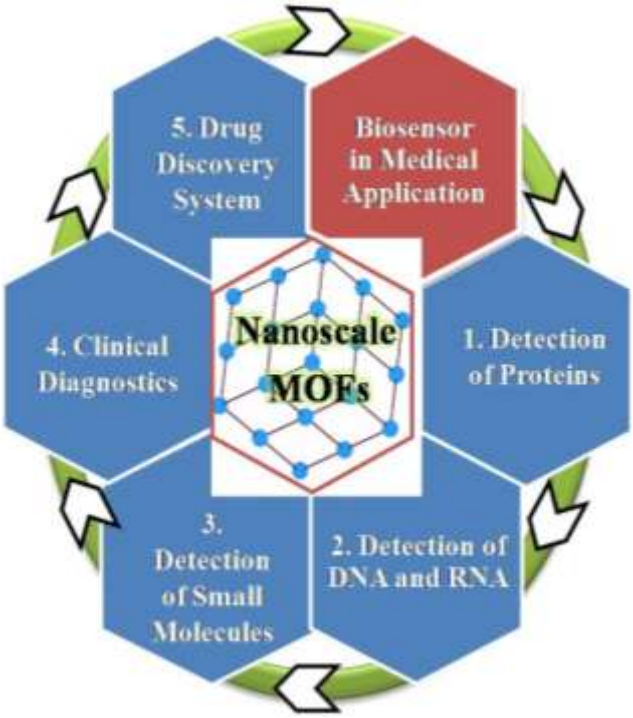
International Journal of Recent Development in Engineering and Technology
Website: www.ijrdet.com (ISSN 2347-6435(Online) Volume 14, Issue 12, December 2025)

Nanoscale MOFs as Biosensors in Medical Application

Ankita Saini[1], Monalisa Bourah[2], Sunil Kumar Saini[3]

[1]*Assistant Professor-Chemistry, Department of Applied Science and Humanities, Ganga Institute of Technology and Management, Kablana, Jhajjar, Haryana-124104, India*
[2]*Associate Professor-Chemistry, Department of Chemistry, Faculty of Physical Sciences, P.D.M. University, Bahadurgarh, Haryana-124507, India*
[3]*Assistant Professor-Zoology, Department of Zoology, School of Basic and Applied Science, Sanskaram University, Patauda, Jhajjar, Haryana-124108, India*



***Abstract*— Metal-organic frameworks (MOFs) are a class of porous materials with high surface area, tunable pore sizes, and unique structural properties, which have attracted considerable attention in biosensors. In particular, the nanoscale MOFs (n-MOFs) with their unique physicochemical properties, have shown great potential as sensing platforms for the detection of biomolecules, drugs, and disease-related molecules. We aim to highlight the recent developments in the design, synthesis, and application of n-MOFs for biomedical sensing. This review provides an overview of the synthesis and functionalization strategies used to tailor the properties of n-MOFs for specific biomedical applications. The review also discusses the different detection mechanisms employed by n-MOF-based biosensors, including fluorescence, electrochemical, and surface-enhanced Raman spectroscopy (SERS). Furthermore, we have described the diverse applications of n-MOF-based biosensors in the detection of various biomolecules, such as proteins, DNA, and small molecules, as well as their potential in clinical diagnostics and drug discovery. We will also address the current challenges and future perspectives in the field of n-MOFs as biosensors.**

***Keywords*— Nanoscale MOFs, Biosensors, Smart Materials, Biomolecules, Medical Application.**

I. INTRODUCTION

Nanotechnology has rapidly emerged as a promising field with transformative potential across various scientific disciplines. Among the fascinating applications of nanomaterials, the development of biosensors for medical purposes stands out. Nanoscale Metal-Organic Frameworks (n-MOFs) have gained considerable attention as highly versatile platforms for biosensing in medicine, amidst the wide array of nanomaterials available. MOFs are crystalline materials composed of metal ions or clusters coordinated to organic ligands, resulting in a three-dimensional porous structure. These structures possess exceptional properties, including high surface areas, tunable pore sizes, and remarkable chemical and thermal stability. Consequently, they have found utility in a diverse range of applications such as gas storage, catalysis, drug delivery, and sensing.

The unique characteristics of n-MOFs have unlocked new avenues for their application as biosensors in medical contexts. Biosensors are analytical devices that combine a biological recognition element, such as enzymes, antibodies, or nucleic acids, with a transducer element to detect and quantify specific analytes. n-MOFs offer several advantages over traditional biosensor materials, including heightened sensitivity, selectivity, stability, and biocompatibility.

International Journal of Recent Development in Engineering and Technology
Website: www.ijrdet.com (ISSN 2347-6435(Online) Volume 14, Issue 12, December 2025)

In the field of medicine, the ability to swiftly and accurately detect and monitor biomarkers, pathogens, and various disease-related analytes holds paramount importance. n-MOFs can be functionalized with specific ligands or biomolecules to create highly sensitive and specific biosensors for medical diagnostics. The substantial surface area of MOFs facilitates efficient immobilization of biomolecules, enabling interactions with target analytes and enhancing sensor performance. Furthermore, the porous nature of MOFs can be tailored to accommodate various guest molecules, enabling controlled release of drugs or therapeutic agents at precise sites within the body. This attribute not only renders n-MOFs valuable for biosensing, but also for targeted drug delivery, imaging, and therapy, thereby providing a multifunctional platform for medical applications. Moreover, n-MOFs can be integrated with different transduction methods, such as optical, electrochemical, and piezoelectric techniques, to convert molecular recognition events into measurable signals. This integration allows for real-time and label-free detection of target analytes, enhancing the speed and accuracy of medical diagnostics.

In this context, the aim of this review is to explore the potential of n-MOFs as biosensors in medical applications. The review will delve into the synthesis methods, functionalization strategies, and sensing mechanisms employed in MOF-based biosensors. Additionally, it will highlight their applications in disease diagnosis, monitoring therapeutic interventions, and shed light on emerging trends in this rapidly evolving field. n-MOFs have emerged as promising biosensing platforms for medical applications, offering unique properties that have the potential to revolutionize disease diagnostics, personalized medicine, and targeted therapies. The development and integration of n-MOF-based biosensors hold tremendous promise for improving patient care, facilitating early detection, and advancing the understanding of complex biological processes.

II. Synthesis And Functionalization Of Nanoscale MOFs

The synthesis and functionalization of n-MOFs are essential steps in customizing their properties for specific applications, particularly in the field of biosensing within medical contexts. This section provides an overview of the synthesis methods and functionalization strategies employed in the fabrication of n-MOFs for biosensing purposes.

2.1 Synthesis Methods

Various techniques have been developed to synthesize n-MOFs with precise control over their size, morphology, and composition. Some commonly used synthesis methods include:

1. Solvothermal or Hydrothermal Synthesis:

This method involves the reaction of metal ions or clusters with organic ligands in a solvent under high temperature and pressure conditions. The choice of solvent and reaction parameters influences the formation of n-MOFs with desired characteristics.

2. Microwave-Assisted Synthesis:

By utilizing microwave irradiation, the synthesis of n-MOFs can be accelerated through rapid and uniform heating. This technique offers advantages such as reduced reaction times and improved control over particle size and morphology.

3. Ultrasound-Assisted Synthesis:

Ultrasonic waves can facilitate the nucleation and growth of MOF crystals by inducing cavitation and microstreaming effects. Ultrasound-assisted synthesis enables the production of n-MOFs with enhanced crystallinity and a narrower size distribution.

4. Spray Drying:

This technique involves atomizing a solution containing metal ions and ligands into a hot air stream, leading to the rapid formation of n-MOF particles. Spray drying offers a continuous and scalable synthesis method for generating n-MOFs.

2.2 Functionalization Strategies

The functionalization of n-MOFs involves the introduction of specific ligands or biomolecules onto the MOF surface to enhance their sensing capabilities or enable targeted applications. Several functionalization strategies have been employed, including:

1. Post-Synthesis Modification

This approach involves modifying pre-synthesized MOFs with functional groups or biomolecules. Surface modification techniques, such as covalent bonding, coordination chemistry, or electrostatic interactions, are utilized to attach ligands or biomolecules onto the MOF surface, imparting specific functionalities.

International Journal of Recent Development in Engineering and Technology
Website: www.ijrdet.com (ISSN 2347-6435(Online) Volume 14, Issue 12, December 2025)

2. Co-Crystallization

In this strategy, functional ligands or biomolecules are co-crystallized with the MOF during the synthesis process. The presence of these additives within the MOF structure can alter the pore properties or provide recognition sites for target analytes, thereby enhancing the sensing capabilities of the nanoscale MOFs.

3. Encapsulation

Nanoscale MOFs can encapsulate guest molecules, including enzymes, antibodies, or DNA strands, within their porous structure. This encapsulation protects the guest molecules from degradation, preserves their activity, and allows for controlled release in response to specific stimuli.

4. Surface Modification

The surface of n-MOFs can be modified with functional groups or biomolecules to enhance their biocompatibility, stability, or affinity towards target analytes. Surface modifications can be achieved through direct covalent or non-covalent interactions with ligands or biomolecules.

The choice of functionalization strategy depends on the desired application and the specific requirements of the biosensing system. By carefully selecting appropriate synthesis methods and functionalization strategies, n-MOFs can be tailored to exhibit enhanced sensing capabilities, improved stability, and compatibility with biological systems. This makes them highly suitable for biosensing applications in medicine.

III. Detection Mechanisms Of Nanoscale MOF-Based Biosensors

n-MOFs based biosensors employ diverse detection mechanisms to achieve high sensitivity and selectivity in sensing and analyzing target analytes. In this section, we will explore several detection mechanisms utilized by n-MOF-based biosensors.

3.1 Fluorescence-Based Biosensors

Fluorescence-based detection stands as one of the most prevalent mechanisms employed in n-MOF-based biosensors. MOFs can be engineered to incorporate fluorescent molecules within their structure or as guest molecules. The interaction between the target analyte and the MOF induces a change in the fluorescence emission properties. This alteration can be measured and quantified to facilitate the detection and quantification of the analyte.

3.2 Electrochemical-Based Biosensors

Electrochemical detection involves measuring electrical signals generated during the interaction between the target analyte and the MOF-based biosensor. MOFs can act as excellent conductive materials or host electroactive species within their structures. The binding of the analyte to the MOF leads to changes in electrical conductivity or electrochemical properties, which can be detected using various electrochemical techniques such as amperometry, voltammetry, or impedance spectroscopy. Electrochemical detection offers high sensitivity, affordability, and compatibility with portable devices.

3.3 Surface-Enhanced Raman Spectroscopy (SERS)-Based Biosensors

Surface-enhanced Raman scattering (SERS) is a powerful spectroscopic technique that amplifies Raman signals of molecules adsorbed on metal surfaces. MOFs can serve as efficient substrates for SERS due to their high surface area and ability to incorporate metal nanoparticles. Interaction between the target analyte and the MOF surface significantly enhances the Raman signals, enabling highly sensitive detection and identification of the analyte molecules.

3.4 Other Detection Mechanisms

Colorimetric detection relies on visually observing a color change in the presence of the target analyte. MOFs can be designed to undergo structural transformations or exhibit specific chemical reactions in response to the analyte, resulting in a distinct color change. This change can be easily observed with the naked eye or measured using simple optical techniques. Colorimetric detection is simple, cost-effective, and suitable for point-of-care applications.

Quartz crystal microbalance (QCM) is a sensitive mass measurement technique based on the principle of the quartz crystal resonator. MOFs can be immobilized onto the surface of the quartz crystal. When the analyte binds to the MOF, it causes a change in the resonance frequency of the crystal. This change can be measured and correlated to the mass of the analyte, enabling label-free and real-time detection of the target analyte.

These represent only a few examples of the detection mechanisms employed by n-MOF-based biosensors. Each mechanism offers unique advantages in terms of sensitivity, selectivity, simplicity, and compatibility with various applications.

International Journal of Recent Development in Engineering and Technology
Website: www.ijrdet.com (ISSN 2347-6435(Online) Volume 14, Issue 12, December 2025)

Researchers continue to harness the remarkable properties of MOFs to develop innovative detection strategies, thereby enhancing performance and broadening the applications of these biosensors in numerous fields of science and technology.

