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## Review

## Design and sensing applications of metal–organic framework composites



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## ABSTRACT

As crystalline molecular materials, metal–organic frameworks (MOFs) have unique chemical and physical properties, such as ultrahigh porosity, tunable structure, and high thermal and chemical stability. These characteristics make MOFs suitable for use in gas storage, separation, catalysis, biomedical imaging and sensing. Precise chemical modifications can especially endow MOFs with specific functions and offer the possibility of designing a new generation of sensing devices. This article focuses on the design of functional MOFs and signal-transduction strategy, including optical, electrochemical, mechanical, and photoelectrochemical schemes, for analytical applications in detection of solvent molecules, metal ions, DNA, proteins, and other important biomolecules.

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## 1. Introduction

As crystalline molecular materials, metal–organic frameworks (MOFs) are formed by association of metal centers or clusters and organic linkers, and offer unique chemical properties with an unprecedentedly large and permanent inner porosity. Moreover, these MOF structures are extremely versatile through the design of the architecture and functionalization of the framework [1–3]. Designed MOFs have shown promising applications in catalysis,

separation, gas storage, biomedical imaging, and drug delivery. Recently, several investigators have begun exploring the potential of MOFs as chemical sensors. The exceptional tunability of MOF structures and properties should constitute an important advantage over other conventional chemo-sensory materials. Therefore, MOF-based sensors have significant potential for developing powerful analytical techniques for the determination of biomolecules in clinical, environmental, and industrial applications.

To achieve specific molecular recognition, the MOFs need additional functionalities. Three different strategies have been identified to modify MOFs easily and endow them with specific functions:

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- the first method is to modify specific organic ligands or dope metal ions in the frame of the MOFs (e.g., lanthanide metal ions are employed as dopants to construct luminescent MOFs for optical sensing) [4];
- the second strategy is post-synthesis modification (PSM), in which the organic linkers with functional groups can be used for subsequent chemical grafting; Kurmoo et al. designed a trifunctional (carboxylate, imidazolite, and hydroxyethyl groups) tag for preparing a single-crystal MOF, and, after dehydration, two consecutive PSMs of elimination and bromination were realized for improving the gas uptake of the MOF [5]; and,
- the third approach is to entrap functional molecules and nanoparticles (NPs) within the framework, whose composites possess multifunctionalities for molecular recognition and signal transduction.

In principle, any changes of MOF properties depending on the guest could be measured as a sensing signal. On the basis of signal transduction, MOF-based sensors are categorized into four types: optical, electrochemical, mechanical, and photoelectrochemical.

It is not surprising that a large number of MOFs have been found to be photoluminescent because the linkers in most MOFs contain aromatic sub-units with luminescent emission. Interestingly, a chiral porous MOF system has been successfully devised for enantioselective fluorescence sensing of chiral amino alcohols with an enantiomeric quenching ratio of 3.12 due to steric confinement of the MOF cavity [6]. Although electrochemical methods have rarely been explored for MOFs due to the insulating properties of the majority of MOFs, the development of conductive MOFs is currently under way by hybridizing with nanomaterials based on carbon and metals [7].

MOF-based mechanical sensors, including surface-acoustic wave (SAW), quartz-crystal microbalance (QCM), and microcantilever devices, are appealing for their advantages of miniaturization and multiplexing. Most recently, a photoelectrochemical strategy was also introduced for the construction of MOF-based sensing devices.

This review highlights the recent advances in MOFs as chemical sensors and biosensors. We briefly examine the design and the functionalization of MOFs with many molecules through dopant modification, post-synthesis methods (PSMs), and entrapping functional NPs (Fig. 1). By incorporating appropriate signal-transduction capabilities, a series of MOF-based sensors, including optical, electrochemical, mechanical, and photoelectrochemical schemes, are summarized for their analytical applications in the selective detection of solvent molecules, metal ion, DNA, protein, and other biologically important targets.

## 2. Design and functionalization of MOFs

### 2.1. Design of MOFs

In general, MOFs are synthesized through the coordination of polydentate-bridging ligands with inorganic centers, which forms

well-defined, low-density networks. Based on the different molecular functionalities and architectures of various ligands and inorganic nodes, the MOFs demonstrate unique chemical and physical properties. Thus, design of specific ligands and doping metal ions in the frame became popular methods for functionalization of MOFs. Typically, Ir, Re, and Ru complexes with dicarboxylic acid functionalities have been incorporated catalytically into a highly stable, porous  $Zr_6O_4(OH)_4(\text{bpdc})_6$  (UiO-67, bpdc = *para*-biphenyldicarboxylic acid) framework using a mix-and-match synthesis strategy. These doped MOFs are highly effective catalysts for water oxidation,  $\text{CO}_2$  reduction, and organic transformations [8]. Doping small amounts of  $\text{Ru}^{\text{II}}$  into a ultramicroporous, fluorescent  $\text{Zn}^{\text{II}}$  coordination polymer produced phosphorescent materials with highly tunable oxygen-quenching efficiency, and were employed to construct a simple, color-changing, ratiometric oxygen sensor [9].

