MOF-biomolecule nanocomposites for electrosensing

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ABSTRACT

Over the last decade, the usage of metal-organic frameworks (MOFs) for electrochemical applications has grown in popularity. The sensitivity of amperometric sensors, which use current as the sensing response for the targeted analyte, is one of the most often encountered electrochemical sensing systems. Electrocatalysts with high reaction rates and the ability to selectively react with the intended analyte are generally required. Since electrochemical reactions may only occur on the surface of an electrode, depositing or immobilizing the electrocatalyst on the surface of the electrode to produce a modified electrode is a typical technique for constructing the active electrode of an amperometric sensor. As we know, multiple chemical functionalities can be incorporated into the entire pore structure of MOFs with different synthetic routes without losing much porosity. However, because most MOFs are not chemically stable in water, and most electrochemical sensing systems require the use of aqueous electrolytes, water stability of MOFs becomes one of the primary issues for MOF usage in electroanalysis. Only lately have significant attempts been made to manufacture MOFs utilizing biomimetic mineralization methods, in which biomolecules are employed as crystallizing and guiding agents to design a variety of MOFs. MOF-based particles containing biomolecules such as enzymes, proteins, peptides, cells, DNA, and viruses have been synthesized using this technique. This review summarizes recent developments of MOF-biomolecule composites with special emphasis on preparative techniques and the synergistic effects of biomolecules and MOFs. The applications of MOF-biomolecule composites in electrosensing are presented as well.

INTRODUCTION

Metal-organic frameworks (MOFs) are crystalline porous compounds formed by using strong connections to join metal ions (or clusters) and organic ligands [1-4]. They have numerous advantages in comparison with other porous materials such as large surface area, unique pore structure, homogeneous pore size, and various chemical functionality. The metal nature and the ligand type can also be altered via adjusting the synthesis process [5]. A huge number of applications are expected for MOFs due to their interesting properties. Some of these applications include gas adsorption, separation of volatile organic compounds (VOCs), contaminant sorption (removing inorganic and organic contaminants from water during purification), sensors, catalysis, and energy storage [6-8].

To improve the conductivity, stability, as well as catalytic activity of MOFs, coupling or scaffolding with various functional materials such as carbon substrates, nanoparticles, enzymes, polymers, and conducting substrates are promising strategies [9-11]. The above-mentioned physicochemical properties are not possible in pristine MOFs. In the past several years, so many MOF composites have been synthesized for sensing applications that are

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pretty stable in hostile environments (very acidic/ basic conditions), improved catalytic performance, and extended signal transduction channels [12]. MOF-polymers, MOF-biomolecules, MOF-metal nanoparticles (NPs), MOF-enzymes, MOF-polyoxometalates (POMs), MOF-carbon nanotubes (CNTs), and MOF-quantum dots (QDs) are some composites that have been reported so far [13-15]. Metal NPs (Pd, Au, Cu, and Ru), metal oxide NPs (Fe_3O_4, TiO_2, Cu_xO_x, and ZnO), POMs ($PMo_{10}V_2$), QDs (CdSe), and carbon nanotubes (SWCNTs (single-wall carbon nanotube) and MWCNTs (multi-wall carbon nanotube)) are all great materials for doping of MOFs' frameworks. The size and shape of NPs can be regulated by engineering MOFs; therefore, they can be used as highly reactive electrocatalysts in electrochemistry [16, 17].

In comparison with inductively coupled plasma mass spectroscopy (ICP-MS), atomic absorption spectroscopy (AAS), chromatography, and atomic emission spectroscopy (AES), electrochemical sensors which are one of the most common types of analytical instrumentation, can provide high sensitivity and selectivity with relatively low-cost equipment [18]. The key to enhancing the sensitivity and selectivity in an electrode toward target molecules is to alter the electrode chemically and this results in low detection limits. Scientists are searching for materials with higher sensitivity and selectivity. The materials that they are looking for (like electrode modifiers) should possess large specific surface areas and great catalytic and electrical capabilities [19]. Electroactive species (including metal ions, organic ligands, or both) in combination with a significant porosity result in great electrochemical redox characteristics composites which contain MOFs. Furthermore, by transporting ions across a high permeability solid, phase changing followed by internal diffusion occurs and this can improve the electrochemical process in MOFs [20]. The combination of large surface areas and excellent electrochemical properties in MOFs has made them ideal choices for synthesizing electrochemical sensors by allowing the analyte to be preconcentrated (to the electrode surface) [21].