IV. Applications Of Nanoscale MOF-Based Biosensors

4.1 Introduction

n-MOFs possess distinct characteristics that set them apart from other inorganic nanomaterials. These unique properties make them highly suitable for various biosensing applications. MOFs demonstrate remarkable attributes such as exceptional porosity, structural flexibility, precise synthesis control, adjustable pore size and wall modifications, as well as relatively low toxicity. One of the key advantages of utilizing MOFs as biosensors is their inherent biodegradability, which makes them environmentally friendly and compatible with biological systems. Additionally, they offer the ability to be employed as bio-compatible building blocks, further enhancing their potential for use in biosensing applications. In this review we discuss about the some important application of MOFs as biosensor in different fields. Table 1 highlights the major documented work on various applications of nanoscale MOF-based biosensors. Herein, we will be covering the following important field of application-

i. Detection of Protein
ii. Detection of DNA and RNA
iii. Detection of Small Molecules
iv. Application on Clinical Diagnostics
v. Application in Drug Delivery System.

Table 1
Major highlights documented on various applications of nanoscale MOF-based biosensors

S. No.	Documented Work	Highlight of Work
For Detection of Protein		
1	Osman et al. (2019), Vikrant et al. (2019)	MOFs as biosensors for nucleic acid and protein detection.
2	Wang et al. (2018)	Electrochemical biosensor using Cu-MOF with Au NPs for miRNA detection.
3	Huang et al. (2018)	Zr-MOF-based fluorescence biosensor for p53 gene and PSA detection with MOF@AuNP@GO nanohybrid.
4	Liu et al. (2017)	Zr-MOF biosensors with tunable pores; low detection limit for lysozyme (3.6 pg mL^{-1}).
5	Chandrasekhar et al. (2016)	Zn-PLA MOF for amino acid detection, with fluorescence quenching specific to histidine.
For Detection of DNA and RNA		
1	Bauer et al. (2017)	Traditional DNA detection through hybridization n of single-stranded DNA.
2	Chen et al. (2016)	Dysprosium-based MOF for detecting Ebolavirus RNA sequences with a detection limit of 160 pM.
3	Qin et al. (2016), Zhao et al. (2016), Yang et al. (2015)	Various MOFs synthesized for virus DNA/RNA detection (e.g., Ebola, HIV, Zika)
4	Wu et al. (2015)	n-MOFs with peptide nucleic acid probes for real-time miRNA detection in living cancer cells.
5	Ye et al. (2014)	Novel MOF biosensor with hairpin-structured oligonucleotides for DNA sequence-specific detection.
6	Zhang et al. (2014)	UiO-66-NH_2 MOF for fluorescent DNA sensing with high selectivity and sensitivity.
7	Zhu et al. (2013)	2D n-MOFs used to detect HIV-1 DNA sequences with high selectivity and sensitivity.
8	Cui et al. (2012)	UiO-66-NH_2 MOF with high chemical and thermal stability for advanced biosensing applications.
For Detection of Small Molecules		
1	Marieeswaran& Panneerselvam (2020)	Mn-MOF biosensors for selective Hg^{2+} detection.
2	Jia et al. (2020)	MOF/aptamer biosensor for aflatoxin B1 detection.
3	Zhang et al. (2020)	ZnO-MOFs for formaldehyde sensing.
4	Ji et al. (2019)	Anion-channel MOFs for heavy metal ion sensing.
5	Zhang et al. (2018)	MOFs with fluorescence quenching for Fe^{3+} detection.
6	Gu et al. (2018); Li et al. (2017)	Functionalized MOFs (-NH_2 , -OH) for Hg^{2+} , Ba^{2+} , and Cd^{2+} detection.
7	Yan et al. (2017)	Cd-MOFs for nitrobenzene and Fe^{3+} detection.
8	Chen et al. (2017)	Cu-MOFs for aniline detection with high selectivity.
9	Su et al. (2017)	Zirconium MOFs with Au nanoclusters for cocaine detection.
10	Wang et al. (2017)	Eu-based MOFs for selective Fe^{3+} , PO_4^{3-} , and F^- detection.
11	Liu et al. (2017)	Lanthanide-MOFs for highly sensitive Fe^{3+} detection.
12	Wu et al. (2017); Gu et al. (2017)	Zn- and Cd-MOFs for Mn^{2+} and $Cr_2O_7^{2-}$ detection.
13	Lustig et al. (2017); Wen et al. (2016); Zhang et al. (2016)	MOFs enhance or quench luminescence for sensitive detection.

International Journal of Recent Development in Engineering and Technology
Website: www.ijrdet.com (ISSN 2347-6435(Online) Volume 14, Issue 12, December 2025)

14	Hu et al. (2016); Cui et al. (2012a, 2014b)	Luminescent MOFs for detecting small molecules and ions.
15	Rudd et al. (2016); Chen et al. (2016)	Zn-MOFs as biosensors for Hg^{2+} and Pb^{2+} ions.
16	Shi et al. (2016)	Lanthanide MOFs for benzaldehyde sensing.
17	Xu et al. (2016)	n-MOFs for oxygen sensing in live cells using dual-emissive probes.
18	Hao et al. (2015)	MIL-121 MOFs for detecting hippuric acid in urine.
19	Zhu et al. (2015)	HKUST-1-based biosensor for dopamine detection.
20	Wang et al. (2015)	Carbon-functionalized MOFs for ultrasensitive dopamine sensing.
21	Zhao et al. (2015)	Tb-based MOFs for sensing metal cations and small molecules.
22	Zhou et al. (2014)	Eu^{3+} -incorporated MOFs for selective Fe^{3+} sensing.
23	Lu et al. (2014)	n-MOF-253s for sensitive Fe^{2+} detection in cells and solutions.
24	Yue et al. (2014)	MOFs for selective pyridine detection.
25	Lin et al. (2013)	Fe_3O_4 @MOF for organic pollutant degradation.
26	Zheng et al. (2011); Cai et al. (2011)	Tb-MOFs for detecting HSO_4^-, F^-, and Fe^{3+} ions.
For Application on Clinical Diagnostics		
1	Kong et al. (2020)	Zr(IV)-MOF for detecting MUC-1 and miRNA-21 in breast cancer cells.
2	Chang et al. (2020)	ZnO@MoS_2 for rapid acetone detection for diabetes diagnosis.
3	Wang et al. (2020)	NiCo-MOF for glucose measurement via nickel/cobalt alloy nanoparticles.
4	Afzalinia & Mirzaee (2020)	La(III)-MOF with Ag NPs for detecting miRNA-155 cancer biomarker.
5	Sheta et al. (2019)	Cu-MOFNPs for early liver cancer diagnosis via AFP quantification.
6	Wang et al. (2019)	MOFs as signal amplifiers for detecting breast cancer cells.
7	Chang et al. (2019)	MOF biosensor for simultaneous tumor biomarker detection
8	Xu et al. (2019)	Fe-MOF-GOx biosensor for ultrasensitive glucose detection.
9	Hu et al. (2017)	GOx/LOx-loaded MOFs for glucose and lactic acid monitoring.
10	Gao et al. (2017)	Fe-MIL-53 for fluorescence imaging of FA-positive cancer cells.
11	Bian et al. (2015)	Fe_3O_4 -based theranostic platform for cancer diagnosis and treatment.
12	Wang et al. (2014)	$Cu_3(BTC)_2$ -MOF for DNA base pair detection via π-π stacking.
13	Chen et al. (2014)	MOFs for acetone detection in diabetes diagnosis.
14	Wei et al. (2013)	Co-MOF/CC/Paper hybrid glucose sensor.
For Application in Drug Delivery System		
1	Su et al. (2022); Zhuang et al. (2014)	pH-sensitive MOFs for controlled drug release and photothermal therapy.
2	Yao et al. (2021); Wu et al. (2020); Orellana-Tavra et al. (2015)	MOFs as versatile drug delivery systems for various therapeutic agents.
3	Jarai et al. (2020); Rojas et al. (2016); Nazari et al. (2016); Vasconcelos et al. (2012)	MOFs with π-stacking interactions for drug loading.
4	Hidalgo et al. (2020); Chen et al. (2017); Wang (2017)	One-pot synthesis for uniform drug distribution in MOFs.
5	Márquez et al. (2016)	Caffeine-loaded MOFs for cosmetic applications.
6	Liedana et al. (2012); Gaudin et al. (2012)	Encapsulation of caffeine in MOFs with controlled release.

4.2. Detection of Protein

Biomacromolecules encompassing proteins and nucleic acids, hold vital significance in biological processes, and their precise detection poses a formidable challenge for disease diagnosis. In response to this challenge, numerous MOFs as biosensors have been developed to detect nucleic acids and proteins effectively (Osman *et al.* 2019, Vikrant *et al.* 2019). In 2018, Wang *et al.* introduced a remarkable origami electrochemical biosensor by modifying Cu-MOF with Au NPs. This biosensor enabled ultrasensitive detection of micro-RNA (miRNA) through a strand displacement reaction. Liu *et al.* (2017) devised three distinct electrochemical biosensors based on Zr-MOF, each featuring tunable pore sizes for detecting proteins. Among the range of biosensors available, one standout is the optimized Zr-MOF-BA, which is composed of Zr^{4+} and 4,4′,4″-s-triazine-2,4,6-triyltribenzoic acid ligands. This particular biosensor demonstrates exceptional qualities, including high selectivity, a broad detection range with low detection limit of 3.6 pg mL^{-1} for lysozyme. Furthermore, in 2018, Huang *et al.* introduced an innovative "three in-one" fluorescence biosensor utilizing a Zr-MOF. This biosensor enabled ratiometric detection of both the p53 gene and prostate-specific antigen.

International Journal of Recent Development in Engineering and Technology
Website: www.ijrdet.com (ISSN 2347-6435(Online) Volume 14, Issue 12, December 2025)

The Zr-MOF acted as a template for the in-situ growth of Au NPs through reduction by $NaBH_4$. Subsequently, an ultrathin graphene oxide layer was applied to the outermost surface through π–π interactions and hydrogen bonds, thus forming the MOF@AuNP@GO nanohybrid structure. Chandrasekhar *et al.* (2016) successfully synthesized Zn-PLA, a homochiral MOF, for the specific detection of amino acids—the fundamental building blocks of proteins. Notably, Zn-PLA displayed unique fluorescence quenching capabilities, particularly when exposed to histidine, among all the other amino acids. The fluorescence quenching phenomenon was observed for both D-(+)- and L-(-) histidine when interacting with Zn-PLA.

4.3. Detection of DNA and RNA

DNA and RNA take part an important role in physiological regulation. Therefore, the level of nucleic acid can give the information about the diseases and can help to diagnose diseases and monitoring biological process. The field of biosensors has been drawn attention to accurate and rapid diagnosis of viral diseases. Viruses pose a severe threat to human life and health, making the detection of viruses essential for preventing and treating associated diseases. The other infectious viral diseases, such as Coronavirus 2 (SARS-CoV-2) and Monkeypox virus (MPXV) has been particularly alarming since the beginning of 2020, leading to the loss of thousands of lives worldwide. As a result, timely and accurate virus detection has become a crucial aspect to combat the outbreaks (Isidro *et al*. 2022, Pastula *et al.* 2022, V'kovski *et al.* 2021). n-MOF based biosensors are extensively developed for detection of DNA and RNA for rapid diagnosis of viral diseases due to its unique properties of possessing high surface area, adjustable pore size and ease in modification.

Research on MOFs for DNA or biomolecule detection remains quite limited. Typically, organic linkers utilized in MOFs possess a conjugated π-electron system, which provides potential sites for forming hydrogen bonds. These interactions enable suitable binding between MOFs and single-stranded DNA (ssDNA). Consequently, MOFs hold promise as candidates for recognizing DNA molecules through fluorescence changes. Traditional DNA detection methods rely on the hybridization of complementary single-strand DNA with each other (Bauer *et al.*, 2017). However, this approach necessitates the prior generation of single-stranded DNA before analysis (Smith *et al.*, 1984). Recent years, triplex DNA technology has attracted considerable attention.