The expansion of organic linkers also provides the possibility of giving MOFs various functionalities. For example, a chiral anionic MOF has been rationally constructed by means of a predesigned size-extended hexatopic ligand, namely, 5,5'-triazine-2,4,6-triyl)tris-(azanediyl)trisophthalate. The luminescence intensity of the designed MOF is significantly enhanced in toluene and benzene, while quenching effects are observed in acetone and ethanol, providing a potential application for luminescent probes [10].

A porous, iron-based MOF, MMPF-6, has been constructed by self-assembly of iron(III) *meso*-tetrakis(4-carboxyphenyl)porphyrin chloride with  $Zr_6O_8(\text{CO}_2)_8(\text{H}_2\text{O})_8$  generated *in situ* under solvothermal conditions. MMPF-6 shows interesting peroxidase activity, comparable to that of heme protein myoglobin [11].

Rosseinsky and co-workers successfully assembled the peptide-based colorless crystals of  $[\text{Zn}(\text{Gly-Thr})_2] \cdot \text{CH}_3\text{OH}$  via the reaction of zinc nitrate and Gly-Thr in a methanolic solution [12]. This peptide-based MOF exhibited selective adsorption of  $\text{CO}_2$  in preference to  $\text{CH}_4$ .

These research efforts open the door to the design of an advanced generation of biomimetic materials for bioanalysis applications.

### 2.2. Functionalization of MOFs by post-synthesis methods

Once the building blocks (ligands and inorganic nodes) for the framework construction are selected, additional functionalities can be imparted to the porous crystals by PSM via chemical reaction [13]. As shown in Fig. 2, when the reaction involves a covalent bond of the organic linker, it is termed a covalent PSM. The concept of post-synthesis deprotection (PSD) is that a protecting group is first introduced onto an organic linker. After the linker is incorporated into a MOF under standard solvothermal conditions, the protecting group is removed in a post-synthesis fashion to reveal the desired functionality.

Covalent PSM has proved to be a powerful, versatile method for introducing a broad range of chemical groups into MOFs. For example, amino, bromo, nitro, and naphthalene-functionalized UiO-66 MOFs have been synthesized through reticular chemistry to generate new, functionalized frameworks via PSM [14]. A

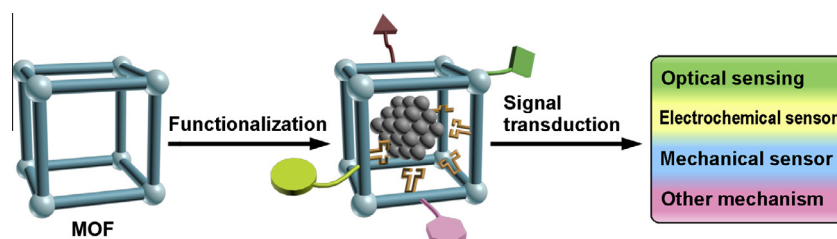


Fig. 1. Functionalization and signal transduction of metal-organic framework (MOF)-based composites for sensing applications.

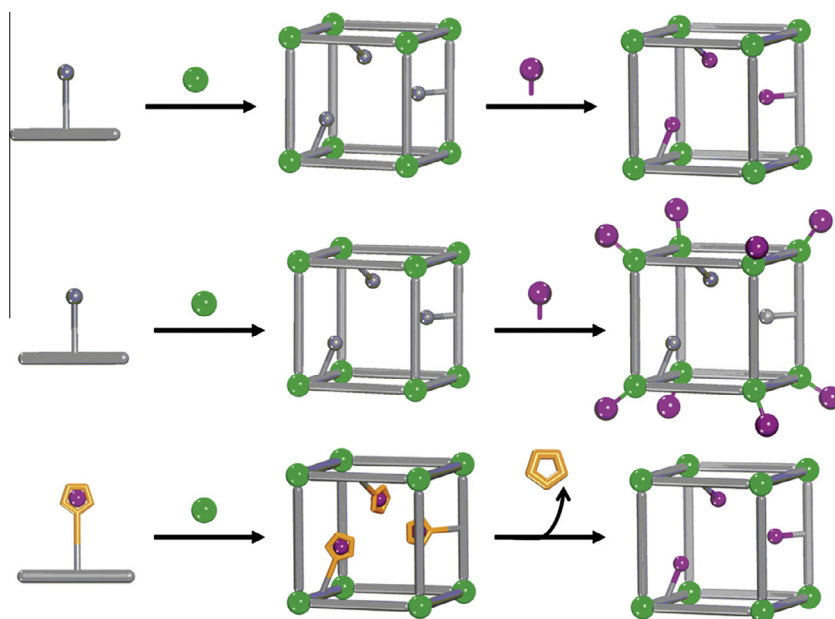


Fig. 2. Generic schemes for covalent PSM, dative PSM, and PSD (Reprinted from [13] with permission from ACS Publications).

composite material has been successfully prepared using an amino-containing MOF as a new type of host-matrix material to anchor hemin and to simulate the peptidic microenvironment of the native peroxidase [15]. It exhibits peroxidase-like activity through catalytic oxidation of the peroxidase substrate 3,3,5,5-tetramethylbenzidine in the presence of  $\text{H}_2\text{O}_2$ , producing a blue-colored solution. The analytical platform for glucose detection shows a linear range of 0.01–0.3 mM [16]. The advantages of amino-acid-based MOFs as biomimetic catalysts extend the applications of MOFs in biosensing.

