surface properties, all directly affecting sensing performance, requiring standardized synthesis protocols, automated systems, and rigorous analytical validation across different biological matrices with comprehensive interference studies and long-term stability assessments[58]. Finally, regulatory and translation barriers encompass complex approval

processes requiring extensive preclinical testing, clinical trials, and comprehensive safety documentation, with the novel nature of MOF materials potentially demanding additional studies to establish safety profiles and appropriate regulatory pathways[59]. The integration of MOF-based devices into existing clinical workflows must be demonstrated through carefully designed clinical trials with appropriate study endpoints, patient populations, and comparison standards, while cost-effectiveness analyses and health economic evaluations become increasingly critical for gaining acceptance by healthcare systems and insurance providers, necessitating clear demonstration of value proposition compared to existing technologies. Successfully addressing these interconnected challenges requires collaborative efforts between materials scientists, biomedical engineers, regulatory experts, and clinicians to develop robust solutions that ensure both technological performance and patient safety while meeting stringent regulatory requirements for medical device approval[60].

5.1. Future Perspectives and Emerging Trends

The next wave of MOF-based biosensors will be driven by advanced architectures that marry sophisticated materials chemistry with intelligent device engineering: stimuli-responsive frameworks capable of reversible, trigger-induced pore opening or catalytic switching under pH, temperature or light control promise self-regulated, on-demand sensing in vivo; parallel efforts toward multifunctional MOFs integrate high-capacity drug reservoirs, diagnostic readouts and multimodal imaging into a single crystalline host, enabling theranostic "sense-and-treat" platforms that tailor therapy to real-time biomarker levels and provide anatomical context for disease management[61]. These material innovations dovetail with wearable and implantable technologies stretchable, textile-woven or biodegradable MOF composites that conform to skin, reside transiently in tissues or dissolve after duty cycles to deliver continuous biochemical data without burdensome retrieval surgeries, thereby supporting personalised medicine and remote monitoring[62]. At the system level, coupling dense MOF sensor arrays to artificial-intelligence engines allows machine-learning algorithms to extract diagnostic patterns from multiplexed outputs, generate real-time clinical alerts and build predictive "digital-twin" models that forecast disease trajectories and optimise therapy. Real-world impact, however, hinges on clinical-translation strategies that adopt staged, low-risk entry points (e.g., research assays or point-of-care strips) before advancing to complex implants, combined with early regulatory engagement, rigorous standardisation of MOF stability and biocompatibility tests, and partnerships with established device manufacturers to streamline scale-up and harmonise global approval pathways[8, 63].

6. Conclusion

This comprehensive review reveals that MOF-based biosensors for reactive oxygen species and hydrogen peroxide detection represent a transformative convergence of advanced materials science and precision medicine, poised to revolutionize healthcare through their unprecedented combination of exceptional porosity, tunable architectures, and intrinsic enzyme-mimicking capabilities that have achieved remarkable detection limits and picomolar sensitivity for various ROS species. The field has witnessed extraordinary progress in developing sophisticated bimetallic nanozymes like Cu@Co-MOFs with 2.8-fold enhanced peroxidase activity, multifunctional composite materials that overcome pristine framework limitations, and dual-mode platforms such as NH_2-UiO-67(Zr/Cu) achieving sub-micromolar detection across colorimetric and fluorescence modalities, collectively demonstrating successful applications in cancer diagnostics, cardiovascular monitoring, inflammatory disease assessment, and innovative point-of-care testing platforms integrated with smartphone technology and 3D-printed devices. However, the path to widespread clinical adoption requires addressing critical challenges including stability under physiological conditions, comprehensive biocompatibility validation, manufacturing reproducibility, and navigating complex regulatory frameworks barriers that demand collaborative efforts between materials scientists, biomedical engineers, clinicians, and regulatory experts to establish standardized testing protocols and appropriate approval pathways. The future of MOF-based biosensors lies in their seamless integration with emerging technologies including artificial intelligence for pattern recognition and predictive modeling, wearable electronics for continuous health monitoring, stimuli-responsive materials for dynamic sensing behaviors, and personalized medicine approaches that leverage real-time biomarker data for individualized treatment optimization. As the healthcare landscape evolves toward proactive, precision-driven care, MOF-based biosensors are uniquely positioned to enable the early detection of life-threatening diseases, facilitate continuous monitoring of chronic conditions, support personalized therapeutic interventions, and ultimately transform healthcare delivery through intelligent, responsive systems centered around individual patient needs promising a future where advanced materials science directly translates into improved patient outcomes, enhanced quality of life, and more effective medical interventions that bridge the gap between cutting-edge research and clinical reality.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] H. Abed, R. Sabouni, M. Ghommem, MOF-based spectrophotometric sensors for cholesterol detection: current trends and challenges, RSC advances 14(53) (2024) 39472-39497. DOI: 10.1039/D4RA07476A