Zhu et al (2013) first developed the two dimensional (2D) n-MOFs for the detection of HIV-1 DNA sequences with high selectivity and sensitivity by incorporation of triplex-forming oligonucleotide with $[Cu(H_2dtoa)]_n$. In this particular investigation, researchers employed MOFs as the sensing platform to detect double-stranded DNA (ds-DNA) in vitro, specifically targeting HIV 16-bp oligopyrimidine-oligopurine proviral DNA. For this purpose, they selected N, N′-Bis(2-hydroxyethyl) dithiooxamida to copper(II) (H2dtoaCu) as an exemplary MOF due to its two-dimensional sheet structure. The H2dtoaCu units were linked in parallel through intermolecular hydrogen bonds, forming a structure wherein a Cu^{2+} ion was surrounded by two S, two N, and one Cu atom. Following this study, the researchers continued their exploration by fabricating various MOFs for detecting virus DNA or RNA. For instance, they utilized the ligands H3CmdcpBr, H3CbdcpBr, and H2dcbbBr to create a series of water-stable MOFs such as $[Cu3(Cmdcp)_2(dps)4(H_2O)_4(SO_4)]_n$, $\{[Dy(Cmdcp)(H_2O)_3].(NO_3).2H_2O\}n$, $\{[Zn(HCbdcp)_2].H_2O\}_n$ and $[Cu(dcbb)_2]_n$ (Qin *et al.*, 2016; Yang *et al.*, 2015; Zhao *et al.*, 2016a, Zhao *et al.*, 2016b).

In 2014, Ye *et al.* introduced a novel biosensor that combines a two-dimensional MOF called N,N-bis(2-hydroxyethyl)dithiooxamidato copper(II) (H2dtoaCu) with hairpin-structured oligonucleotides showcasing its potential for detecting multiple sequence-specific DNA targets. The main element of this biosensor, referred to as MOF–MBs, is the hairpin-structured fluorescent oligonucleotide. This unique design allows the MOFs to serve as both a nanoscaffold for the oligonucleotide and a nanoquencher of the fluorophore, enabling effective and sensitive detection of specific DNA sequences. Model systems included a reverse-transcription RNA oligonucleotide sequence of HIV (T2) and a wild-type HBV (T1) oligonucleotide sequence. Dye fluorescence was recovered by forming a double-strand structure while the targets were present. Synchronous scanning fluorescence spectrometry is capable of performing multiplex DNA detection showing no cross-reaction between the two probes. Recent years, MOF based technology has been widely exploited as a sensing platform for effective detection of various viruses involving HIV ss-DNA (Pan *et al.* 2018), HIV ds-DNA (Chen *et al.* 2013), H5N1 virus (Wei *et al.* 2013), Sudan virus (Yang *et al.* 2015), Respiratory syncytial virus (Guo *et al.* 2015), Ebola virus (Qin *et al.* 2016), Dengue virus(Xie *et al.* 2018), Zika virus (Xie *et al.* 2018) and Hepatitis A virus (HAV) (Luo *et al.* 2020) etc.

International Journal of Recent Development in Engineering and Technology
Website: www.ijrdet.com (ISSN 2347-6435(Online) Volume 14, Issue 12, December 2025)

In 2014, Zhang *et al.* developed an amine-functionalized MOF known as UiO-66-NH_2 (UiO-University of Oslo). This MOF served as a highly effective fluorescent sensing platform for DNA detection. The biosensor demonstrated exceptional capabilities in distinguishing between complementary and mismatched target sequences, exhibiting both high selectivity and sensitivity. The free single-stranded DNA (ssDNA) labeled with a fluorophore at its 5′ end emitted strong fluorescence at 518 nm (λ_{max}= 480 nm). However, when brought into proximity with UiO-66-NH_2, the aromatic nucleotide bases in the ssDNA and the MOF exhibited a noteworthy fluorescence quenching effect (off-state). This quenching was attributed to several factors, including electrostatic attractions, hydrogen bond interactions, and possibly photoinduced electron transfer. In a related work by Cui *et al.* in 2012, they constructed UiO-66-NH_2 using Zr(IV) and 2-amino-1,4-benzenedicarboxylic acid (NH_2-BDC), which resulted in a MOF with high chemical and thermal stability. The framework was composed of $Zr_6O_4(OH)_4$ oxoclusters interconnected by 12 NH_2-BDC ligands, forming a 3D network structure with tetrahedral and octahedral cages measuring 6 and 11 Å, respectively. These cages were accessible through microporous windows measuring 4–6 Å.

MOF-based technology has found applications in detecting microRNAs (miRNAs), which are emerging biomarkers used for diagnostics and prognostics. miRNAs are small, endogenous, non-protein-coding RNAs, typically comprising around 18 to 25 nucleotides, and are present in the genomes of plants, animals, and certain virus species (Cullen 2006, Landgraf *et al.* 2007, Mallory and Vaucheret 2006).

In 2015, Wu *et al.* introduced a novel sensing strategy utilizing n-MOFs conjugated with peptide nucleic acid (PNA) probes labeled with fluorophores, enabling the multiplexed detection of miRNAs in living cancer cells. The n-MOF acted as a fluorescence quencher for the labeled PNA, forming a strong binding with the metal. Upon the presence of target miRNA, the PNA was hybridized and released from n-MOF, leading to the restoration of fluorescence. This miRNA sensor facilitated quantitative and highly specific detection of multiple miRNAs in living cancer cells. Meanwhile, it allowed precise and real-time monitoring of changes in miRNA expression over space and time.

In 2016, Chen *et al.* developed a distinctive water-stable 3D dysprosium-based MOF using a zwitterionic carboxylate ligand called N-carboxymethyl-(3,5-dicarboxyl) pyridinium bromide (H3CmdcpBr).

This MOF demonstrated the ability to interact non-covalently with probe single-stranded DNA (ss-DNA), serving as an efficient fluorescent sensing platform for detecting complementary Ebolavirus RNA sequences. Remarkably, the detection limit achieved by this MOF-based sensor was an impressive 160 pM.

4.4. Detection of Small Molecules

The detection and sensing of small molecules are crucial tasks in environmental science, medicinal science, life sciences, and the nuclear industry (Chan *et al.*, 2012; Changela *et al.*, 2003; Kong *et al.*, 2000; Waldron *et al.*, 2009). Over the years, numerous methods have been developed for this purpose. Among these methods, n-MOF approach has garnered attention due to its rapid and accurate detection of trace amounts of impurities. Particularly, Luminescent MOFs have been extensively studied for its highly sensitive response to small organic molecules, metal ions and anionic ions (Cui *et al.*, 2012a, 2014b; Hu *et al.*, 2016).

The interactions between these n-MOFs and guest molecules or ions are strongly influenced by factors such as chemical composition, pore size and surface environment of n-MOFs. These unique properties render n-MOFs highly suitable for selective uptake, recognition, and detection of specific molecules or ions. Remarkably, the presence of guest components within MOFs can either enhance or reduce the luminescent emission of the framework as observed in studies by Lustig *et al.* (2017), Wen *et al.* (2016), and Zhang *et al.* (2016). This characteristic provides several advantages, including improved sensitivity, selectivity, response time, and excellent anti-interference performance. Additionally, n-MOFs exhibit remarkable recyclability and operability comparable to traditional methods, as demonstrated by Liu *et al.* (2015) and Lustig *et al.* (2017). Certain n-MOFs exhibit strong luminescent signals with visible emission colors, making them highly promising candidates for chemical sensors.

Among the various n-MOFs, lanthanide-based MOFs (Ln-MOFs) show particular promise for such applications. These Ln-MOFs offer unique optical properties including excellent color purity, visible color detectable with the naked eye, a large Stokes shift value and relatively long luminescence lifetimes attributed to f-f transitions facilitated by an "antenna effect" (Hu *et al.*, 2014; Li *et al.*, 2014; Zhao *et al.*, 2015). For instance, Wang *et al.* (2017) developed a luminescent Eu(III)-based metal-organic framework using 5-(2-carboxy-phenoxy)-1,3-benzenedicarboxylic acid and 1,10-phenanthroline as an efficient fluorescent sensor for detecting metal ions.

International Journal of Recent Development in Engineering and Technology
Website: www.ijrdet.com (ISSN 2347-6435(Online) Volume 14, Issue 12, December 2025)

This sensor exhibited high selectivity for detecting Fe^{3+}, PO_4^{3-}, and F^- in an aqueous medium, with a long excitation wavelength of 348 nm.

Similarly, Zhao *et al.* (2015) designed a luminescent porous Terbium(III)-metal-organic framework $[Tb_3(L)_2(HCOO)(H_2O)_5].DMF.4H_2O$ [H4L = 4,4′-(pyridine-3,5-diyl)diisophthalic acid] for sensing metal cations and small molecules. In this n-MOF model, the unsaturated pyridyl group acts as an excellent functional site for responding to metal cations and small Lewis acidic molecules. The rigid ligand, H4L, enables the formation of robust porous frameworks. Furthermore, the pure and sharp green emission from Tb^{3+} cations, arising from characteristic 4f electronic transitions, serves as a sensitive optical signal in this system.

All organisms require iron species because they function as cofactors in key cellular functions such respiration, DNA synthesis and repair, ribosome biogenesis, and metabolism. But as fluorescence imaging technology develops, it becomes more difficult to probe iron ions properly (Fleming 2009; Takahashi-Makise *et al.* 2009; Que *et al.* 2008).

By inserting Eu^{3+} cations into the pores of MIL-53-COOH (Al) nanocrystals, Zhou *et al.* (2014) demonstrated how to fabricate a luminous lanthanide-functionalized MOF. The parented framework's sensitization and protection allowed these Eu^{3+}-incorporated n-MOFs to demonstrate exceptional luminescence and fluorescence stability in water. It was the first time that Fe^{3+} was detected using a lanthanide-functionalized n-MOF, and the resulting Eu^{3+} coupled nanocrystals shown to be a highly sensitive and selective probe for detecting Fe^{3+} in aqueous solutions.

In a related investigation, Lu *et al.* (2014) created the effective n-MOF-253s n-MOF for detecting Fe^{+2}. According to their findings, these n-MOF-253s exhibited extremely sensitive and focused sensing capacities for Fe^{2+} in aqueous conditions. They created three types of n-MOF-253s with varying particle sizes (range from 300 to 50 nm) by altering the amount of base and acid in the reaction system. In HeLa cells, the 50 nm n-MOF-253 was successfully used for intracellular Fe^{2+} detection. The MOF-253 structure consists of an infinite one-dimensional chain of bpydc (bpydc = 2,20-bipyridine-5,50-dicarboxylic acid) linkers that connect corner-sharing AlO_6 octahedra to form rhombic-shaped pores.

In an inorganic host (tetraethoxysilane), Zheng *et al.* (2011) proposed a novel terbium 2-(3-pyridyl) imidazole-4,5-dicarboxylic acid complex for sensing HSO_4^- and F^- anions. Similarly, Cai *et al.* (2011) designed a terbium(III) coordination polymer $\{Tb_3(\mu3\text{-}HPyIDC)4(H_2O)8]\cdot NO_3\cdot 4H_2O\}n$ (H_3PyIDC = 2-(4-pyridyl)-1H-imidazole-4,5-dicarboxylic acid) which exhibited selective identification for Fe^{3+} ions.

In order to detect Fe(III), Liu *et al.* (2017) developed an effective luminous sensing method based on a lanthanide-MOF based on 4,5-imidazole dicarboxylate. Additionally, Yue *et al.* (2014) created 3D-MOF, $\{[Cd_2(p\text{-}ClPhHIDC)2(4,4'\text{-bipy})]\cdot H_2O\}n$ (4,4′-bipy = 4,4′-bipyridine), including the selective ligand 2-(4-chlorophenyl)-1H-imidazole-4,5-dicarboxylic acid (p-$ClPhH_3IDC$), which displayed specific recognition properties for pyridine.

In order to create highly sensitive and precise iron(III) sensors, Zhang *et al.* (2018) created two luminous transition-MOF: [Cd(p-CNPhHIDC)(4,4'-bipy)0.5]n (1) and [Zn(p-CNPhHIDC)(4,4'-bipy)]n (2) (4,4'-bipy = 4,4'-bipyridine). These n-MOFs demonstrated remarkable fluorescence quenching-based selective sensing for Fe^{3+} ions as well as resistance to interference from other metals and quick reaction times.

While luminescent porous MOFs functionalized with -COOH groups, responsive to metal ions such as Hg^{2+}, Ba^{2+}, Cu^{2+}, Cd^{2+}, and others, remain relatively limited in development (Gu *et al.* 2018, Li *et al.* 2017, Tseng *et al.* 2012), functionalized MOFs (-NH2, -OH, -CHO, and -N3) have been widely used in various metal ion detection systems. Ji *et al.* (2019) developed two distinctive anion channel-type n-MOFs with the molecular formula $\{[Et_2NH_2][M1.5(Ina)(HIna)(\mu2\text{-}OH)(TPTC)0.5]\}n$ (M = Co-SXNU-J1, Ni-SXNU-J2, SXNU = Shanxi Normal University) under solvothermal conditions employing $M(Ac)_2.4H_2O$ and mixed ligands of H_4TPTC (p-terphenyl-3,3",5,5'"-tetracarboxylic acid) and (HIna) isonicotinic acid. The blue luminescence of these MOFs revealed promising luminescence sensor properties for the targeted and accurate detection of Fe^{3+}.