When vacant coordination sites at the metal are available, the dative PSM can be accomplished as follows:

- (1) replacement of cationic guests with metal cations;
- (2) exchange of a hydroxy proton for a  $\text{Li}^+$  ion;
- (3) chemical reduction with Li;
- (4) cooperative addition of metal salts to anion and cation binding sites [17].

The interesting example is the PSM of HKUST-1 ( $[\text{Cu}_3(\text{TMA})_2(\text{H}_2\text{O})_3]_n$ ), in which the aqua ligands can be replaced by pyridines to generate HKUST-1 derivative that cannot be directly synthesized by solvothermal methods [18]. Compared with conventional PSM, the PSD model has proved to be a distinct, useful approach for modifying MOFs.

### 2.3. Entrapment of nanoparticles within the framework

The alternative functionalization method is to combine functional NPs into MOF architectures, to create advanced composite materials with multiple properties (luminescent, magnetic, and catalytic). A carbon nanotube (CNT)-MOF was synthesized by incorporating CNTs into  $[\text{Cu}_3(\text{C}_9\text{H}_3\text{O}_6)_2(\text{H}_2\text{O})_3] \cdot x\text{H}_2\text{O}$  ( $[\text{Cu}_3\text{-(BTC)}_2$ , BTC = 1,3,5-benzenetricarboxylate). Due to its open metal sites and high thermal stabilities, and its sorption properties, the hybrid shows highly effective  $\text{CO}_2$  and  $\text{CH}_4$  uptakes that are increased by about 305% and 200%, respectively, compared to the unmodified MOF [19].

Hybrid composites based on MOFs and graphene enable integration of the unique properties of these two fascinating materials. For example, a nanocomposite material was assembled with azobenzene-functionalized graphene oxide (GO) and stilbene-MOF. This unique system displayed selectivity to dinitrotoluene (71% quenching) over trinitrotoluene (20% quenching) with sub-ppm sensitivity and response times of less than 1 min [20]. A tunable hybrid of GO and zeolitic imidazolate frameworks (ZIF-8) was also prepared via direct growth of ZIF-8 nanocrystals on the GO surface [21]. The GO@ZIF-8 nanocomposites obtained had tunable surface areas and pore volumes depending on the proportion of GO.

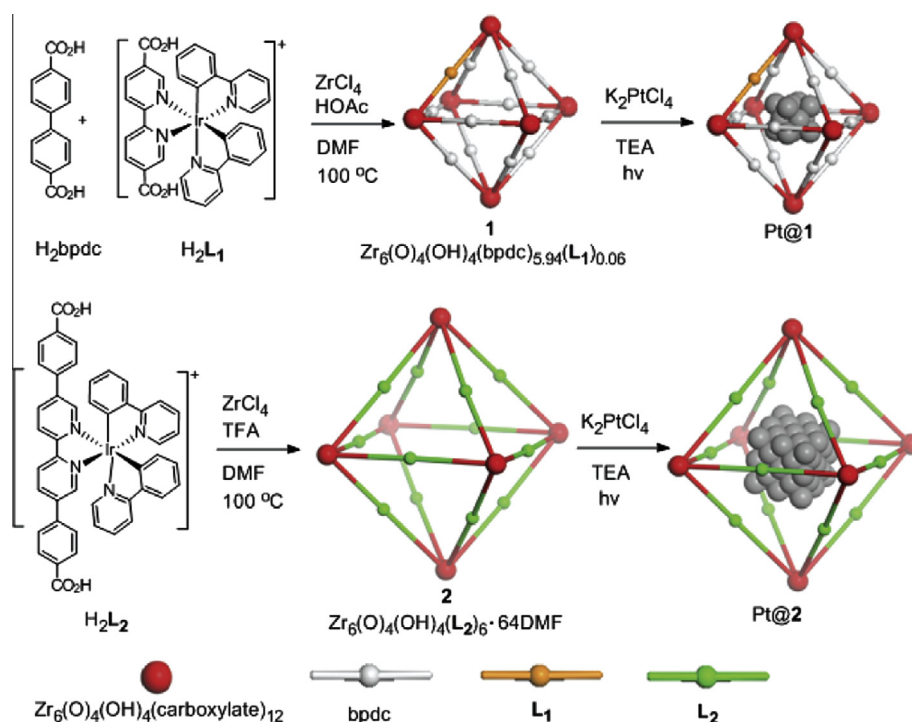
A PtNP@photoactive MOF nanohybrid was designed by *in-situ* loading PtNPs into the cavities of MOFs (**1** and **2**) built from  $[\text{Ir}(\text{ppy})_2(\text{bpy})]^+$ -derived dicarboxylate ligands (**L1** and **L2**) and secondary building units of  $\text{Zr}_6(\mu_3\text{-O})_4(\mu_3\text{-OH})_4(\text{carboxylate})_{12}$ , via MOF-mediated photoreduction of  $\text{K}_2\text{PtCl}_4$  (Fig. 3). The resulting Pt@MOF **2** assemblies could serve as effective photocatalysts for hydrogen evolution with a turnover number of 7000 due to synergistic photoexcitation of the MOFs and electron injection into the PtNPs [22].