The reason for the great electrocatalytic capacities of MOF-contained composites is their porosity, crystalline structure, presence of positive metal coordination nodes, and accessibility to diverse chemical functionalization. One thing which is crucial for industrial electrocatalysts and electrode-active materials is the inorganic nano or microparticle stability of composites [22-24]. Despite non-porous/microporous materials, electrochemically active MOFs have more metal ions that are in contact with the electrolyte and it results in enhanced electrochemically active surface area. This is because of their high surface area and porosity. But unfortunately, due to limited access to the electrolyte by metal atoms on non-porous/microporous materials, they have highly limited electroactive surface and this could be one of their disadvantages. The special design of MOF-contained composites exposes almost all of the electrochemically active sites to the electrolyte ions and allows the composites to be more sensitive to the required levels of electronic and ionic conductivities [25, 26].

The mentioned composites act as electrode modifiers in electrochemical sensor applications. The presence of MOF composites on the electrode surface is pretty beneficial [27]. They can improve selectivity, anti-interference capabilities, and sensitivity (or decrease LODs (limit of detection)) in catalytic systems. Interestingly, they can change the analytes' oxidation/reduction potentials to lower values as well. Scientists have explored considerably in the field of MOF composites and their application in electrochemical sensing platforms in the last few years. We try to explain the electrochemical sensing capabilities of MOF composites in this review. Various functional materials can be used in synthesizing MOF-contained composites, but here we mainly focus on enzyme-based composites [28].

BIOMOLECULES

Biomolecules are pretty important in a bunch of energy, biotechnological, and environmental applications including catalysis, fluorescence, ion exchange, biosensors, and nonlinear optics [29, 30]. But their widespread use is limited because of some issues like negligible robustness, utilizable stability, selectivity/specificity, and recyclability. In 1916, scientists' efforts to reach enzyme immobilization on solid support resulted in adsorbed invertase enzyme on charcoal and aluminum hydroxide [29]. Although we can call this a success, the mentioned structure didn't affect the enzyme's activity [31].

Biomolecule development

Biomolecules face so many challenges which

limit their reusability and recovery (the extraction of high-value components such as proteins, polysaccharides, fibers, flavor compounds, and phytochemicals, which can be re-used as nutritionally and pharmacologically functional ingredients) when used in different applications. Some of these challenges are the necessity of precise conditions for desirable biological activity, fragile structures, and strong reactivity toward non-specific components [10]. The key factor in developing a biorecognition element for a sensor is to determine a fine immobilization platform for physiologically active materials like antibodies, enzymes, or nucleic acid. It is also noteworthy that the platform should not hinder the activity, accuracy, sensitivity, and stability of these materials [32]. As an example, the sensitivity of an electrochemical biosensor is determined by the activity of the electrode surface and the mass transferability of the analyte, which is designed by the interfacial properties of the immobilizing matrix and the biorecognition structures like enzymes for developing biomolecule features such as synthesizing MOF-based composites and biomolecules could be used [17].

Enzyme/MOF embedded structures

De novo and post-synthetic approaches are two methods for mounting enzymes on MOFs. The de novo method involves in situ or one-pot synthesis of enzyme- MOF composites. In this protocol, the larger enzyme molecules (compared to the apertures or channel size of the MOFs) can be immobilized into the cavities of MOFs. Enzyme-MOF composites prepared through this method are

also beneficial to stabilize the tertiary structure of an enzyme. In some cases, auxiliary stabilizers were required for an enzyme during the preparation of enzyme-MOF composites. A de novo approach was used for the size-selective covering of catalase. The difference between these approaches is that the post-synthetic methods involve immobilizing enzymes onto a pre-existing MOF while De novo methods require arranging MOFs around the enzymes [17]. The resulting composites have shown enhanced enzymes' operating stability in several applications and it occurred for both de novo and post-synthetic approaches. Some important factors can affect substrate diffusion in aqueous/non-aqueous solutions during certain applications. The crystallite characteristics and size of MOFs (as an immobilizing matrix) are two of those factors that influence substrate diffusion. One of the embedding methods that was used to synthesize catalase enzyme into ZIF-90, is the de novo method [33-35].