Among various pollutants documented in the literature, organic solvents, organochlorine pesticides, and heavy metal ions are significant contributors to environmental pollution. Toxic heavy metals are continuously released into the environment due to agricultural and development and expansion of chemical industries.

International Journal of Recent Development in Engineering and Technology
Website: www.ijrdet.com (ISSN 2347-6435(Online) Volume 14, Issue 12, December 2025)

The source intake of contaminants with toxic metals leads to various health issues including DNA damage and overall damage to the central nervous system (Liu *et al.* 2020, Ma *et al.* 2020). Additionally, chemicals like acetylacetone (Hacac) and nitrobenzene (NB) are extremely toxic and acutely carcinogenic, posing environmental risks and human health hazards (Esrafili *et al.* 2021, Kang *et al.* 2019, Liu *et al.* 2020, Yang *et al.* 2020). Overuse of organochlorine pesticides (OCPs) during plantation due to high demand for cereal and vegetable production also contributes to environmental concerns. To ensure environmental safety, rapid and selective detection of trace amounts of these harmful pollutants is crucial. The unique properties of MOF nanostructures make them highly sensitive in MOF-based sensors, as they facilitate the adsorption of a large number of target analytes, thereby providing enhanced detection capabilities.

Rudd *et al.* (2016) and Chen *et al.* (2016) presented an isoreticular series of Zn-based Luminescent MOFs that acted as sensitive and selective biosensors for detecting heavy metal ions (Hg^{2+} and Pb^{2+}) in water at very low concentrations. Wu *et al.* (2017) and Gu *et al.* (2017) developed Zn- and Cd-based Luminescent MOFs to create luminescent sensors for sensing Mn^{2+} and $Cr_2O_7^{2-}$ ions, respectively. Marieeswaran and Panneerselvam (2020) designed a novel fluorescent biosensor, comprising a magnetic nanoscale metal-organic framework (Mn-MOF) functionalized with fluorescein amidite (FAM)-labeled ssDNA, which exhibited excellent sensitivity and selectivity for Hg(II) cations over other co-existing metal ions. Lin *et al.* (2013) successfully developed Fe_3O_4@MOF (MIL-53(Fe)) for degrading organic pollutants.

Shi *et al.* (2016) demonstrated two dimethylphenyl imidazole dicarboxylate-based lanthanide MOFs for luminescence sensing of benzaldehyde. Yue *et al.* (2014) synthesized a new 3D MOF, {[Cd_2(p-ClPhHIDC)2(4,4′-bipy)]·H_2O}n (4,4′-bipy = 4,4′-bipyridine), using a newly designed ligand, 2-(4-chlorophenyl)-1H-imidazole-4,5-dicarboxylic acid (p-ClPhH_3IDC), for selective pyridine detection in samples.

Yan *et al.* (2017) designed highly selective luminescent metal MOFs for the detection of nitrobenzene and Fe^{+3} ions. They prepared the MOFs using V-shaped rigid multicarboxylate 2,4-di(3′,5′-dicarboxylphenyl)benzoic acid (H5L) and Cd(II) salts in various solvent systems, resulting in the formation of three different coordination fashions and a diversity of targeted MOFs.

Chen *et al.* (2017) fabricated Copper(II) based metal MOFs (CP-MOFs) for detecting aniline. CP-MOF [Cu_4(tdhb)] (BUT-155) displayed great porosity, high hydrolytic stability, and high performance for selectively adsorbing soft base type aniline over water or phenol, with a detectable color change for the MOF.

Xu *et al.* (2016) developed novel n-MOFs for sensing ratiometric oxygen in live cells, using a phosphorescence/fluorescence dual-emissive n-MOF, R-UiO, containing a Pt(II)-porphyrin ligand as an O_2-sensitive probe and a Rhodamine-B isothiocyanate (RITC) ligand as an O_2-insensitive reference probe.

Su *et al.* (2017) designed 2D zirconium-based MOF nanosheets embedded with Au nanoclusters (2D AuNCs@521-MOF) for detecting cocaine employing the bio-affinity of nanosheets toward biomolecule-bearing phosphate groups to immobilize a large amount of cocaine aptamer strands forming a biosensitive platform for cocaine detection.

Jia *et al.* (2020) developed a MOF/aptamer system as a fluorescent biosensor for detecting aflatoxin B1 in food samples. The fluorescent aptasensor utilized metal-organic frameworks (UiO-66-NH_2) and TAMRA-labeled aptamer as a sensing platform for AFB1 detection, based on changes in fluorescence signal upon aptamer binding to AFB1. Zhang *et al.* (2020) derived a novel MOF-hierarchical ZnO structures as efficient sensing materials for detecting formaldehyde.

Hao *et al.* (2015) used MIL-121 to develop a fluorescent probe for detecting hippuric acid (HA) in urine, employing Eu ions introduced into the MIL-121 channels to create fluorescent Eu^{3+} @MIL-121, suitable for analyzing HA in human urine.

Zhu *et al.* (2015) developed a sensitive biosensor for dopamine (DA) based on the catalytic chemiluminescence of HKUST-1, observing that HKUST-1 enhanced the chemiluminescence intensity of the luminol-H2O2 system, which was inhibited by DA. Wang *et al.* (2015) utilized carbon-functionalized Al-MIL-53-$(OH)_2$ for ultrasensitive determination of DA, creating a Nafion/C/Al-MIL-53-$(OH)_2$ modified electrode as an electrocatalyst for DA oxidation.

4.5. Application on Clinical Diagnostics

The definite amounts of physiological species are playing a significant role to cellular functions and normal physiological activities.

International Journal of Recent Development in Engineering and Technology
Website: www.ijrdet.com (ISSN 2347-6435(Online) Volume 14, Issue 12, December 2025)

The detection of physiological biomarkers is crucial for identifying metabolic disorders or pathological disturbances. Timely and precise diagnosis through qualitative or quantitative methods is essential for effective treatment and preventing severe conditions (Xu *et al.*, 2022). Recently, n-MOF biosensors have gained attention for their unique properties, especially in fluorescence-based detection, which offers high sensitivity, selectivity, and real-time response (Zhang *et al.*, 2020; Wang *et al.*, 2018; Li *et al.*, 2019). Many n-MOF-based fluorescent nanoprobes have been developed as biosensors, capable of recognizing and transducing signals from guest species (Wu *et al.*, 2020; Wang *et al.*, 2019).

Cancer poses a significant threat to health worldwide causing millions of deaths annually (Ding *et al.*, 2020). Early cancer diagnosis is crucial for improving treatment outcomes and saving lives (Abánades Lázaro *et al.*, 2019). n-MOFs have been extensively synthesized and studied for cancer detection. For instance, Kong *et al.* (2020) developed a green-emission Zr(IV)-MOF (BUT-88) nanoprobe (drDNA-BUT-88) that could precisely detect dual tumor biomarkers (MUC-1 and miRNA-21) in breast cancer cells (MCF-7 cells) with high sensitivity. Sheta *et al.* (2019) used a magnetic n-MOF-based platform (Cu-MOFNPs) for early diagnosis of liver cancer through quantification of alpha-fetoprotein (AFP) in serum samples from healthy and hepatitis patients. Bian and his coworkers (2015) created a novel theranostic platform for cancer diagnosis and treatment, combining Fe_3O_4@polyacrylic acid/Au nanoclusters/zeolitic imidazolate framework-8 nanoparticles (Fe_3O_4@PAA/AuNCs/ZIF-8 NPs). Additionally, Gao *et al.* (2017) employed Fe-MIL-53-NH2-FA-5-FAM/5-FU DDS as a theranostic platform for detecting cancer cells using fluorescence imaging of FA-positive cancer cells (MGC-803 cells).

Afzalinia and Mirzaee (2020) designed a novel La(III)-MOF combined with silver nanoparticles (Ag NPs) as a fluorescence resonance energy transfer (FRET) strategy for detecting MicroRNA-155 (miRNA-155) expression levels as a cancer biomarker. Wang *et al.* (2014) studied the electro-chemical behavior of adenine and guanine using Cu_3(BTC)2-MOF, which interacted with DNA base pairs through π-π stacking which enable the distinction of different base pairs. Moreover, MOFs have been reported as excellent signal amplifiers in MOFTA sensors for detection of breast cancer cells (Wang *et al.*, 2019; Luan *et al.*, 2018; Chen *et al.*, 2017).

To achieve early and accurate cancer diagnosis, simultaneous detection of multiple tumor biomarkers is essential (Munawar *et al*., 2023, Guo *et al*. 2020, Wang *et al*.2021, Zhou *et al*.2022, Hu *et al*. 2021, Li *et al*.2021, Biswas *et al*.2021, Zhang *et al*. 2019, Bhardwaj *et al* 2017, Ehzari *et al*. 2020, Tang *et al*. 2022, Yola *et al*. 2021, Sheta *et al*. 2019). Chang *et al.* (2019) developed a novel MOFs-based homogeneous electrochemical biosensor for simultaneous detection of multiple tumor biomarkers. The functionalized MOFs used porous UIO-66-NH_2 as nano-containers to load electroactive dyes with dsDNA acting as a receptionist to cap the MOFs.

A serious hazard to human health is diabetes, a chronic disease that affects people all over the world. Type I (TIDM) and type II (T2DM) diabetes are two types that are distinguished by insulin insufficiency. Diabetes is often discovered by checking the body's levels of exhaled acetone or blood glucose. Due to their distinctive characteristics, MOFs have attracted interest for acetone detection (Chen *et al.*, 2014).

Chang and his colleagues (2020) created a new MOF for acetone detection called ZnO@MoS_2 nanosheets core/shell heterojunctions. Due to the quick gas diffusion rates in the porous MoS_2 nanosheets, the n-MOF system responded to acetone with response times of 9 s/17 s at 500 ppb and 60 s/40 s at 5 ppb. The MOF makes an effective sensor for diabetes diagnosis since the green emission is quenched in the presence of acetone.

To measure blood glucose, Wang *et al.* (2020) created a nanohybrid MOF based on nickel and cobalt. The nickel/cobalt (NiCo) alloy nanoparticles were created by pyrolyzing a bimetallic (Ni and Co) framework (NiCo-MOF) at 800^0C in a nitrogen environment. In the meantime, Wei *et al.* (2013) created a hybrid non-enzyme sensor for glucose detection called the Co-MOF/CC/Paper.

By in situ growing AuNPs inside MIL-101, Hu *et al.* (2017) created two GOx/ lactate oxidase (LOx)-loaded MOF-based biosensors with good selectivity and sensitivity for monitoring glucose and lactic acid in living tissues. Fe-MIL-88B-NH_2 (Fe-MOF) biosensor for ultrasensitive glucose detection in human serum was created by Zhu and colleagues (Xu *et al.* 2019). Fe-MOF-GOx was created by immobilizing GOx on Fe-MIL88B-NH_2 by covalent binding caused by EDC/NHS.

International Journal of Recent Development in Engineering and Technology
Website: www.ijrdet.com (ISSN 2347-6435(Online) Volume 14, Issue 12, December 2025)

4.6. Application in Drug Delivery System

MOFs have garnered significant interest as primary drug delivery carriers due to their exceptional drug loading capacity. The physical properties of MOFs, such as void volume, surface area, pore size, and structural dynamics, play a crucial role in efficiently loading drugs into the material (Horcajada *et al.*, 2006). The release of drug molecules from MOFs involves a reaction-diffusion mechanism rather than a pure diffusion approach (Han *et al.*, 2012). Fick's first and second laws of diffusion, commonly used for quantitatively describing diffusional mass transfer, are also applicable to nanoporous materials like MOFs (Titze *et al.*, 2015). The interaction of guest molecules with MOFs is of significant importance in the reaction-diffusion process. MOFs can have either rigid or flexible pores, depending on the alignment of guest-host interactions and the MOF structure (Horcajada *et al.*, 2010). Some drug molecules, such as Ibuprofen and others can induce changes in the unit cell structures of MOFs when loaded, resulting in "swelling" behavior (McKinlay *et al.*, 2013; Pham *et al.*, 2020).