[2] D.M. Teleanu, A.-G. Niculescu, I.I. Lungu, C.I. Radu, O. Vladâcenco, E. Roza, B. Costăchescu, A.M. Grumezescu, R.I. Teleanu, An overview of oxidative stress, neuroinflammation, and neurodegenerative diseases, International journal of molecular sciences 23(11) (2022) 5938. DOI: 10.3390/ijms23115938

[3] H.-S. Wang, Y.-H. Wang, Y. Ding, Development of biological metal–organic frameworks designed for biomedical applications: from bio-sensing/bio-imaging to disease treatment, Nanoscale advances 2(9) (2020) 3788-3797. DOI: 10.1039/D0NA00557F

[4] H. Chai, K. Yu, Y. Zhao, Z. Zhang, S. Wang, C. Huang, X. Zhang, G. Zhang, MOF-On-MOF dual enzyme-mimic nanozyme with enhanced cascade catalysis for colorimetric/chemiluminescent dual-mode aptasensing, Analytical Chemistry 95(28) (2023) 10785-10794. DOI:10.1021/acs.analchem.3c01905

[5] A. Vahdatkhah, H. Hosseinzadeh, S. Javanbakht, R. Mohammadi, Fantastic composition of metal-organic frameworks with layered double hydroxides: Insights into synthesis, applications, and synergistic effects, Chemical Engineering Journal Advances (2025) 100768. DOI: 10.1016/j.ceja.2025.100768

[6] Y. Yan, M. Ni, F. Wang, Y. Yu, X. Gong, Y. Huang, W. Tao, C. Li, F. Wang, Metal–organic framework-based biosensor for detecting hydrogen peroxide in plants through color-to-thermal signal conversion, ACS nano 16(9) (2022) 15175-15187. DOI:10.1021/acsnano.2c06481

[7] J. Yang, Y.W. Yang, Metal–organic frameworks for biomedical applications, Small 16(10) (2020) 1906846. DOI:10.1002/smll.201906846

[8] Z. Zhang, Y. Li, Z. Yuan, L. Wu, J. Ma, W. Tan, Y. Sun, G. Zhang, H. Chai, MOF nanozymes: active sites and sensing applications, Inorganic Chemistry Frontiers 12(2) (2025) 400-429. DOI:10.1039/D4QI02555E

[9] L. Gorgani, M. Mohammadi, G.N. Darzi, J.B. Raoof, Metal-organic framework (MOF)-based biosensors for miRNA detection, Talanta 273 (2024) 125854. DOI:10.1016/j.talanta.2024.125854

[10] P. Sezgin, E. Gulcay-Ozcan, M. Vuckovski, A.M. Bondžić, I. Erucar, S. Keskin, Biomedical Applications of Metal–Organic Frameworks Revisited, Industrial & Engineering Chemistry Research 64(4) (2025) 1907-1932. DOI:10.1021/acs.iecr.4c03698

[11] L. Yang, Z. Fu, J. Xie, Z. Ding, Portable sensing of hydrogen peroxide using MOF-based nanozymes, Food Research International 197 (2024) 115272. DOI:10.1016/j.foodres.2024.115272

[12] B. Dou, H. Shen, Z. Li, H. Cheng, P. Wang, A chemically modified DNAzyme-based electrochemical sensor for binary and highly sensitive detection of reactive oxygen species, Chemical Science 16(8) (2025) 3470-3478. DOI: 10.1039/D4SC05512H