ELECTROCHEMICAL SENSING PLATFORM

Electrochemical biosensors have the potential to detect specific analytes. Owing to this potential, they have a wide range of beneficial applications in quality control, disease diagnosis, food safety, and environmental monitoring. Ease of downsizing, sensitivity, fast response, and selectivity are some of the unique electrochemical features of biosensors that aid them in their sensing applications [36, 37]. As mentioned before, the stability of the biomolecule needs to be improved by immobilizing with a proper matrix to reach better performance under hard reaction circumstances. The biocatalytic
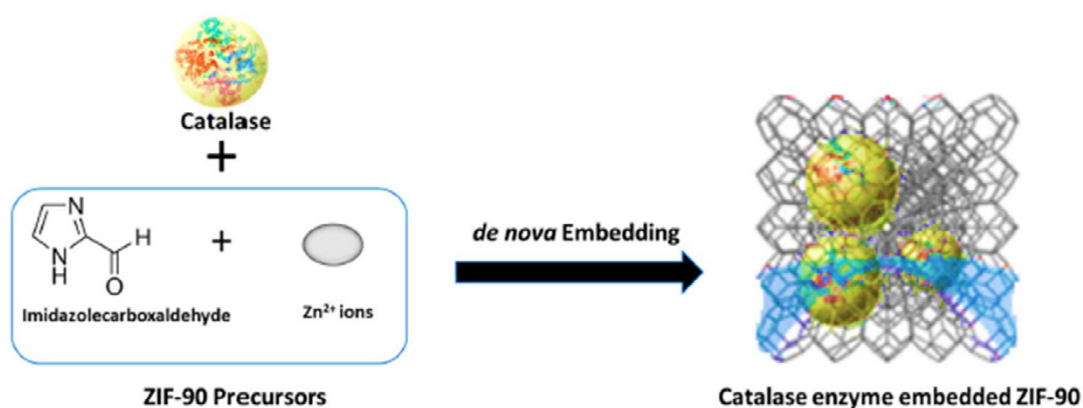

Fig. 1. De novo approach for enzyme/ZIF-90 embedded catalyst, in which the catalase enzyme was encapsulated inside the MOF. Reproduced with permission from reference [35], copyright (2015), ACS Publication.

activity of the electrode surface and the mass transferability of the analyte in an electrochemical biosensor depends on two factors. First, the interfacial qualities of the biorecognition material, and second, the type of host matrix utilized. Because MOFs are effective matrices to immobilize host materials and a wide range of biomolecules, they can be used as an electrode in electrochemical biosensors [37, 38].

MOF/biomolecule composite as an electrochemical platform

Scientists have developed in-vivo glucose monitoring sensing by using zeolitic imidazolate frameworks (ZIFs) and dehydrogenase-based electrochemical platforms in 2013 [39]. Different porosity, morphological, and surface features of ZIFs, have convinced scientists to choose ZIF-67, ZIF-68, ZIF-70, and ZIF-7 to immobilize both methylene green (MG) and glucose dehydrogenase (GDH) electrocatalysts [39, 40]. Their advanced qualities were fitted for electrocatalysis. Such qualities include electrostatic interactions between functional groups of ZIFs and enzymes, simple surface/physical adsorption of electrocatalysts, and excellent chemical stability of ZIFs. The sensitivity and selectivity of the ZIF-70/MG/GDH biosensor for detecting glucose in a continuous flow system were extremely high. ZIF-70 is used for glucose sensing in this system due to its better adsorption capacities for MG and GDH than other ZIF analogs. The adsorption capacities (mg/g) for MG were estimated to be 5.65 (ZIF-7), 6.79 (ZIF-8), 6.98 (ZIF-67), 3.82 (ZIF-68), and 7.11 (ZIF-69) (ZIF 70). In addition, the GDH adsorption capabilities (mg/g) were 88.3, 110.4, 584.9, and 441.4 for ZIF-

8, ZIF-67, ZIF-68, and ZIF-70, respectively. The selectivity of the sensor was tested with endogenous electroactive species in a brain system and the sensor was successfully used for sensing glucose in dialysate samples from guinea pig brains [39].