Further, AuNi-alloy NPs were immobilized to a chromium-based MOF (MIL-101) with size and location control by the double-solvent method combined with a liquid-phase concentration-controlled reduction strategy [23]. The ultrafine AuNi-alloy NPs inside the mesoporous MIL-101 showed high activity for hydrogen generation from the catalytic hydrolysis of ammonia borane.

A new class of nanocomposites with a silica shell and a MOF core ( $\text{Ln}(\text{BDC})_{1.5}(\text{H}_2\text{O})_2$ ), where Ln =  $\text{Eu}^{3+}$ ,  $\text{Gd}^{3+}$ , or  $\text{Tb}^{3+}$  and BDC = 1,4-benzenedicarboxylate, was synthesized using a reverse microemulsion system. These shells increased MOF core stability and allowed for the controlled release of metal constituents. The silica-coated MOFs could be further functionalized for the luminescence sensing of dipicolinic acid [24].

Incorporation of highly luminescent core-shell quantum dots (QDs) within a MOF was achieved through a one-pot method [25]. The resulting QD@MOF-5 composites effectively preserved the fluorescence characteristics of the QD emitters.

Hupp et al. reported the functionalization of porphyrin-based MOFs with CdSe/ZnS core/shell QDs for the enhancement of light



**Fig. 3.** Synthesis of phosphorescent Zr-carboxylate metal–organic frameworks (MOFs) (1 and 2) and subsequent loading of Pt nanoparticles inside MOF cavities via MOF-mediated photoreduction of  $K_2PtCl_4$  to form the Pt@1 and Pt@2 assemblies (Reprinted from [22] with permission from ACS Publications).

**Table 1**  
Selected examples of metal–organic frameworks (MOFs) for sensing applications

MOF formula	Mechanism of detection	Analytes	Linear range/ DL	Ref.
MIL-53(Al)	Fluorescence quenching based on cation exchange	$Fe^{3+}$	3–200 $\mu M$ 0.9 $\mu M$	[32]
$H_2dtoaCu$	Fluorescence recovery after forming a rigid triplex structure	DNA	4–200 nM 1.3 nM	[36]
Adenine-based lanthanide MOF	Fluorescence enhancement via suppression of the PET process by coordination of $Hg^{2+}$ with adenine	$Hg^{2+}$	0.2–100 nM 0.2 nM	[38]
UiO-66	Visual detection (Olive green)	$Bi^{3+}$	0.95–470 nM 5.31 nM	[33]
Fe-MIL-88NH <sub>2</sub>	Colorimetric method using MOF as peroxidase mimic	Glucose	2.0–300 $\mu M$ 0.48 $\mu M$	[15]
ZIF-70	Two-electron reduction of methylene green into leucomethylene green	Glucose	0.1–2 mM Not available	[43]
MWCNTs@Cu <sub>3</sub> (BTC) <sub>2</sub>	Differential pulse anodic stripping voltammetry in a lab-on-valve format	$Pb^{2+}$	1–50 nM 0.79 nM	[44]
Au-SH-SiO <sub>2</sub> @Cu-MOF	Electrocatalytic oxidation	L-cysteine	0.02–300 $\mu M$ 8.0 nM	[46]
Au-SH-SiO <sub>2</sub> @Cu-MOF	Electrocatalytic oxidation	hydrazine	0.04–500 $\mu M$ 0.01 $\mu M$	[47]
SWNT@Zn MOF	Electrochemical reduction	Methyl parathion	0.034–6.9 $\mu M$ 7.9 nM	[45]
ZIF-8 film	Refractive index	Ethanol	Not available 100 ppm	[39]
Fe-BTC	Impedance	Water	0 to 2.5 vol% Not available	[42]

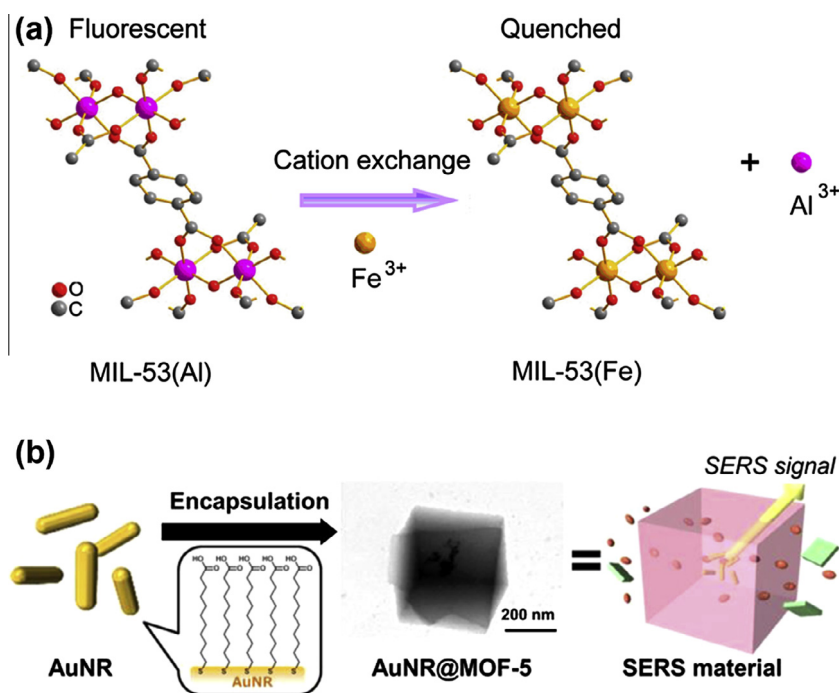
harvesting. Time-resolved emission demonstrated that photoexcitation of the QDs was followed by energy transfer to the MOFs with efficiencies of more than 80% [26].