[13] Q. Jiang, Y. Xiao, A.N. Hong, Z. Gao, Y. Shen, Q. Fan, P. Feng, W. Zhong, Bimetallic Metal–Organic Framework Fe/Co-MIL-88 (NH2) exhibiting high peroxidase-like activity and its application in detection of extracellular vesicles, ACS Applied Materials & Interfaces 14(37) (2022) 41800-41808. DOI:10.1021/acsami.2c12115

[14] X. Guo, C. Lin, M. Zhang, X. Duan, X. Dong, D. Sun, J. Pan, T. You, 2D/3D Copper-based metal-organic frameworks for electrochemical detection of hydrogen peroxide, Frontiers in Chemistry 9 (2021) 743637. DOI:10.3389/fchem.2021.743637

[15] S. Götz, U. Karst, Recent developments in optical detection methods for microchip separations, Analytical and Bioanalytical Chemistry 387(1) (2007) 183-192. DOI:10.1007/s00216-006-0820-8

[16] S.E. Miller, M.H. Teplensky, P.Z. Moghadam, D. Fairen-Jimenez, Metal-organic frameworks as biosensors for luminescence-based detection and imaging, Interface Focus 6(4) (2016) 20160027. DOI:10.1098/rsfs.2016.0027

[17] D. Ren, X. Wang, Y. Dai, M. Li, Y. Lu, J. Wang, Efficient fluorescence quenching and low-limit detection of HIV-1 DNA via morphology controlled ZIF-8 crystals, Journal of Luminescence 276 (2024) 120867. DOI:10.1016/j.jlumin.2024.120867

[18] A. Ko, C. Liao, based colorimetric sensors for point-of-care testing, Analytical Methods 15(35) (2023) 4377-4404. DOI:10.1039/D3AY00943B

[19] L. Jiang, C.-H. He, H.-Y. Chen, C.-Y. Xi, E.K. Fodjo, Z.-R. Zhou, R.-C. Qian, D.-W. Li, M.E. Hafez, In situ monitoring of hydrogen peroxide released from living cells using a ZIF-8-based surface-enhanced Raman scattering sensor, Analytical Chemistry 93(37) (2021) 12609-12616. DOI:10.1021/acs.analchem.1c02233

[20] A. Elgazar, R. Sabouni, M. Ghommem, A.F. Majdalawieh, Novel metal–organic framework biosensing platform for detection of COVID-19 RNA, Scientific Reports 14(1) (2024) 25437. DOI:10.1038/s41598-024-75668-8

[21] Y.-S. Li, Q.-Y. Lv, Z.-D. Ding, X. Song, J. Chen, H.-F. Cui, Luminescent gold nanoclusters loaded on iron metal–organic framework with enhanced peroxidase-like activity for the colorimetric/fluorescent determination of H2O2, Microchemical Journal 201 (2024) 110675. DOI:10.1016/j.microc.2024.110675

[22] S. Carrasco, Metal-organic frameworks for the development of biosensors: A current overview, Biosensors 8(4) (2018) 92. DOI:10.3390/bios8040092

[23] H. Hu, X. Huang, Y. Dai, K. Zhu, X. Ye, S. Meng, Q. Zhang, X. Xie, Organic metal matrix Mil-88a nano-enzyme for joint repair in the osteoarthritis mouse model, Frontiers in Bioengineering and Biotechnology 11 (2023) 1164942. DOI:10.3389/fbioe.2023.1164942

[24] Y. Hou, C. Lv, W. Liu, Y. Guo, Y. Jin, B. Li, Y. Zhang, Y. Liu, In situ synthesis of copper metal-organic framework on paper-based device for dual-mode detection of volatile sulfur compounds in exhaled breath, Sensors and Actuators B: Chemical 352 (2022) 131008. DOI:10.1016/j.snb.2021.131008

[25] M. Pietrzak, P. Ivanova, Bimetallic and multimetallic nanoparticles as nanozymes, Sensors and Actuators B: Chemical 336 (2021) 129736. DOI:10.1016/j.snb.2021.129736