In another study, scientists employed a copper-based MOF (Cu-H$_2$BDC) (1,4-benzene dicarboxylic acid) tyrosinase (try) chitosan composite modified glassy carbon electrode (GCE) to detect bisphenol A (BPA) (Fig. 2) [41]. This MOF is perfect for both enzyme (try) adsorption and BPA detection with enhanced sensitivity owing to its 3D structure which can provide high surface area. Because of the π-π stacking interactions, the BPA sites were improved, and, as a result, its reaction with tyrosinase on the electrode surface was increased. The recovery rate of the sensor ranged from 94.0 to 101.6 percent. The analysis of the results of detecting BPA through this technology was very promising. Scientists also examined other BPs, like bisphenol Z (BPZ), bisphenol B (BPB), bisphenol F (BPF), and bisphenol E (BPE) by the above-mentioned nanocomposite as an electrochemical sensor [42]. The sensitivity of BP nano-sensors significantly depends on the n-octanol/water partition coefficients logarithms. Although the response of the nanocomposite was considerable toward BPAP, BPS, and BPAF, it was insufficient to some other bisphenols including bisphenol AF (BPAF), tetra bromobisphenol A, bisphenol AP (BPAP), and bisphenol S (BPS). Scientists figured out that the substituent groups on the bisphenol structure affect electrochemical response of the nanocomposite in different BPs detection processes. The oxidation of the accessible ortho hydroxyl groups on phenol by tyrosinase is affected by the other substituents on
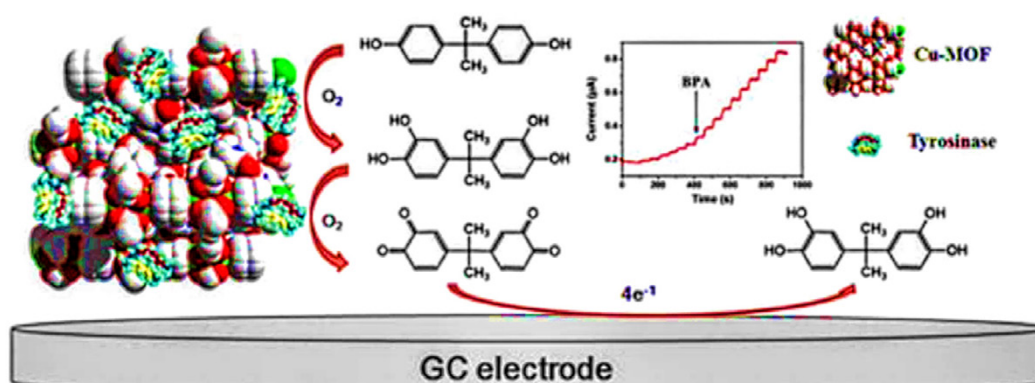

Fig. 2. 3D-MOFs as a biosensor for ultrasensitive and rapid detection of BPA. The large surface area of MOFs exhibited a favorable effect on the adsorption of both tyrosine enzyme and BPA which led to improving the sensor activity for ultrasensitive detection of 50 nM to 3 μM BPA. Reproduced with permission from reference [41]copyright (2015) ELSEVIER.

phenol, which controls the electron density of the hydroxyl group of phenol. The biopolymer chitosan film's exceptional film-forming capability, the ultra-stable Cu-small MOF's pore size distribution (4.9 OA), and extraordinary adsorption characteristics for a variety of heavy metal ions, are the reasons for restricting the diffusion of large hydrated heavy metal ions [42-44].

MOF/Hemin composite as an electrochemical sensor

One of the natural metalloporphyrins which has both catalytic and redox mediator properties is hemin. The catalytic activity of this structure is because of its peroxidase-like activity and also the redox mediator features of this structure are referred to as the reversible redox reactions of the Fe^{3+}-Fe^{2+} couple [45]. Unfortunately, hemins have their disadvantages in catalysis too. Insolubility in neutral/alkaline buffer solutions and short lifespan are some examples of these drawbacks. Therefore,, to face this challenge, hemin needs to be immobilized in matrix-like polymeric films, zeolites, and sol-gels [46]. The named matrixes can improve the hemin's catalytic performance. But the point is that these compounds have low sensitivity as electrochemical sensors. The reason for this low sensitivity is the poor hemin loading/leaching of the loaded substrate during functional operation [47].