Chemical stability is crucial in drug delivery systems over time. Various parameters, including pH value, buffer composition, nanoparticle size, and surface adaptation, play a critical role in controlling MOF stability. Chemical stability in MOFs refers to their ability to maintain long-range ordered structures in specific environments. Two main ways of measuring material degradation are decomposition to the original building blocks and amorphization. The stability of MOFs depends on factors like pH, time, and temperature, and the optimal stability is influenced by the intended application and drug administration route.

MOFs with ligands containing aromatic structures exhibit favorable π-stacking interactions, enabling the loading of molecules like rhodamine, mitoxantrone, doxorubicin, and 5-fluorouracil (Jarai *et al.*, 2020; Rojas *et al.*, 2016; Vasconcelos *et al.*, 2012; Nazari *et al.*, 2016). Small drug molecules and nucleic acids interact with the surface of MOFs, typically co-precipitating during one-pot synthesis methods, leading to even distribution throughout the mesopores of MOFs (Chen *et al.*, 2017; Hidalgo *et al.*, 2020; Wang, 2017).

Caffeine, a liporeductor and amphiphilic drug, has been combined with MOFs to create cosmetic-containing composites and MOF-based patches for cosmetic applications (Márquez *et al.*, 2016).

Studies have investigated the encapsulation of caffeine drugs in MOFs like ZIF-8 and MIL-88B_2OH, showing differences in delivery rates based on MOF interactions (Liedana *et al.*, 2012; Gaudin *et al.*, 2012). pH-sensitive MOFs have been developed for drug delivery, demonstrating controlled drug release and photothermal efficiency (Su *et al.*, 2022; Zhuang *et al.*, 2014).

In various studies, MOFs like UiO-66, MIL-88, and ZIF-8 have been utilized as drug delivery systems for a range of therapeutic agents, including photosensitizers, chemotherapy drugs, and hydrophilic fluorescent molecules (Wu *et al.*, 2020; Yao *et al.*, 2021; Orellana-Tavra *et al.*, 2015). These studies highlight the potential of MOFs as versatile drug delivery carriers with tunable properties for various biomedical applications.

In summary, the utilization of MOFs as biosensors in the medical domain shows tremendous potential in transforming disease diagnosis, monitoring, and treatment. Ongoing research and development efforts are poised to propel the integration of MOF-based biosensors into mainstream clinical applications, leading to substantial progress in personalized healthcare solutions.

V. Challenges And Future Prospects Of Nanoscale MOFs As Biosensors

n-MOFs have emerged as promising materials for biosensing applications due to their unique properties. However, several challenges need to be addressed to fully exploit the potential of n-MOFs as biosensors. Additionally, there are exciting future prospects for further enhancing their performance and expanding their applications. Let's discuss both the challenges and future prospects in detail:

5.1 Challenges of Nanoscale MOFs as Biosensors:

1. *Selectivity and Specificity:* Biosensors based on n-MOFs should exhibit high selectivity and specificity towards target analytes. Achieving selective molecular recognition within the porous structure of MOFs can be challenging, particularly in the presence of complex biological samples. Functionalization of MOFs with appropriate recognition elements, such as aptamers or antibodies, can enhance selectivity and specificity but requires careful design and optimization.
2. *Stability and Degradation:* One of the key challenges is the stability of n-MOFs in complex biological environments.

International Journal of Recent Development in Engineering and Technology
Website: www.ijrdet.com (ISSN 2347-6435(Online) Volume 14, Issue 12, December 2025)

MOFs are typically synthesized under controlled conditions, but they can be prone to degradation or structural collapse when exposed to various physiological conditions, such as changes in pH, temperature, or the presence of enzymes. Stability enhancement strategies, including surface modifications and encapsulation techniques, need to be developed to ensure the long-term stability of MOFs in biosensing applications.

3. *Biocompatibility and Cytotoxicity:* Before MOFs can be widely used in biological systems, it is essential to evaluate their biocompatibility and potential cytotoxic effects. Some MOFs may release metal ions or organic linkers, which can be toxic to cells. Comprehensive biocompatibility studies are required to assess the safety of n-MOFs and minimize any adverse effects on living organisms.
4. *Signal Transduction and Detection Limits:* Efficient signal transduction and detection methods are crucial for biosensing applications. Incorporating suitable transduction elements, such as fluorescence, electrochemistry, or SERS is necessary for converting the molecular recognition event into a measurable signal. Additionally, improving the sensitivity and detection limits of MOF-based biosensors is important for the accurate detection of analytes, especially in low-concentration samples.

5.2 Future Prospects of Nanoscale MOFs as Biosensors

1. Multifunctional MOFs: Researchers are actively exploring the integration of different functionalities into MOFs to expand their biosensing capabilities. This includes incorporating catalytic sites for simultaneous sensing and catalysis, introducing luminescent or plasmonic properties for enhanced signal transduction, or integrating nanomaterials for synergistic effects. Multifunctional MOFs can enable more versatile and efficient biosensing platforms.

2. Stimuli-Responsive MOFs: Stimuli-responsive MOFs can undergo structural changes in response to external stimuli, such as temperature, pH, or the presence of specific molecules. These dynamic properties can be harnessed to develop smart biosensors with on-demand control and improved sensitivity. Stimuli-responsive MOFs offer the potential for real-time monitoring and selective release of analytes, leading to enhanced biosensing performance.

3. In vivo Applications: The development of n-MOFs as biosensors for in vivo applications holds significant promise. By combining the unique properties of MOFs with the ability to target specific tissues or cells, MOFs can be used for real-time monitoring of biological processes, disease diagnosis, and drug delivery. In vivo biosensing with MOFs can provide valuable insights into complex biological systems and enable personalized medicine approaches.

4. Integration with Nanotechnology: n-MOFs can be integrated with other nanomaterials and nanotechnologies to create hybrid biosensing platforms with enhanced performance. For example, coupling MOFs with nanoparticles or nanowires can improve signal amplification, sensitivity, and multiplexing capabilities. Integration with microfluidics, nanoelectronics, or wearable devices can lead to portable, point-of-care biosensing systems with high precision and convenience.

In summary, while nanoscale MOFs show great potential as biosensors, addressing the challenges related to stability, biocompatibility, selectivity, and signal transduction is essential for their successful implementation. However, with ongoing research and technological advancements, the future prospects of n-MOFs as biosensors look promising, offering exciting opportunities for advanced sensing capabilities in various fields, including healthcare, environmental monitoring, and food safety.

VI. Conclusion

In conclusion, nanoscale MOFs exhibit tremendous promise as biosensors in medical applications. Their exceptional characteristics, including high surface area, adjustable porosity, and versatile functionality, position them as compelling candidates for various sensing and diagnostic purposes in healthcare. By effectively addressing challenges related to stability, biocompatibility, selectivity, and signal transduction, n-MOFs can be harnessed to great effect in medical settings. The future outlook for n-MOFs as biosensors in medical applications is highly promising. Advancements in the development of multifunctional MOFs, which integrate catalytic, luminescent, or plasmonic properties, can unlock enhanced sensing capabilities. Stimuli-responsive MOFs offer the potential for precise and controlled diagnostics through real-time monitoring and selective analyte release.

Furthermore, by integrating MOFs with nanotechnology, such as nanoparticles or wearable devices, portable and point-of-care biosensing systems can be created, enabling rapid and accurate medical diagnostics. In medical applications, n-MOFs can find application in in vivo monitoring, disease diagnosis, and targeted drug delivery. Their ability to target specific tissues or cells, coupled with their high sensitivity, allows for real-time monitoring of biological processes and early detection of diseases. Additionally, the integration of MOFs with other nanomaterials and nanotechnologies has the potential to enhance their performance, enabling advanced sensing capabilities and personalized medicine approaches. Thus, n-MOFs as biosensors possess the potential to bring about revolutionary advancements in medical diagnostics and monitoring.

Acknowledgment

The authors would like to express their heartfelt gratitude to the management of Institute/ University HoD, and everyone who helped us directly and indirectly throughout the project.

Declaration Of Competing Interest

We, the authors of the publication titled "Nanoscale MOFs as Biosensors in Medical Application" thus declare that the work featured in the above review paper is original. Furthermore, we affirm that the work provided has not previously been published or is currently being considered for publication in any other journals.

Credit Author Statement

Ankita Saini and Monalisa Bourah: Conceptualization, Data curation, Visualization, Investigation, Writing-Original draft preparation, Writing- Reviewing and Editing. Sunil Kumar Saini: Visualization, Investigation, Supervision, Validation.

REFERENCES

[1] Abánades Lázaro, I.; Forgan R.S. Application of zirconium MOFs in drug delivery and biomedicine. Coord. Chem. Rev. 2019; 380: 230–59.

[2] Afzlinia A and Mirzaee M, Ultrasensitive Fluorescent miRNA Biosensor Based on a “Sandwich” Oligonucleotide Hybridization and Fluorescence Resonance Energy Transfer Process Using an Ln(III)-MOF and Ag Nanoparticles for Early Cancer Diagnosis: Application of Central Composite Design, ACS Appl. Mater. Interfaces, 2020; 12: 16078-87.

[3] Bauer CA, Timofeeva T VT. Settersten B, Patterson BD, Liu V H,Simmons B A, *et al*. Influence of Connectivity and Porosity on Ligand-Based Luminescence in Zinc Metal−Organic Frameworks J. Am. Chem. Soc. 2007; 129: 7136–44.

[4] Bhardwaj SK, Sharma AL, Bhardwaj N, Kukkar M, Gill AA, Kim K-H. A. Deep, TCNQ-doped Cu-metal organic framework as a novel conductometric immunosensing platform for the quantification of prostate cancer antigen, Sens. Actuators, B 2017; 240:10–17.

[5] Bian R, Wang T, Zhang L, Li L, Wang C. A combination of tri-modal cancer imaging and in vivo drug delivery by metal-organic framework based composite nanoparticles. Biomater. Sci. 2015; 3: 1270–78.

[6] Biswas S, Lan Q, Xie Y, Sun X, Wang Y, Label-free electrochemical immunosensor for ultrasensitive detection of carbohydrate antigen 125 based on antibody-immobilized biocompatible MOF-808/CNT, ACS Appl. Mater. Interfaces. 2021; 13 (2): 3295–3302.

[7] Bůžek D, Adamec S, Lang K, Demel J. Metal–organic frameworks vs. buffers: Case study of UiO-66 stability. Inorg. Chem. Front. 2021; 8: 720–34.

[8] Cai S L, Zheng S R, Fan J, Xiao T T, Tan J B and Zhang W G. A new sensor based on luminescent terbium–organic framework for detection of Fe^{3+} in water. Inorg. Chem. Commun., 2011; 14: 937-39.

[9] Cao J, Gao Y, Wang Y, Du C. and Liu Z. A microporous metal-organic open framework containing uncoordinated carbonyl groups as postsynthetic modification sites for cation exchange and Tb3+ sensing. Chem. commun. 2013; 49: 6897-99.

[10] Chan J, Dodani S C, Chang C. Reaction-based small-molecule fluorescent probes for chemoselective bioimaging. J. Nat. Chem. 2012; 4(12): 973−84.

[11] Chandrasekhar P, Mukhopadhyay A, Savitha G, Moorthy JN, Remarkably selective and enantiodifferentiating sensing of histidine by a fluorescent homochiral Zn-MOF based on pyrene-tetralactic acid. Chem. Sci. 2016; 7: 3085–91.

[12] Chang J, Wang X, Wang J, Li H, and Li F. Nucleic Acid Functionalized Metal-Organic FrameworksBased Homogeneous Electrochemical Biosensor for Simultaneous Detection of Multiple Tumor Biomarkers, Anal. Chem. 2019; 91 (5); 3604-10

[13] Chang X, Li X, Qiao X, Li K, Xiong Y, Li X, Guo T, Zhu L, Xue Q. Metal-organic frameworks derived ZnO@MoS2nanosheets core/shell heterojunctions for ppb-level acetone detection: Ultra-fast response and recovery. Sens. Actuators B Chem. 2020; 304: 127430-33.

[14] Changela A, Chen K, Xue Y, Halschen J, Outten CE, O’halloran, T V, *et al*. Molecular basis of metal-ion selectivity and zeptomolar sensitivity by CueR. Science 2003; 301: 1383−87.

[15] Chen D, Yang D, Dougherty CA, Lu W, Wu H, He X, Hong H. In vivo targeting and positron emission tomography imaging of tumor with intrinsically radioactive metal–organic frameworks nanomaterials., ACS Nano 2017; 11 (4): 4315–4327.

[16] Chen EX, Yang H, Zhang J. Zeolitic imidazolate framework as formaldehyde gas sensor. Inorg. Chem. 2014; 53: 5411–5413.