[26] S. Li, L. Liang, L. Tian, J. Wu, Y. Zhu, Y. Qin, S. Zhao, F. Ye, Enhanced peroxidase-like activity of MOF nanozymes by co-catalysis for colorimetric detection of cholesterol, Journal of Materials Chemistry B 11(33) (2023) 7913-7919. DOI:10.1039/D3TB00958K

[27] Y. Gu, J. Han, N. Zhang, W. Yan, Y. Guo, H. Tan, C. Yang, F. Wang, H. Yao, Bimetallic Cu@ Co-MOFs mimic peroxidase for colorimetric detection of glutathione, ACS Applied Nano Materials 7(21) (2024) 24683-24696. DOI:10.1021/acsanm.4c04563

[28] J. Wang, M. Bao, T. Wei, Z. Wang, Z. Dai, Bimetallic metal–organic framework for enzyme immobilization by biomimetic mineralization: Constructing a mimic enzyme and simultaneously immobilizing natural enzymes, Analytica chimica acta 1098 (2020) 148-154. DOI:10.1016/j.aca.2019.11.039

[29] V.N. Palakollu, D. Chen, J.-N. Tang, L. Wang, C. Liu, Recent advancements in metal-organic frameworks composites based electrochemical (bio) sensors, Microchimica Acta 189(4) (2022) 161. DOI:10.1007/s00604-022-05238-0

[30] W. Zhang, X. Li, X. Ding, K. Hua, A. Sun, X. Hu, Z. Nie, Y. Zhang, J. Wang, R. Li, Progress and opportunities for metal–organic framework composites in electrochemical sensors, Rsc Advances 13(16) (2023) 10800-10817. DOI: 10.1039/D3RA00966A

[31] L. Ndlwana, N. Raleie, K.M. Dimpe, H.F. Ogutu, E.O. Oseghe, M.M. Motsa, T.A. Msagati, B.B. Mamba, Sustainable hydrothermal and solvothermal synthesis of advanced carbon materials in multidimensional applications: a review, Materials 14(17) (2021) 5094. DOI:10.3390/ma14175094

[32] A. Yari, P. Tabei, Innovative advancement of the MIL-101 (Fe) metal-organic framework nanocomposite and application as a sensing element of an electrochemical sensor targeting the detection and quantification of Methadone in actual samples, Journal of Alloys and Compounds Communications (2025) 100090. DOI:10.1016/j.jacomc.2025.100090

[33] M. Morsy, S.S. Hassan, H.M. Shaker, K.M. Ismail, Synthesis and characterization of MIL-88B (Fe) MOF for high-performance humidity sensing, Sensors and Actuators B: Chemical 438 (2025) 137806. DOI:10.1016/j.snb.2025.137806

[34] I. Ibadi, A. Naseri, B. Khalilzadeh, Development of an electrochemical biosensor based on MOF@ AuNPs nanocomposite for early-stage evaluation of ovarian cancer via CA125 oncomarker in human serum samples, Sensing and Bio-Sensing Research (2025) 100838. DOI:10.1016/j.sbsr.2025.100838

[35] J. Sengupta, C.M. Hussain, Early detection of cancer utilizing biosensors based on "Green Graphene": An innovative and sustainable methodology for advancing cancer diagnosis, TrAC Trends in Analytical Chemistry 167 (2023) 117254. DOI:10.1016/j.trac.2023.117254

[36] S. Thakur, M. Bhattacharjee, A.K. Dasmahapatra, D. Bandyopadhyay, Acoustic wave catalyzed urea detection utilizing a pulsatile microdroplet sensor, ACS Sustainable Chemistry & Engineering 7(14) (2019) 12069-12082. DOI:10.1021/acssuschemeng.9b01123

[37] Y. Deng, M. Guo, L. Zhou, Y. Huang, S. Srivastava, A. Kumar, J.-Q. Liu, Prospects, advances and biological applications of MOF-based platform for the treatment of lung cancer, Biomaterials Science 12(15) (2024) 3725-3744. DOI:10.1039/D4BM00488D