### 3. Sensing applications

#### 3.1. Optical sensors

Optical MOFs have received great attention in sensing applications, (Table 1) because the linkers in most MOFs contain aromatic

sub-units for luminescent emission, UV or visible adsorption. A visible color change of material, such as solvatochromism, is one of the simplest, most powerful sensing strategies. For example, a nanotubular MOF,  $\{[(WS_4Cu_4)I_2(dptz)_3] \cdot DMF\}_n$  ( $dptz = 3,6$ -di-(pyridin-4-yl)-1,2,4,5-tetrazine,  $DMF = N,N$ -dimethylformamide) was presented for sensing small solvent molecules. When accommodating different solvent molecules as guests, the resulting inclusion compounds exhibited different colors depending on the solvent guests, showing a new way of signal transduction as a new kind of sensor [27].



**Fig. 4.** (a) The cation exchange mechanism for the use of MIL-53(Al) as a fluorescent probe for sensing Fe<sup>3+</sup> (Reprinted from [32] with permission from ACS Publications). (b) AuNR@MOF-5 as suspension-based SERS sensor (Reprinted from [40] with permission from ACS Publications).

The majority of MOF sensors are based on luminescence quenching of lanthanide ions (Ln<sup>3+</sup>) or aromatic fluorophores. A prototype luminescent MOF (MOF-76) exhibited high-sensitivity sensing with respect to fluoride. The mechanism of MOF-76 for recognition and sensing of anions is to make use of O–H moieties within the terminal solvents for their recognition of anions [28].

Chen et al. reported the example of microporous Eu(BTC), which made use of luminescent open Eu<sup>3+</sup> sites for sensing small molecules [29]. To make use of the preferential binding of Ln<sup>3+</sup> to carboxylate oxygen atoms over pyridyl nitrogen atoms in Ln<sup>3+</sup>–pyridine–carboxylate complexes, the same group designed luminescent MOFs, [Eu(pdc)<sub>1.5</sub>(dmf)]·(DMF)<sub>0.5</sub>(H<sub>2</sub>O)<sub>0.5</sub> (pdc = pyridine-3,5-dicarboxylate), with Lewis basic pyridyl sites for the sensing of metal ions [30]. A dual functional luminescent sensor based on luminescent MOF [Zn<sub>3</sub>(TDPAT)·(H<sub>2</sub>O)<sub>3</sub>] [TDPAT = 2,4,6-tris(3,5-dicarboxyl phenylamino)-1,3,5-triazine] was also designed for quantitative detection of the concentration of nitrobenzene and temperature [31].

Several mechanisms have been explored for luminescent MOFs to sense metal ions on the basis of metal–ligand coordination interactions (weak binding of metal ions to heteroatom (N or O) within the ligands) and intramolecular energy transfer from the ligand to metal ion. A fluorescent MIL-53(Al) was designed for highly selective, sensitive detection of Fe<sup>3+</sup> in aqueous solution [32]. As shown in Fig. 4a, the cation exchange between Fe<sup>3+</sup> and the framework metal ion Al<sup>3+</sup> in MIL-53(Al) led to quenching of the fluorescence of MIL-53(Al) due to the transformation of strong-fluorescent MIL-53(Al) to weak-fluorescent MIL-53(Fe). The linear range and limits of detection (LODs) are 3–200 μM and 0.9 μM, respectively. The method developed can be applied to the determination of Fe<sup>3+</sup> in human urine samples with the quantitative spike recoveries of 98.2–106.2%.

Azzazy et al. constructed a highly sensitive UiO-66 sensor for simple, simultaneous colorimetric detection of toxic heavy-metal ions, such as Bi(III), Pb(II), Zn(II), Hg(II) and Cd(II) ions, in aquatic samples with the naked eye. The sensor displayed a wide range of detectable metal analytes up to 10<sup>−10</sup> M with a rapid response

[33]. A highly specific, distinct color change in the crystals of a MOF with pendant allyl thioether units in response to Pd species was discovered for colorimetric detection and quantification of Pd(II) ions [34].