[17] Chen L, Zheng H, Zhu X, Lin Z, Guo L, Qiu B, Chen G, Chen Z.-N. Metal–organic frameworks-based biosensor for sequence-specific recognition of double-stranded DNA. The Analyst. 2013; 138 (12): 3490–93.

[18] Chen M M, Chen L, Li H X, Brammer L and Lang J P, Highly selective detection of Hg^{2+} and MeHgI by di-pyridin-2-yl-[4-(2-pyridin-4-yl-vinyl)-phenyl]-amine and its zinc coordination polymer. Inorg. Chem. Front., 2016; 3: 1297–05.

[19] Chen M. Gan N, Zhou Y, Li T, Xu Q, Cao Y. and Chen Y. A novel aptamer- metal ions- nanoscale MOF based electrochemical biocodes for multiple antibiotics detection and signal amplification. Sens. Actuators B Chem., 2017; 242: 1201–09.

[20] Chen Y, Wang B, Wang X, Xie L-H, Li J, Xie Y, and Li J-R J, A Copper(II)-Paddlewheel Metal-Organic Framework with Exceptional Hydrolytic Stability and Selective Adsorption and Detection Ability of Aniline in Water ACS Applied Materials & Interfaces, 2017; 9(32): 27027–35

[21] Cui Y J, Chen B L, Qian GD. Lanthanide metal-organic frameworks for luminescent sensing and light-emitting applications Coord. Chem. Rev. 2014b; 273- 274: 76−86.

[22] Cui Y J, Yue Y F, Qian G D and Chen BL. Luminescent Functional Metal–Organic Frameworks. Chem. Rev., 2012; 112: 1126-62

[23] Cullen B R, Viruses and microRNAs, Nat. Genet. 2006; 38: S25-30.

[24] Dai Q, Ren E, Xu D, Zeng Y, Chen C, Liu G. Indocyanine green-based nanodrugs: A portfolio strategy for precision medicine. Prog. Nat. Sci. 2020; 30: 577–88.

[25] Ding S; He L; Bian, XW, Tian G. Metal-organic frameworks-based nanozymes for combined cancer therapy. Nano Today 2020; 35: 100920-23.

[26] Ehzari H, Amiri M, Safari M. Enzyme-free sandwich-type electrochemical immunosensor for highly sensitive prostate specific antigen based on conjugation of quantum dots and antibody on surface of modified glassy carbon electrode with core–shell magnetic metal-organic frameworks, Talanta. 2020; 210:120641.

[27] Esrafili L, Firuzabadi F D, Morsali A and Hu M L, Reuse of predesigned dual-functional metal organic frameworks (df-mofs) after heavy metal removal. Hazard J. Mater. 2021; 403: 123696-98.

[28] Eubank A, J, Wuttke S, Xiao B, Wheatley P, Bazin P, De Weireld G, Nitric oxide adsorption and delivery in flexible MIL-88 (Fe) metal–organic frameworks. Chem. Mater. 2013; 25 (9): 1592–99.

[29] Fleming R E. Iron sensing as a partnership: HFE and Transferrin receptor 2. Cell Metab. 2009; 9: 211-12

[30] Gao X, Zhai M, Guan W, Liu J, Liu Z, Damirin A. Controllable synthesis of a smart multifunctional nanoscale metal-organic framework for magnetic resonance/optical imaging and targeted drug delivery. ACS Appl. Mater. Interfaces 2017; 9: 3455–62.

[31] Gaudin C, Cunha D, Ivanoff E, Horcajada P, Chevé G, Yasri, A, *et al*. Quantitative structure activity relationship approach to probe the influence of the functionalization on the drug encapsulation of porous metal-organic frameworks. Microporous Mesoporous Mater. 2012; 157: 124–130.

[32] Gautam S, Singhal J, Lee H, Chae K, Drug delivery of paracetamol by metalorganic frameworks (HKUST-1): Improvised synthesis and investigations, Mater. Today Chem. 2022; 23:100647-48.

[33] Gu B, Ye M, Nie L, Fang Y, Wang Z, Zhang X, Zhang H, Zhou Y and Zhang Q. Organic-dye-modified upconversion nanoparticle as a multichannel probe to detect Cu^{2+} in living cells. ACS Appl. Mater. Interfaces. 2018; 10:1028-1032.

[34] Gu T-Y, Dai M, Young D J, Ren Z G and Lang J P. Luminescent Zn(II) coordination polymers for highly selective sensing of Cr(III) and Cr(VI) in water. Inorg. Chem., 2017; 56(8): 4668–78.

[35] Guo JF, Fang RM, Huang CZ, Li YF. Dual amplifying fluorescence anisotropy for detection of respiratory syncytial virus DNA fragments with sizecontrol synthesized metal–organic framework MIL-101. RSC Adv. 2015; 5 (57): 46301–06.

[36] Guo L, Mu Z, Yan B, Wang J, Zhou J, Bai L. A novel electrochemical biosensor for sensitive detection of non-small cell lung cancer ctDNA using NG-PEICOFTAPB-TFPB as sensing platform and Fe-MOF for signal enhancement, Sens. Actuators, B 2022; 350:130874-76.

[37] Gutiérrez M, Möslein AF, Tan JC. Facile and fast transformation of nonluminescent to highly luminescent metal-organic frameworks: Acetone sensing for diabetes diagnosis and lead capture from polluted water. ACS Appl. Mater. Interfaces. 2021; 13: 7801–11.

[38] Han S, Hermans T M, Fuller P E, Wei Y and Grzybowski B A. Transport into Metal-Organic Frameworks from solution is not purely diffusive. Angew. Chem. In. Ed., 2012, 51: 2662-66.

[39] Hao J-N, Yan B, Recyclable lanthanide-functionalized MOF hybrids to determine hippuric acid in urine as a biological index of toluene exposure. Chem. Commun. 2015; 51:14509–12.

[40] Harris A L. Hypoxia- a key regulatory factor in tumour growth. Nat. [4Rev. Cancer 2002; 2: 38-47.

[41] Hidalgo T, Alonso-Nocelo M, Bouzo B, Reimondez-Troitino S, AbuinRedondo de la Fuente ˜ C M, Horcajada P, Biocompatible iron (III) carboxylate metal–organic frameworks as promising RNA nanocarriers. Nanoscale. 2020; 12 (8): 4839–45.

[42] Horcajada P, Chalati T, Serre C, Gillet B, Sebrie C, Baati T, Kreuz C, Porous metal–organic-framework nanoscale carriers as a potential platform for drug delivery and imaging, Nat. Mater. 2010; 9 (2) :172–78.

[43] Horcajada P, Serre C, Vallet-Regí M, Sebban M, Taulelle F, F´erey G. Metal–organic frameworks as efficient materials for drug delivery, Angew. Chem. 2006; 118(36): 6120–24.

[44] Hou L, Qin Y, Li J, Qin S, Huang Y, Lin T, *et al*., A ratiometric multicolor fluorescence biosensor for visual detection of alkaline phosphatase activity via a smartphone, Biosens. Bioelectron. 2019; 143:111605--.

[45] Hu M, Zhu L, Li Z, Guo C, Wang M, Wang C, Du M. CoNi bimetallic metal–organic framework as an efficient biosensing platform for miRNA 126 detection. Appl. Surf. Sci. 2021; 542:148586-88.

[46] Hu Y, Cheng H, Zhao X, Wu J, Muhammad F, Lin S, *et al*. Surface-enhanced raman scattering active gold nanoparticles with enzyme-mimicking activities for measuring glucose and lactate in living tissues. ACS Nano 2017; 11:5558-61.

[47] Hu Z C, Deibert BJ, Li J. Luminescent metal–organic frameworks for chemical sensing and explosive detection. Chem. Soc. Rev. 2014; 43: 5815−40.

[48] Huang X, He Z, Guo D, Liu Y, Song J, Yung B C, *et al*., "Three-in-one" nanohybrids as synergistic nanoquenchers to enhance no-wash fluorescence biosensors for ratiometric detection of cancer biomarkers. Theranostics 2018; 8: 3461-73.

[49] Ikeda E. Cellular response to tissue hypoxia and its involvement in disease progression. Pathol. Int. 2005; 55: 603-10.

[50] Isidro J, Borges V, Pinto M, Sobral D, Santos JD, Nunes A, *et al*. Phylogenomic characterization and signs of microevolution in the 2022 multi-country outbreak of monkeypox virus. Nat. Med. 2022; 28: 1569–72.

[51] Jarai BM, Stillman Z, Attia L, Decker GE, Bloch ED, Fromen CA, Evaluating UiO-66 metal–organic framework nanoparticles as acid-sensitive carriers for pulmonary drug delivery applications, ACS Appl. Mater. Interfaces. 2020; 12 (35): 38989–004.

[52] Ji W-J, Pei W-W, Wang Q-B, Liu G-F, Yan B, Yao S-Q, Zhai Q-G, Decoration of bare carboxyl group on the pore surface of metal-organic frameworks for high selective fluorescence Fe^{3+} detection. Journal of Solid State Chemistry 2019; 274: 18-25

[53] Jia Y, Zhou G, Wang X, Zhang Y , Li Z , Liu P, Yu B, and Zhang J, A metal-organic framework/aptamer system as a fluorescent biosensor for determination of aflatoxin B1 in food samples. Talanta, 2020; 219:121342-50

[54] Jo EJ, Byun JY, Mun H, Bang D, Son JH, Lee JY, Lee LP, Kim MG, Singlestep LRET aptasensor for rapid mycotoxin detection, Anal. Chem. 2018; 90:716–22.

[55] Jung HS, Verwilst P, Sharma A, Shin J, Sessler JL, Kim JS. Organic molecule-based photothermal agents: An expanding photothermal therapy universe. Chem. Soc. Rev. 2018; 47: 2280–97.

[56] Kang X M, Fan X Y, Hao P Y, Wang W M and Zhao B. A stable zinc–organic framework with luminescence detection of acetylacetone in aqueous solution. Inorg. Chem. Front., 2019; 6: 271–77.

[57] Kong J, Franklin N R, Zhou C, Chapline M G, Peng S, Cko K, *et al*. Nanotube molecular wires as chemical sensors. Science 2000; 287: 622−25.

[58] Kong XJ; Ji X; He T; Xie LH; Zhang YZ; Lv H, Ding C; Li JR. A Green-Emission Metal-Organic Framework-Based Nanoprobe for Imaging Dual Tumor Biomarkers in Living Cells. ACS Appl. Mater. Interfaces 2020; 12: 35375–84.

[59] Landgraf P, Rusu M, Sheridan R, Sewer A, N. Iovino, Aravin A. *et al.*, A Mammalian microRNA Expression Atlas Based on Small RNA Library Sequencing, Cell 2007; 129 : 1401-14.

[60] Lei B, Wang M, Jiang Z, Qi W, Su R, He Z, Constructing redox-responsive metal–organic framework nanocarriers for anticancer drug delivery, ACS Appl. Mater. Interfaces. 2018; 10 (19): 16698–706.

[61] Li DS, Wu Y P, Zhao J, Zhang J, Lu J Y. Metal-organic frameworks based upon non-zeotype 4-connected topology. Coord. Chem. Rev. 2014; 261: 1 −27.

[62] Li H, Feng X, Ma D, Zhang M, Zhang Y, Liu Y, *et al*. Stable aluminum metal-organic frameworks (Al-MOFs) for balanced CO_2 and water selectivity. ACS Appl. Mater. Interfaces. 2018; 10: 3160-63.

[63] Li L, Lv L and Huang RD. A series of coordination polymers based on terphenyl tetracarboxylates and bis-pyridyl ligands with water vapor sorption properties. RSC Adv. 2017; 7: 975-84.

[64] Li L, Shen S, Lin R, Bai Y. and Liu H. Rapid and specific luminescence sensing of Cu(II) ions with a porphyrinic metal-organic framework. Chem. commun. 2017; 53: 9986-89.

[65] Li S, Hu C, Chen C, Zhang J, Bai Y, Tan CS, Ming D. Molybdenum disulfide supported on metal–organic frameworks as an ultrasensitive layer for the electrochemical detection of the ovarian cancer biomarker CA125, ACS Appl. Bio Mater. 2021; 4 (7):5494–02.

[66] Liédana N, Galve A, Rubio C, Téllez C, Coronas J. CAF@ZIF-8: One-step encapsulation of caffeine in MOF. ACS Appl. Mater. Interfaces. 2012; 4: 5016–21.