[38] E. Panieri, M. Santoro, ROS homeostasis and metabolism: a dangerous liason in cancer cells, Cell death & disease 7(6) (2016) e2253-e2253. DOI:10.1038/cddis.2016.105

[39] T. Ahmad, A. Iqbal, S.A. Halim, J. Uddin, A. Khan, S. El Deeb, A. Al-Harrasi, Recent advances in electrochemical sensing of hydrogen peroxide (H2O2) released from cancer cells, Nanomaterials 12(9) (2022) 1475. DOI:10.3390/nano12091475

[40] S. Dong, Y. Chen, L. Yu, K. Lin, X. Wang, Magnetic hyperthermia–synergistic H2O2 self-sufficient catalytic suppression of osteosarcoma with enhanced bone-regeneration bioactivity by 3D-printing composite scaffolds, Advanced Functional Materials 30(4) (2020) 1907071. DOI:10.1002/adfm.201907071

[41] E. Dubois-Deruy, V. Peugnet, A. Turkieh, F. Pinet, Oxidative stress in cardiovascular diseases, Antioxidants 9(9) (2020) 864. DOI:10.3390/antiox9090864

[42] A. Bigham, N. Islami, A. Khosravi, A. Zarepour, S. Iravani, A. Zarrabi, MOFs and MOF-based composites as next-generation materials for wound healing and dressings, Small 20(30) (2024) 2311903. DOI:10.1002/smll.202311903

[43] W. Xu, M. Sakran, J. Fei, X. Li, C. Weng, W. Yang, G. Zhu, W. Zhu, X. Zhou, Electrochemical biosensor based on HRP/Ti3C2/Nafion film for determination of hydrogen peroxide in serum samples of patients with acute myocardial infarction, ACS Biomaterials Science & Engineering 7(6) (2021) 2767-2773. DOI:10.1021/acsbiomaterials.1c00242

[44] A. Li, X. Yang, J. Chen, A novel route to size-controlled MIL-53 (Fe) metal–organic frameworks for combined chemodynamic therapy and chemotherapy for cancer, RSC advances 11(18) (2021) 10540-10547. DOI: 10.1039/D0RA09915E

[45] B. Mohan, R.K. Gupta, A.J. Pombeiro, P. Ren, Advanced luminescent metal–organic framework (MOF) sensors engineered for urine analysis applications, Coordination Chemistry Reviews 519 (2024) 216090. DOI:10.1016/j.ccr.2024.216090

[46] K. Djordjevic, A. Milojevic Samanovic, M. Veselinovic, V. Zivkovic, V. Mikhaylovsky, M. Mikerova, V. Reshetnikov, V. Jakovljevic, T. Nikolic Turnic, Oxidative stress mediated therapy in patients with rheumatoid arthritis: a systematic review and meta-analysis, Antioxidants 12(11) (2023) 1938. DOI:10.3390/antiox12111938

[47] C.N. Young, J.I. Koepke, L.J. Terlecky, M.S. Borkin, S.L. Boyd, S.R. Terlecky, Reactive oxygen species in tumor necrosis factor-α-activated primary human keratinocytes: implications for psoriasis and inflammatory skin disease, Journal of Investigative Dermatology 128(11) (2008) 2606-2614. DOI:10.1038/jid.2008.122

[48] B. Yang, H. Yao, J. Yang, C. Chen, J. Shi, Construction of a two-dimensional artificial antioxidase for nanocatalytic rheumatoid arthritis treatment, Nature Communications 13(1) (2022) 1988. DOI:10.1038/s41467-022-29735-1

[49] W. Pan, Z. Li, S. Qiu, C. Dai, S. Wu, X. Zheng, M. Guan, F. Gao, Octahedral Pt-MOF with Au deposition for plasmonic effect and Schottky junction enhanced hydrogenothermal therapy of rheumatoid arthritis, Materials Today Bio 13 (2022) 100214. DOI:10.1016/j.mtbio.2022.100214