Because of this, scientists have employed MOFs to immobilize hemin molecules. The multifunctional bioconjugate electrochemical sensor which was used for sensing thrombin (TB) was Au/hemin@MOF–TBA II (thrombin binding aptamer)–GOx (glucose oxidase) [48]. The step-by-step synthesis process of the composite and the detection of tuberculosis are shown in Fig. 3. Au/hemin@MOF–TBA II–GOx composites in this aptasensor are secondary bioconjugates and sandwiched between the self-assembled amino-terminated TBA I on gold nanoparticles (AuNPs) modified electrode and TB. H_2O_2 was produced after converting glucose to gluconic acid by GOx. The hemin electrochemical signal was amplified after electrocatalysis of the as-produced H_2O_2 by the hemin@MOFs. In conclusion, hemin@MOFs acted as a multifunctional material, especially for three purposes: redox mediators, enzyme catalysts, and enzyme loading platforms [48].
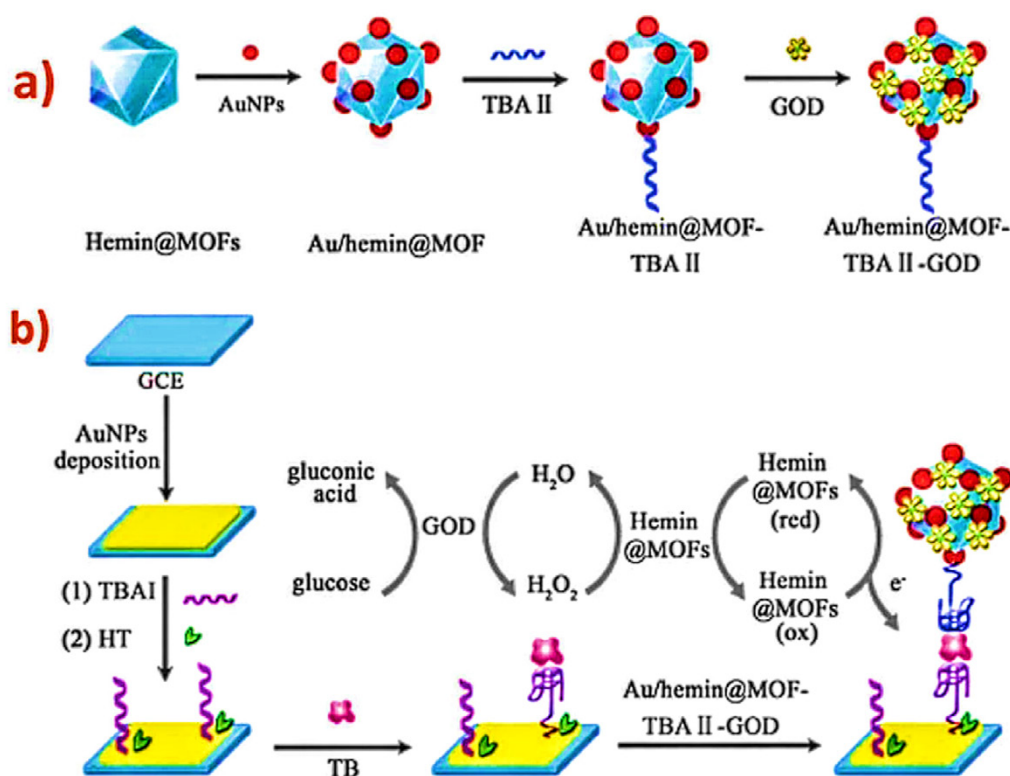

Fig. 3. Electrochemical aptasensor preparation and detection principle: (a) The preparation of Au/hemin@ MOF–TBA II–GOD preparation (b) Schematic of the stepwise assembly procedure and electrocatalytic detection principle of the proposed electrochemical aptasensor. Reproduced with permission from reference [48], copyright (2015) ELSEVIER.

MOF/GOx composite as an electrochemical sensor

An electrochemical biosensor using a Pt-NPs/ MOF/GOD (glucose oxidase dehydrogenase) nanocomposite matrix was reported. The application of this sensor was to detect glucose [17]. The modified nanocomposite electrode exhibited excellent performance in detecting glucose and this is because of electrocatalytic features of Pt-NPs and MIL-100(Fe). Because of the intrinsic peroxidase activity of the Fe^{3+} centers in MIL-100(Fe), these centers are responsible for the electrocatalytic oxidation capabilities of the sensor towards glucose. After replacing Fe with Al and Cr in the MOF, the sensitivity decreased and the response time increased for the electrocatalytic oxidation of glucose in comparison with MIL-100(Fe). One strategy for determining the activity of GOx in the composite is to use Michaelis–Menten constant (K_m). K_m was determined 2.4 and 33–110 mM for immobilized GOx and free GOx, respectively. Lower K_m values mean that the enzyme has a stronger connection to the substrate. So, it is proof for GOx/MIL-100(Fe)/Pt NP nanocomposite high sensitivity, and, as a result, it can provide a biocompatible milieu for enzymatic biosensing of glucose [49].