[67] Lin Z H, Zhu G, Zhou Y S, Yang Y, Bai P., Chen J and Wang Z L, A self-powered triboelectric nanosensor for mercury ion detection Angew. Chem., Int. Ed., 2013; 52:5065–69.

[68] Liu C-S, Zhang Z-H, Chen M, Zhao H, Duan F-H, Chen D-M, *et al*. Pore modulation of zirconium–organic frameworks for high-efficiency detection of trace proteins.Chem. Commun. 2017: 53: 3941-44.

[69] Liu FH, Qin C, Ding Y, Wu H, Shao K Z, Su Z M. Pillared metal organic frameworks for the luminescence sensing of small molecules and metal ions in aqueous solutions. Dalton Trans. 2015; 44:1754−60.

[70] Liu G C, Li Y, Chi J, Xu N, Wang X L, Lin H Y and Chen Y Q. Multi-functional fluorescent responses of cobalt complexes derived from functionalized amide-bridged ligand. Dyes Pigm., 2020; 174, 108064.

[71] Liu J Q, Luo Z D, Pan Y, Singh A K, Trivedi M and Kumar A, Recent developments in luminescent coordination polymers: Designing strategies, sensing application and theoretical evidences. Coord. Chem. Rev., 2020; 406: 213145.

[72] Liu L-H, Qiu X-T, Wang Y-J, Shi Q, Sun Y-Q, Chen Y-P. NIR emission and luminescent sensing of a lanthanide–organic framework with Lewis basic imidazole and pyridyl sites. Dalton. Trans. 2017; 46: 12106-13.

[73] Lu K, He C, Lin W, A chlorin-based nanoscale metal–organic framework for photodynamic therapy of colon cancers, J. Am. Chem. Soc. 2015; 137 (24):7600–03.

[74] Lu Y, Yan B. and Liu J-L, Nanoscale metal–organic frameworks as highly sensitive luminescent sensors for Fe^{2+} in aqueous solution and living cells. Chem. Commun., 2014; 50: 9969-72.

[75] Luan Q, Xiong X, Gan N, Cao Y, Li T, Wu D, Dong Y and Hu F. A multiple signal amplified colorimetric aptasensor for antibiotics measurement using DNAzyme labeled Fe-MIL-88-Pt as novel peroxidase mimic tags and CSDP target-triggered cycles. Talanta, 2018; 187:27–34.

[76] Luo L, Zhang F, Chen C, Cai C,. Molecular imprinting resonance light scattering nanoprobes based on pH-responsive metal-organic framework for determination of hepatitis A virus. Mikrochim. Acta 2020; 187 (2): 140---

[77] Lustig W P, Mukherjee S, Rudd ND, Desai A V, Li J, Ghosh S K. Metal–organic frameworks: functional luminescent and photonic materials for sensing applications. Chem. Soc. Rev. 2017; 46: 3242-85

[78] Ma J X, Xu N, Liu Y, Wang Y, Li H., Liu G C, Wang X L and Li J R. A Stable 3D Zn-Coordination Polymer Sensor Based on Dual Luminescent Ligands for Efficient Detection of Multiple Analytes under Acid or Alkaline Environment. Inorg. Chem., 2020; 59: 15495–03.

[79] Mallory AC, Vaucheret H, Functions of microRNAs and related small RNAs in plants. Nat. Genet. 2006; 38(7): S31-36.

[80] Marieeswaran M. and Panneerselvam P, A magnetic nanoscale metal–organic framework (MNMOF) as a viable fluorescence quencher material for ssDNA and for the detection of mercury ions via a novel quenching–quenching mechanism. RSC Adv., 2020; 10: 3705–14.

[81] Márquez AG, Hidalgo T, Lana H, Cunha D, Blanco-Prieto MJ, Álvarez-Lorenzo C, *et al*. Biocompatible polymer–metal–organic framework composite patches for cutaneous administration of cosmetic molecules. J. Mater. Chem. B 2016; 4: 7031–40.

[82] Morris W, Doonan C J, Furukawa H, Banerjee R. and Yaghi O-M. Crystals as molecules: postsynthesis covalent functionalization of zeolitic imidazolate frameworks. J. Am. Chem. Soc. 2008; 130: 12626-27

[83] Mulfort K L, Farha O K, Stern C L, Sarjeant A A and Hupp J T. Post-synthesis alkoxide formation within metal-organic framework materials: a strategy for incorporating highly coordinatively unsaturated metal Ions. J. Am. Chem. Soc. 2009; 131: 3866-68.

[84] Munawar J, Khan M, Syeda S. E Z , Nawaz S, Janjhi F A, Haq H U *et al*. Metal-organic framework-based smart nanoplatforms for biosensing, drug delivery, and cancer theranostics, Inorg. Chem. Comm. 2023; 147: 110145-58.

[85] Nasrollahi M, Nabipour H, Valizadeh N, Mozafari M, The role of flexibility in MOFs metal-organic frameworks for biomedical applications, Elsevier, 2020; 93–110.

[86] Nazari M, Rubio-Martinez M, Tobias G, Barrio JP, Babarao R, Nazari F, Hill A J, Metal-organic-framework-coated optical fibers as light-triggered drug delivery vehicles. Adv. Funct. Mater. 2016; 26 (19): 3244–49.

[87] Orellana-Tavra C, Baxter EF, Tian T, Bennett TD, Slater NKH, Cheetham AK. Fairen-Jimenez D. Amorphous metal– organic frameworks for drug delivery. Chem. Commun. 2015; 51:13878–81.

[88] Osman D I, El-Sheikh S M, Sheta S M, Ali O I, Salem A M, Shousha WG, *et al*., Nucleic acids biosensors based on metal-organic framework (MOF): Paving the way to clinical laboratory diagnosis. Biosens. Bioelectron. 2019, 141, 111451.

[89] Pan Y, Zhan S, Xia F. Zeolitic imidazolate framework-based biosensor for detection of HIV-1 DNA. Anal. Biochem. 2018; 546: 5–9.

[90] Pastula DM, Tyler KL. An Overview of Monkeypox Virus and Its Neuroinvasive Potential. Ann. Neurol. 2022; 92:527–31.

[91] Pham H, Ramos K, Sua A, Acuna J, Slowinska K, Nguyen T, Tian F, Tuning crystal structures of iron-based metal–organic frameworks for drug delivery applications, ACS Omega. 2020; 5 (7): 3418–3427.

[92] Qin L, Lin LX, Fang ZP, Yang SP, Qiu GH, Chen JX, Chen WH. A waterstable metal-organic framework of a zwitterionic carboxylate with dysprosium: a sensing platform for Ebolavirus RNA sequences. Chem. Commun. 2016; 52 (1): 132–35.

[93] Que E L, Domaille D W and Chang C J. Metals in Neurobiology: Probing Their Chemistry and Biology with Molecular Imaging. Chem. Rev. 2008; 108: 4328.

[94] Rojas S, Carmona FJ, Maldonado CR, Horcajada P, Hidalgo T, Serre C, Barea E, Nanoscaled zinc pyrazolate metal–organic frameworks as drug-delivery systems, Inorg. Chem. 2016; 55 (5): 2650–2663.

[95] Rudd N D, Wang H, Fuentes-Fernandez E M A, Teat S J, Chen F, Hall G, *et al*. Highly Efficient Luminescent Metal–Organic Framework for the Simultaneous Detection and Removal of Heavy Metals from Water. ACS Appl. Mater. Interfaces, 2016; 8: 30294–03

[96] Schneemann A, Bon V, Schwedler I, Senkovska I, Kaskel S, Fischer RA, Flexible metal–organic frameworks., Chem. Soc. Rev. 2014; 43 (16): 6062–96.

[97] Sheta SM, El-Sheikh SM, Abd-Elzaher MM. A novel optical approach for determination of prolactin based on Pr-MOF nanofibers, Anal. Bioanal. Chem. 2019; 411 (7):1339–1349.

[98] Sheta SM; El-Sheikh SM, Abd-Elzaher MM; Salem SR, Moussa HA, Mohamed RM, Mkhalid I A. A novel biosensor for early diagnosis of liver cancer cases using smart nano-magnetic metal–organic framework. Appl. Organomet. Chem. 2019; 33: e5249.

[99] Shi B B, Zhong Y H, Guo L L, Li G, Two dimethylphenyl imidazole dicarboxylate-based lanthanide metal–organic frameworks for luminescence sensing of benzaldehyde. Dalton Trans., 2015; 44: 4362-69.

[100] Silva IM, Carvalho MA, Oliveira CS, Profirio DM, Ferreira RB, Corbi PP, Formiga A L, Enhanced performance of a metal-organic framework analogue to MIL-101 (Cr) containing amine groups for ibuprofen and nimesulide controlled release. Inorg. Chem. Commun. 2016; 70:47–50.

[101] Smith J K, Cywinski A, and Taylor J M, Initiation of plus-strand DNA synthesis during reverse transcription of an avian retrovirus genome. J. Virol., 1984, 49, 200–204.

[102] Su F, Zhang S, Ji H, Zhao H, Tian J-Y, Liu CS, *et al*., Two-Dimensional Zirconium-based Metal-Organic Framework Nanosheet Composites Embedded with Au Nanoclusters: a Highly Sensitive Electrochemical Aptasensor towards Detecting Cocaine. ACS Sens., 2017; 2(7): 998–05

[103] Su Y, Ni W, Zhang H, Jiang K, Wen F, One-pot synthesis of ICG&Cur@ ZIF-8 nanocomposites with pH-controlled drug delivery and good photothermal performance, Zeitschrift für anorganische und allgemeine Chemie 2022; 648 (9): e202100345.

[104] Sun W, Wang J, Zhang G. and Liu Z. A luminescent terbium MOF containing uncoordinated carboxyl groups exhibits highly selective sensing for Fe^{3+} ions. RSC Adv. 2014; 4: 55252-55.

[105] Takahashi-Makise N, Ward D M and Kaplan J. On the mechanism of iron sensing by IRP2: new players, new paradigms. Nat. Chem. Biol. 2009; 5: 874-75

[106] Tang T, Liu M, Chen Z, Wang X, Lai C, Ding L, Zeng C, Highly sensitive luminescent lanthanide metal–organic framework sensor for L-kynurenine, J. Rare Earths. 2022; 40 (3): 415–20.

[107] Titze T, Lauerer A, Heinke L, Chmelik C, Zimmermann N E R, Keil F J, *et al*. Transport in nanoporous materials including MOFs: the applicability of Fick's Laws. Angew. Chem. In. Ed., 2015; 54: 14580-83.

[108] Tseng T W, Luo T T, Chen S Y, Su C-C, Chi K M and Lu K L. Porous metal-organic frameworks with multiple cages based on tetrazolate ligands: synthesis, structures, photoluminescence, and gas adsorption properties. Cryst. Growth Des. 2012; 13: 510-517.

[109] V'kovski, Kratzel A, Steiner S, Stalder H, Thiel V. Coronavirus biology and replication: Implications for SARS-CoV-2. Nat. Rev. Microbiol. 2021; 19:155–70.

[110] Van H, Jeffrey F, Donald M, Thomas M. Jing X F, Wiers B M, *et al*. Ammonia capture in porous organic polymers densely functionalized with Brønsted acid groups. J. Am. Chem. Soc. 2014; 136: 2432-40.

[111] Vasconcelos IB, da Silva TG, Militao GC, Soares ˜ TA, Rodrigues NM, Rodrigues M O, Junior SA, Cytotoxicity and slow release of the anti-cancer drug doxorubicin from ZIF-8, RSC Adv. 2012; 2 (25): 9437–42.

[112] Vikrant K, Bhardwaj N, Bhardwaj SK, Kim K.-H, Deep A. Nanomaterials as efficient platforms for sensing DNA. Biomaterials 2019; 214: 119215

[113] Waldron KJ, Rutherford J C, Ford D, Robinson NJ. Metalloproteins and metal sensing. Nature. 2009; 460: 823−30.

[114] Wang FY, Han YM, Wang SM, Ye ZJ, Wei L, Xiao LH. Single-particle LRET aptasensor for the sensitive detection of aflatoxin B1 with upconversion nanoparticles, Anal. Chem. 2019; 91: 11856–11863.

[115] Wang H, Jian Y, Kong Q, Liu H, Lan F, Liang L, Ge S, Yu J, Ultrasensitive electrochemical paper-based biosensor for microRNA via strand displacement reaction and metal-organic frameworks. Sens. Actuators, B 2018; 257: 561-69.