[50] B. Heidt, W.F. Siqueira, K. Eersels, H. Diliën, B. van Grinsven, R.T. Fujiwara, T.J. Cleij, Point of care diagnostics in resource-limited settings: A review of the present and future of PoC in its most needed environment, Biosensors 10(10) (2020) 133. DOI:10.3390/bios10100133

[51] O. Kammona, E. Tsanaktsidou, C. Kiparissides, Recent developments in 3D-(bio) printed hydrogels as wound dressings, Gels 10(2) (2024) 147. DOI:10.3390/gels10020147

[52] T. Li, Y. Li, J. Mao, Transition metal supported UiO-67 materials and their applications in catalysis, Frontiers in Chemistry 13 (2025) 1596868. DOI:10.3389/fchem.2025.1596868

[53] J. Galvão Duarte, A.P. Piedade, B. Sarmento, F. Mascarenhas-Melo, The Printed Path to Healing: Advancing Wound Dressings through Additive Manufacturing, Advanced Healthcare Materials 14(6) (2025) 2402711. DOI:10.1002/adhm.202402711

[54] S.C. Moore, I.L. Hubble, A.L. Ritchie, J.E. Barzach, M.L. Sarazen, UiO (Zr)-based MOF catalysts for light-driven aqueous pollutant degradation, Reaction Chemistry & Engineering 9(9) (2024) 2333-2344. DOI: 10.1039/D4RE00172A

[55] G.K. Ali, K.M. Omer, Nanozyme and stimulated fluorescent Cu-based metal–organic frameworks (Cu-MOFs) functionalized with engineered aptamers as a molecular recognition element for thrombin detection in the plasma of COVID-19 patients, ACS omega 7(41) (2022) 36804-36810. DOI:10.1021/acsomega.2c05232

[56] X. Yang, C. Jin, J. Zheng, F. Chai, M. Tian, Portable intelligent paper-based sensors for rapid colorimetric and smartphone-assisted analysis of hydrogen peroxide for food, environmental and medical detection applications, Sensors and Actuators B: Chemical 394 (2023) 134417. DOI:10.1016/j.snb.2023.134417

[57] S. Wang, X. Li, X. Wang, X. Wu, D. Jiang, H. Zhou, S. Gao, J. Liu, A triple read-out visible biosensing platform based on multifunctional nanozyme and bipolar electrode for multi-mode detection and imaging of CEA, Biosensors and Bioelectronics 253 (2024) 116170. DOI:10.1016/j.bios.2024.116170

[58] S.B. Park, J.H. Shin, Open-source spring-driven syringe pump with 3D-printed components for microfluidic applications, HardwareX 19 (2024) e00550. DOI:10.1016/j.ohx.2024.e00550

[59] [59] B. Rai, J. Srivastava, P. Saxena, Challenges in translating laboratory findings to drug development, Protein Misfolding in Neurodegenerative Diseases, Elsevier2025, pp. 319-354. DOI:10.1016/B978-0-443-18716-2.00009-0

[60] A. Wang, M. Walden, R. Ettlinger, F. Kiessling, J.J. Gassensmith, T. Lammers, S. Wuttke, Q. Peña, Biomedical metal–organic framework materials: perspectives and challenges, Advanced functional materials 34(43) (2024) 2308589. DOI:10.1002/adfm.202308589

[61] E. Saygili, M. Ucuncu, N. Horzum, Colorimetric detection of hydrogen peroxide using nanozymes, Nanozymes, Elsevier2024, pp. 295-314. DOI:10.1016/B978-0-443-13788-4.00007-8

[62] S. De Vincentiis, F. Merighi, P. Blümler, J.G. De La Ossa Guerra, M. Di Caprio, M. Onorati, M. Mainardi, V. Raffa, M. Carbone, 3D-printed weight holders design and testing in mouse models of spinal cord injury, Frontiers in Drug Delivery 4 (2024) 1397056. DOI:10.3389/fddev.2024.1397056

[63] Y. Ma, Q. Yang, Smartphone Image Recognition of Dual-Emitting Electrospun Mof@[Ru (Byp) 3] 2+ Nanofibres for Effective Detection And Adsorptionof Aflatoxin B1. DOI:10.2139/ssrn.4657899.