The structure of GOx/Cu-Hemin-MOFs is similar to a ball flower-like structure with hollow cages. Due to their high specific surface area and many mesopores, they were chosen for the electrocatalytic oxidation of glucose [50]. Scientists believed that the probable accommodation of a large number of GOx molecules is because of Cu-hemin MOFs' pores. Cu-Hemin/GCE exhibited considerably better electrocatalytic performance than GOD/Cu-hemin MOF/GCE. Both composites were tested in a special condition to detect glucose. In the presence of 10-fold higher quantities of other sugars (galactose, fructose, and mannose), uric acid (UA), ascorbic acid (AA), and glucose, the GCE-contained structure selectivity toward glucose was remarkably higher than the other structure. Fortunately, when it came to real-world application, the sensor's performance was great. In an experiment, the blood samples of diabetes patients were used to determine the sensitivity, selectivity, and accuracy of the sensor in glucose detection. According to the results, the sensor showed a glucose level of 8.3 mM which was quite close to the clinical outcomes. As mentioned above, the main characteristics of any biosensor are long-term stability and reproducibility. This biosensor

was held at 4 °C for 48 hours, and the long-term stability described 99.6% of the original current; after 30 days, it was 87.5 percent of the original current. Moreover, the RSD (relative standard deviations) value was estimated to be 4.27 percent when the system's repeatability was evaluated with five different electrodes [50].

MOF/ DNA enzyme as an electrochemical sensor

In another study, a composite material based on HP3 (marked as hairpin probe 3) / AuNPs / MOF (Cu-2-aminoterptahlic acid) was synthesized as a ratiometric electrochemical aptasensor for detecting lipopolysaccharide (LPS). AuNP/ CuMOF compounds acted as both nanocarriers and nano-active materials for signal reporting. The properties of LPS in the presence of procalcitonin (PCT), C-reactive protein (CRP), and human serum albumin (HSA) were exposed by the aptasensor. AuNP/CuMOF compounds acted as an immobilized matrix for many HP3s and were also used for signal transmission. In addition, they made it easier for glucose oxidation catalysis to amplify the signal without the use of enzymes [51].

In another work, Ce-based AuNP/MOFs (Ce-2-aminotepthalic acid) and Zn^{2+} dependent DNA enzyme-assisted recycling were used as dual signal amplifiers in an electrochemical aptasensor for detecting LPS. In this research, scientists preferred DNA enzymes rather than the protein ones due to their facile synthesis process, non-toxic features, and being cost-effective. The role of Au nanoparticles in this study was to trap -SH ended hairpin probes 2 (HP2) to act as HP2/AuNP/Ce-MOF signal probes and Ce-MOFs also aided signal amplification via oxidizing AA. MOF-contained nanoparticles exposed catalytic activity in the ascorbic acid oxidation reaction.[51].

The sensitivity and selectivity of the aptasensor toward LPS in the presence of other proteins including HAS, CRP, and PCT were checked. Interestingly, the signal patterns related to LPS remained unchanged. Moreover, the above-mentioned proteins were employed as interfering molecules while LPS sensing was in progress. They didn't significantly change the sensor when it was tested with 10 ng.mL^{-1} LPS. In addition, the aptasensor was used for detecting LPS in human serum and it showed good recoveries (93.6 to 104.4 %).