[116] Wang L, Hou C, Yu H, Zhang Q, Li Y, Wang H. Metal–organic framework-derived nickel/cobalt-based nanohybrids for sensing non-enzymatic glucose. ChemElectroChem 2020; 7: 4446–52.

[117] Wang M, Guo L, Cao D, Amino-functionalized luminescent metal–organic framework test paper for rapid and selective sensing of SO2 gas and its derivatives by luminescence turn-on effect, Anal. Chem. 2018; 90:3608–14.

[118] Wang Q-S, Li J-J, Zhang M-N, Li X, A luminescent Eu(III)-based metal-organic framework as a highly effective sensor for cation and anion detections Sensors and Actuators B: Chemical, 2017; 258:358-64.

[119] Wang X, Fan W, Zhang M, Shang Y, Yutong W, Liu D *et al.*, Ligand controlled structure of cadmium(II) metal-organic frameworks for fluorescence sensing of Fe^{3+} ion and nitroaromatic compounds, Chin. Chem. Lett. 2019; 30:801–05

[120] Wang Y, Chen H., Wu Y, Ge H, Ye G and Hu X. Metal–organic frameworks and β-cyclodextrin-based composite electrode for simultaneous quantification of guanine and adenine in a lab-on-valve manifold. Analyst, 2014; 139: 6197–03.

[121] Wang Y, Ge H, Ye G, Chen H, Hu X, Carbon functionalized metal organic framework/Nafion composites as novel electrode materials for ultrasensitive determination of dopamine. J. Mater. Chem. B 2015; 3: 3747-53

[122] Wang Y, Li Y., Zhuang X, Tian C, Fu X, Luan F. Ru $(bpy)_3^{2+}$ encapsulated cyclodextrin based metal organic framework with improved biocompatibility for sensitive electrochemiluminescence detection of CYFRA21-1 in cell, Biosens. Bioelectron. 2021; 190: 113371.

[123] Wang Y, Zhang Y, Sha H, Xiong X, and Jia N., Design and Biosensing of a Ratiometric Electrochemiluminescence Resonance Energy Transfer Aptasensor between a g-C3N4 Nanosheet and Ru@MOF for Amyloid-β Protein. ACS Appl. Mater. Interfaces, 2019; 11: 36299–306.

[124] Wang Z, Fu Y, Kang Z, Liu X, Chen N, Wang Q, Ling D., Organelle-specific triggered release of immunostimulatory oligonucleotides from intrinsically coordinated DNA–metal–organic frameworks with soluble exoskeleton. J. Am. Chem. Soc. 2017; 139 (44):15784–91.

[125] Wei X. Fluorescence biosensor for the H_5 N_1 antibody based on a metal–organic framework platform. J. Mater. Chem. B 2013; 1(13): 1812–1817.

[126] Wen GX, Wu Y P, Dong W W, Zhao J, D. S. Li, and Zhang J. An Ultrastable Europium(III)–organic framework with the capacity of discriminating Fe^{2+}/Fe^{3+} ions in various solutions. Inorg. Chem. 2016; 55:10114-17.

[127] Wu B, Fu J, Zhou Y, Luo S, Zhao Y, Quan G, Pan X, Wu C. Tailored core-shell dual metal-organic frameworks as a versatile nanomotor for effective synergistic antitumor therapy. Acta Pharm. Sin. B 2020; 10: 2198–11.

[128] Wu L, Ding F, Yin WM, Ma J, Wang BR, Nie A, Han HY. From electrochemistry to electroluminescence: development and application in a ratiometric aptasensor for aflatoxin B1, Anal. Chem. 2017; 89:7578–85.

[129] Wu S, Min H, Shi W, Cheng P, Multicenter metal-organic framework-based ratiometric fluorescent sensors, Adv. Mater. 2020; 32: 1805871

[130] Wu Y, Han J, Xue P, Xu R, and Kang Y. Nano metal–organic framework (NMOF)-based strategies for multiplexed microRNA detection in solution and living cancer cells. Nanoscale, 2015; 7:1753-59

[131] Wu Y, Wu J, Luo Z-D, Wang J, Li Y-L, Han Y-Y and Liu J-Q. Fluorescence detection of Mn^{2+}, $Cr_2O_7^{2-}$ and nitroexplosives and photocatalytic degradation of methyl violet and rhodamine B based on two stable metal–organic frameworks. RSC Adv., 2017; 7: 10415–23.

[132] Xie BP, Qiu GH, Hu PP, Liang Z, Liang YM, Sun B, Bai LP, Jiang ZH, Chen JX. Simultaneous detection of Dengue and Zika virus RNA sequences with a three-dimensional Cu-based zwitterionic metal–organic framework, comparison of single and synchronous fluorescence analysis. Sensor. Actuator. B Chem. 2018; 254:1133–40.

[133] Xie HL, Wang XP, Zhang LX, Wang T, Zhang W, Jiang J, *et al*. Monitoring metabolite production of aflatoxin biosynthesis by orbitrap fusion mass spectrometry and a D-optimal mixture design method, Anal. Chem. 2018; 90:14331–14338.

[134] Xu Q-Y, Tan Z , Liao X-W, Wang C. Recent advances in nanoscale metal-organic frameworks biosensors for detection of biomarkers. Chin. Chem. Lett. 2022; 33(1):, 22-32

[135] Xu R, Wang Y, Duan X, Lu K, Micheroni D, Hu A, and Lin W, Nanoscale metal-organic frameworks for ratiometric oxygen sensing in live cells. J Am. Chem. Soc, 2016; 138(7): 2158–61.

[136] Xu W, Jiao L, Yan H, Wu Y, Chen L, Gu W, *et al*. Glucose oxidase-integrated metal-organic framework hybrids as biomimetic cascade nanozymes for ultrasensitive glucose biosensing, ACS Appl. Mater. Interfaces. 2019; 11:22096.

[137] Yan Y-T, Liu J, Yang G-P, Zhang F, Fan Y-K, Zhang W-Y and Wang Y-Y, Highly selective luminescence sensing for the detection of nitrobenzene and Fe^{3+} by new Cd(II)- based MOFs. Cryst. Eng. Comm, 2018; 20: 477-86.

[138] Yang C, Xu, J, Yang D, Wang X, Liu B, He N, Wang Z. ICG@ZIF-8: One-step encapsulation of Indocyanine Green in ZIF-8 and use as a therapeutic nanoplatform. Chin. Chem. Lett. 2018; 29: 1421–24.

[139] Yang D, Lu L, Feng S and Zhu M. First Ln-MOF as a trifunctional luminescent probe for the efficient sensing of aspartic acid, Fe^{3+} and DMSO. Dalton Trans., 2020; 49: 7514–24.

[140] Yang S-P, Chen S-R, Liu S-W, Tang X-Y, Qin L, Qiu G.-H, *et al*. Platforms formed from a three-dimensional cu-based zwitterionic metal-organic framework and probe ss-DNA: selective fluorescent biosensors for human immunodeficiency Virus1 ds-DNA and Sudan virus rna sequences. Chen, Anal. Chem. 2015; 87: 12206–14.

[141] Yang SP, Chen SR, Liu SW, Tang XY, Qin L, Qiu GH, Chen JX, Chen WH., Platforms formed from a three-dimensional Cu-based zwitterionic metal–organic framework and probe ss-DNA: selective fluorescent biosensors for human immunodeficiency virus 1 ds-DNA and Sudan virus RNA sequences. Anal. Chem. 2015; 87 (24): 12206–14.

[142] Yao, L, Tang Y, Cao W, Cui YY, Qian G. Highly efficient encapsulation of doxorubicin hydrochloride in metal–organic frameworks for synergistic chemotherapy and chemodynamic therapy. ACS Biomater. Sci. Eng. 2021; 7: 4999–006.

[143] Ye R P, Zhang X, Zhang L, Zhang J. and Yao YG. Solvent and pH driven self-assembly of isomeric or isomorphic complexes: crystal structure and luminescent change upon desolvation. Cryst. Growth Des. 2016; 16: 4012-20.

[144] Ye T, Liu Y, Luo M, Xia X, Ji X, Zhou G, and He Z. Metal–organic framework-based molecular beacons for multiplexed DNA detection by synchronous fluorescence analysis. Analyst, 2014; 139: 1721-25.

[145] Yola ML, Sensitive sandwich-type voltammetric immunosensor for breast cancer biomarker HER2 detection based on gold nanoparticles decorated Cu-MOF and Cu_2ZnSnS_4 NPs/Pt/g-C_3N_4 composite. Microchim. Acta. 2021; 188 (3): 1–13.

[146] Yue Z F, Chen Z N, Yao M J, Wang H L and Li G, RSC Adv. 2014; 4: 33537-40.

[147] Zhang HJ, Fan R Q, Chen W, Fan J Z, Dong Y W, Song Y, *et al*., Cryst. Growth Des., 2016; 16: 5429-40.

[148] Zhang H-T, Zhang J-W, Huang G, Dub Z-Yand Jiang H-L, Chem. Commun., 2014; 50: 12069-71.

[149] Zhang J., Zhao L, Liu Y, Li M, Li G and Meng X. Two luminescent transition-metal−organic frameworks with predesigned ligand as highly sensitive and selective iron(III) sensors. New J. Chem., 2018; 42: 6839-47.

[150] Zhang N, Yan L, Lu Y, *et al.*, Metal-organic frameworks-derived hierarchical ZnO structures as efficient sensing materials for formaldehyde detection, Chin. Chem. Lett. 2020; 31: 2071–76.

[151] Zhang S, Pei X, Gao H, Chen S, Wang J, Metal-organic framework-based nanomaterials for biomedical applications, Chin. Chem. Lett. 2020; 31:1060–70

[152] Zhang X, Fang L, Jiang K, He H, Yang Y, Cui Y, Qian G, Nanoscale fluorescent metal–organic framework composites as a logic platform for potential diagnosis of asthma, Biosens. Bioelectron. 2019; 130: 65–72.

[153] Zhao HQ, Qiu GH, Liang Z, Li MM., Sun B, Qin L,*et al*. A zinc(II)-based two-dimensional MOF for sensitive and selective sensing of HIV-1 ds-DNA sequences. Anal. Chim. Acta 2016; 922: 55–63.

[154] Zhao HQ, Yang SP., Ding NN, Qin L, Qiu GH., Chen JX., *et al*. Dalton Trans. 2016; 45: 5092–100.

[155] Zhao J, Wang YN, Dong WW, Wu Y P, Li DS, Liu B, Zhang QC. A new surfactant-introduction strategy for separating the pure single-phase of metal–organic frameworks. Chem. Commun. 2015; 51: 9479 −82.

[156] Zhao J, Wang Y-N, Dong W-W, Wu Y-P, Li D-S, and Zhang Q-C, A robust luminescent Tb(III)-MOF with lewis basic pyridyl sites for the highly sensitive detection of metal ions and small molecules. Inorg.Chem. 2016; 55(7): 3265–3271

[157] Zheng Y H, Tan C L, Wang Q M, Zhang CC, 2-(3-Pyridyl)imidazole-4,5-dicarboxylic acid based lanthanide luminescent anion sensor. Solid State Sci. 2011; 13: 1687-91.

[158] Zhou Y, Chen H-H and Yan B, An Eu^{3+} post-functionalized nanosized metal–organic framework for cation exchange-based Fe^{3+}-sensing in an aqueous environment. J. Mater. Chem. A, 2014; 2: 13691-97.

[159] Zhou Z, Wang Y, Peng F, Meng F, Zha J, Ma L, Zhang Q. IntercalationActivated Layered MoO3 Nanobelts as Biodegradable Nanozymes for TumorSpecific Photo-Enhanced Catalytic Therapy. Angew. Chem. 2022; 134 (16): e202115939.

[160] Zhu Q, Chen Y, Wang W, Zhang H, Ren C, Chen H, Chen X, A sensitive biosensor for dopamine determination based on the unique catalytic chemiluminescence of metal–organic framework HKUST-1. Sens. Actuators, B 2015; 210: 500–07.

[161] Zhu X, Zheng H, Wei X, Lin Z, Guo L, Qiu B, Chen G. Metal–organic framework (MOF): a novel sensing platform for biomolecules. Chem. Commun. 2013; 49 (13): 1276–78.

[162] Zhuang J, Kuo C H, Chou L Y, Liu D Y, Weerapana E, Tsung C K, Optimized Metal–Organic-Framework Nanospheres for Drug Delivery: Evaluation of Small-Molecule Encapsulation. ACS Nano 2014; 8:2812-19.