In MOFs, the ligands usually contain a conjugated π-electron system, allowing for binding single-stranded DNA molecules. Hence, MOFs may have an ability similar to carbon nanostructures for quenching fluorescence. A MOF, *N,N'*-bis(2-hydroxyethyl) dithiooxamidatocopper(II) [Cu(H<sub>2</sub>dtoa)], was introduced as a sensing platform for the detection of biomolecules, which acted to absorb probe DNA and to quench fluorescence from FAM by photoinduced electron transfer (PET). The sensing method for target DNA showed a linear relationship in the range 10–100 nM with an LOD of 3 nM. For thrombin, the fluorescence intensity was found to be linear with the logarithm of thrombin concentration in the range 5–100 nM with an LOD of 1.3 nM [35]. Further, a cost-efficient, simple, sensitive fluorescent biosensor was successfully developed for HIV DNA based on triplex-DNA technology with an LOD of 1.3 nM [36]. Coupling the protection of H5N1 antibody against the hydrolysis of Exo I, the fluorescent biosensor was applied to detect the H5N1 antibody in the range 1.0 μM–5.0 nM with an LOD of 1.6 nM [37].

A turn-on fluorescent biosensor was prepared on the basis of adenine-based lanthanide coordination polymer NPs (CPNPs), which comprised adenine, terbium ion (Tb<sup>3+</sup>), and dipicolinic acid (DPA) as an auxiliary linking molecule that can sensitize the fluorescence of Tb<sup>3+</sup>. The fluorescence of the CPNPs was very weak due to the existence of PET from adenine to DPA. However, in the presence of Hg<sup>2+</sup>, significant enhancement in the fluorescence of CPNPs was observed because of the suppression of the PET process by the coordination of Hg<sup>2+</sup> with adenine. As a kind of Hg<sup>2+</sup> nanosensor, the CPNPs exhibited excellent selectivity and ultra-high sensitivity up to the 0.2 nM LOD [38].

Different from luminescence and solvatochromic measurements, other optical methods, such as interferometry, surface-enhanced Raman scattering (SERS) and localized surface-plasmon resonance (LSPR) spectroscopy, do not involve absorption or

emission of light by the MOF. Lu and Hupp developed a MOF-based Fabry-Pérot device by growing micrometer-thick homogeneous ZIF-8 films on a silicon substrate. By monitoring shifts of the interference peaks in the transmission spectrum, the ZIF-8 based sensor could respond to ethanol in water with an LOD of  $\sim 0.3$  vol%, corresponding to an ethanol-vapor concentration of  $\sim 100$  ppm [39].

SERS is a powerful new analytical tool used extensively in research. Sada et al. prepared cubic gold nanorod (AuNR)@MOF-5 nanocrystals by using the 11-mercaptoundecanoic acid (MUA)-capped AuNR as seeds for direct growth of MOF-5. Clearly, AuNR was incorporated at the center of the cubic crystals with the formation of MOF shell (Fig. 4b). The obtained AuNR@MOF-5 nanocrystals were dispersible and stable in organic solvents and were demonstrated to be reproducible SERS materials for size-selective detection of pyridine derivatives [40].

LSPR spectroscopy has generally been restricted to large biological analytes. Sensing smaller molecules is a compelling target for this technique. Duyne et al. proposed a novel strategy for amplifying the sensing signal by coating  $\text{Cu}_3(\text{BTC})_2(\text{H}_2\text{O})_3$  on AgNPs using a layer-by-layer method. Preferential concentration of  $\text{CO}_2$  within the MOF pores produces a 14-fold signal enhancement for  $\text{CO}_2$  sensing. In principle, MOFs can be tailored for sorbing different analytes, making them ideal materials for this amplification strategy [41].

### 3.2. Electrochemical sensors

MOFs have rarely been utilized for conductivity-based sensing applications, because the majority of MOFs are insulating materials. Achmann et al. used Fe-BTC to construct a first impedance sensor for small-molecule sensing with a linear response of 0–2.5% for water, 0–18% for ethanol, and 1–35% for methanol at low temperature [42]. Mao et al. designed an integrated dehydrogenase-based electrochemical biosensor by using ZIFs-70 as the matrix for *in-vivo* measurement of neurochemicals, such as glucose (Fig. 5). ZIFs-70 can serve as a matrix for coimmobilizing electrocatalysts (i.e., methylene green, MG) and dehydrogenases (i.e., glucose dehydrogenase, GDH) onto the electrode surface. In a continuous-flow system, the ZIF-based biosensor prepared is highly sensitive to glucose with a linear range of 0.1–2 mM [43]. This biosensor is capable of selectively monitoring dialysate glucose from the brain of guinea pigs in a near real-time way.

With the development of nanoscience and nanotechnology, nanocomposites of NPs and MOFs show great application in electrochemical sensing, especially for conductive NPs, such as CNTs and metal NPs. The nanocomposite of multi-walled CNTs and

MOFs (MWCNTs@ $\text{Cu}_3(\text{BTC})_2$ ) has been used to modify an electrode for the determination of trace levels of lead by accumulating lead on the electrode surface and subsequently measuring with differential pulse anodic stripping voltammetry in a lab-on-valve format. Under optimum conditions, the oxidation peak current displayed a calibration response for lead over a concentration range 1.0–50 nM with an excellent LOD of 0.79 nM [44].

By integrating with transition-metal ions on single-walled carbon nanotubes (SWCNTs), a porous inorganic-organic hybrid framework (SWCNT@Zn) was designed. Due to the porous structure and its inherent conductive characteristics, the SWCNT@Zn was employed as sorbent for separation and detection of organophosphate compounds via a two-electron reduction process of the nitro group into the hydroxylamine group [45].

An electrochemical sensor based on Au-SH- $\text{SiO}_2$ NPs supported on Cu-MOF was developed for electrocatalytic oxidation of L-cysteine with a linear range of 0.02–300  $\mu\text{M}$  and an LOD of 8.0 nM [46].

Similarly, Au-SH- $\text{SiO}_2$ @Cu-MOF showed good electrocatalytic activity toward the oxidation of hydrazine in neutral solution and exhibited a low LOD (0.01  $\mu\text{M}$ ) and a wide linear range (0.04–500  $\mu\text{M}$ ) [47].

### 3.3. Mechanical sensors

Mechanical sensors, such as SAW sensors, QCMs, and microcantilevers are the devices that can transduce mass or molecular adsorption changes into vibration frequency or mechanical energy signals. In each case, signal detection requires the analyte to be adsorbed onto the surface of the sensor. Robinson and co-workers designed a thin film of Cu-BTC to functionalize a SAW device for gas detection. The MOF-coated SAWs exhibited a rapid, reversible response to water-vapor concentrations, spanning four orders of magnitude from  $-85^\circ\text{C}$  to  $+10^\circ\text{C}$  frost point (0.28–14800 ppm at local elevation) [48].

One of the most straightforward approaches to devise a sensor is to use QCM equipment. Indeed, MOF thin films can be easily deposited on QCMs because their hydroxylated surface provides reactive sites for binding linkers and metal ions. Biemmi et al. performed the first detailed study of water sorption in an HKUST-1 film grown directly on 11-mercaptoundecanol-modified gold QCM electrodes. The weight of the water adsorbed into the film was detected as a frequency shift, which was translated into a mass uptake using the Sauerbrey equation [49].

Ameloot et al. directly coated HKUST-1 on top of QCM substrates by electrochemical deposition that allowed tuning the size

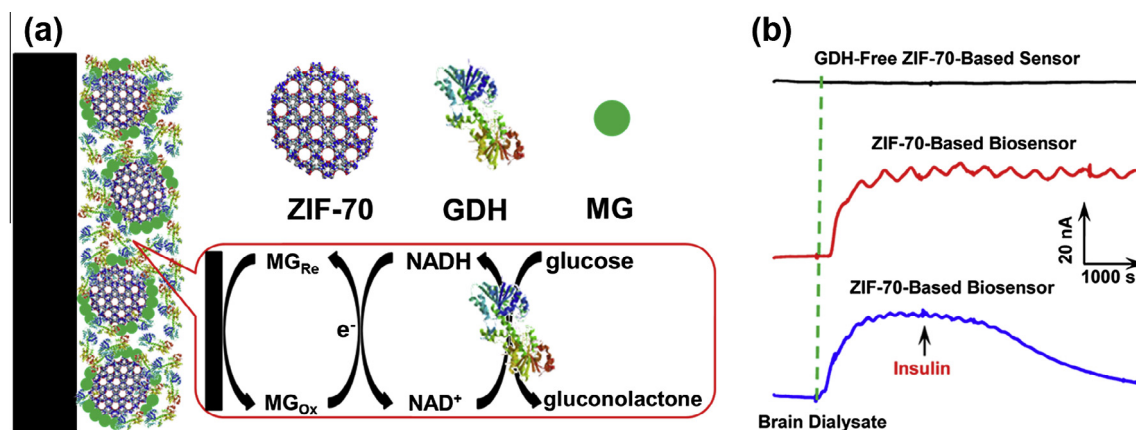
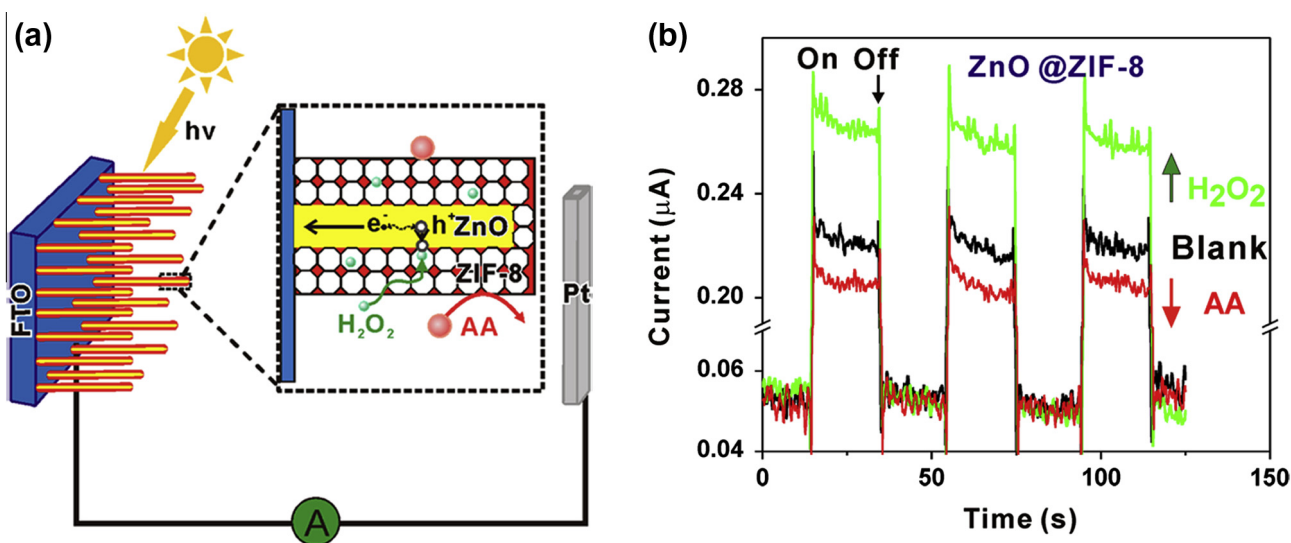


Fig. 5. (a) The ZIF-70-based biosensor. (b) Online current–time response recorded for the brain microdialysates of guinea pig with the MG/ZIF-70-modified GC electrode (i.e., GDH-free ZIF-70-based sensor, black line) and ZIF-70-based biosensor (red and blue line) as the detector. The electrodes were polarized at 0 V (Reprinted from [43] with permission from ACS Publications).



**Fig. 6.** (a) PEC sensor. (b) Photocurrent responses of the ZnO@ZIF-8 nanorod array in the presence of H<sub>2</sub>O<sub>2</sub> (0.1 mM) and AA (0.1 mM) (Reprinted from [53] with permission from ACS Publications).

of the densely-packed crystallites. The water-sorption capacity of the films was found to be 25–30 wt%. Significantly, the high reproducibility of the signal was obtained upon sequentially cycling dry and water-containing nitrogen flows [50].

Allendorf et al. proposed the concept of stress-induced chemical detection by integrating a thin film of HKUST-1 with a microcantilever surface. Upon inclusion of molecules in the pores, the energy of molecular adsorption within a porous MOF could be efficiently converted to mechanical energy to create a highly responsive, reversible, selective sensor for water vapor [51].

### 3.4. Other mechanisms

Compared with pure MOFs, the heterostructures integrating MOFs with other functional materials show great advantages due to their synergistic effects. Many metal oxides are very important functional materials with semiconducting properties, especially for applications in photoelectrochemistry. A series of MOF films with tetra(4-carboxyphenyl)porphyrin, trimesic-acid ligands and Cu<sup>2+</sup> ions have been grown layer-by-layer on TiO<sub>2</sub>-modified indium-tin-oxide electrodes to generate the cathodic short-circuit photocurrent [52].

Such semiconductor@MOFs heterostructures should have potential applications in photoelectrochemical (PEC) sensors with a highly-selective response toward molecules of different sizes. As shown in Fig. 6a, ZnO@ZIF-8 NRs with core-shell structures were successfully synthesized on the basis of a self-template strategy, where ZnO NRs not only act as the template but also provide Zn<sup>2+</sup> ions for the formation of ZIF-8 [53]. Interestingly, the photocurrent responses of the ZnO@ZIF-8 NR arrays display opposite changes with the addition of H<sub>2</sub>O<sub>2</sub> or ascorbic acid (AA) (Fig. 6b). The photocurrent response of the ZnO@ZIF-8 NR arrays is positively enhanced by the addition of H<sub>2</sub>O<sub>2</sub>, while the photocurrent response is markedly reduced by the addition of AA. The semiconductor@MOFs heterostructure therefore has promising applications in many electronic and electrochemical devices.

## 4. Conclusion and outlook

As a new kind of crystalline molecular material, MOFs have excellent advantages, such as ultrahigh porosity, high thermal

and chemical stability, and tunable structure. The functionalized MOFs with multitudinous biomolecules offer excellent platforms as signal transduction for detecting a range of organic molecules, ions, DNA and other biomolecules. To optimize the performance of MOF-based sensors, a series of improvements should be made as follows:

- (1) to realize the specific functionality of MOFs, it is desirable to design rational building blocks with various functionalities for assembly of MOF structures;
- (2) biocompatibility is important parameter in biosensing, so a significant direction for MOF materials is to explore a mild biofunctional way to fix the biomolecules on the surface of MOFs;
- (3) to expand their applicability, it is necessary to employ other signal-transduction methods, involving magnetic, electrochemical, mechanical and other physical properties, suitable for any MOF material without concern for its properties or structure;
- (4) for MOF-based devices, well-organized or patterned MOF fabrication is required, so it is a critical to develop a well-controlled growth method in a modular fashion, such as a layer-by-layer technique and the Langmuir-Blodgett method; and,
- (5) MOFs assembled with NPs show some significant properties and a new direction for constructing MOF-based devices.

With the achievements of nanoscience and biotechnology, MOF-based devices show very promising applications and provide a proof of concept in bioanalysis and biosensing.

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