For detecting mutations in the FGFR3 gene (a pathogenic gene from achondroplasia), another
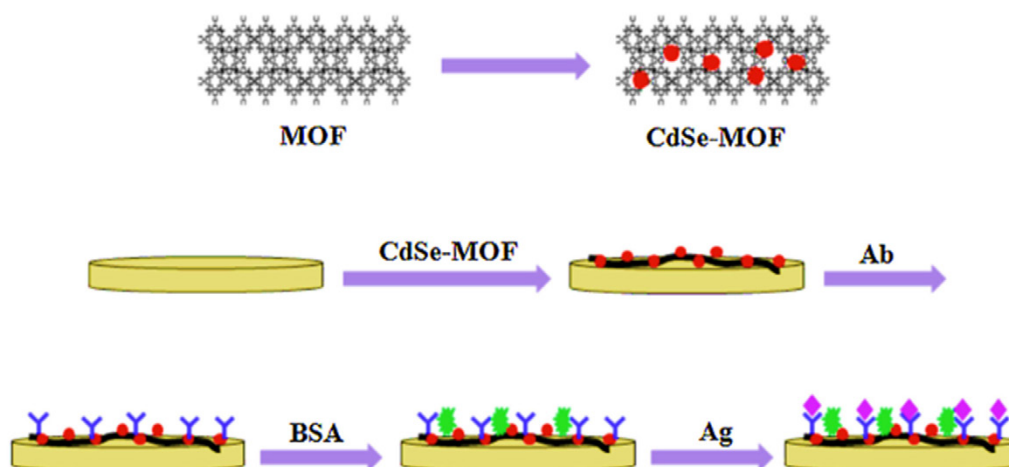
Fig. 5. The fabricating steps of the ECL immunosensor. Reproduced with permission from reference [52], copyright (2017) ELSEVIER.

DNA sensor was developed in 2017. In addition to the biocatalytic signal materials, a biotin-streptavidin system was suspected for the sensing signals. Because of the excellent catalyzing performance of Hemin-MOF/Pt NPs composites in oxidizing O_2 and their fine conductivity, they were synthesized and utilized in that project to amplify the signal. It is notable that several materials such as AuNP, streptavidin, and rGO-tetra ethylene pentaamine (rGO-TEPA; rGO = reduced graphene oxide), were used to modify the electrode for amplifying the sensor signals. This aptasensor was applied to other oligonucleotides like noncomplementary targets (random), and mismatch oligonucleotides (i.e., single-base, double-base, and three-base mismatch) because it has displayed good selectivity to the target DNA. The current response did not show any changes similar to the response of the blank for oligonucleotides with a 10-fold higher concentration than the target DNA. Even so, the current signals increased in the existence of target DNA. Healthy maternal serum samples spiked with target DNA were detected using the DNA sensor. The obtained recovery values ranged from 97.4% to 105.2%. [47].

Other examples of multi-enzyme system sensors

MIL-101/CdSe/GCE nanocomposite is an electrochemiluminescence (ECL) immunosensor which is another type of electrochemical sensor based on MOF and it was used to detect the carcinoembryonic antigen (CEA) (Fig. 5) [52]. The following synthesized CdSe QD/MIL-101 composite was entrusted on GCE for the sensing of immunogens. Owing to the presence of QDs in MIL-101/CdSe/GCE and selective adsorption and efficient accumulation of CEA by MIL-101, the mentioned composite demonstrated great ECL activity and selectivity through CEA. ECL immunosensor are utilized for interfering molecules like human IL-6, BSA (bovine serum albumin), and their mixture because of their selective response. In the presence of interfering molecule concentrations of 10^{-6}–10^{-3} mg mL^{-1}, the performance of the sensor was investigated and a relative signal deviation of 1.46–3.46% was observed [52].

In another study, for electrochemical detection of glucose, a multi-enzyme system was developed from MOFs and GOx [53]. Polydopamine (PDA) and ZIF-8 were composed together via aiding $CaCO_3$ templates as the mimetic enzymes. Then, for reclaiming the electron transfer between composite and electrode, reduced graphene oxide (rGO) was attached to the PDA/ZIF-8 via π-π interactions and hydrogen bonding. As a result, the electrocatalytic activity of produced PDA/ZIF-8@rGO was perfect toward H_2O_2. A multi-enzyme biosensor (GOx/PDA/ZIF-8@rGO/GCE) for detecting glucose was prepared by immobilizing the GOx enzyme on PDA/ZIF-8@rGO microcapsule. These biosensors which were based on microcapsule exposed excellent selectivity in real examples in the field of glucose detection.

PCN-333(Al) (porous coordination network) encapsulated MP-11(Microperoxidase-11) and the resulting structure grew on a 3D-kenaf stem-derived porous carbon (3D–KSC) (kenaf stem
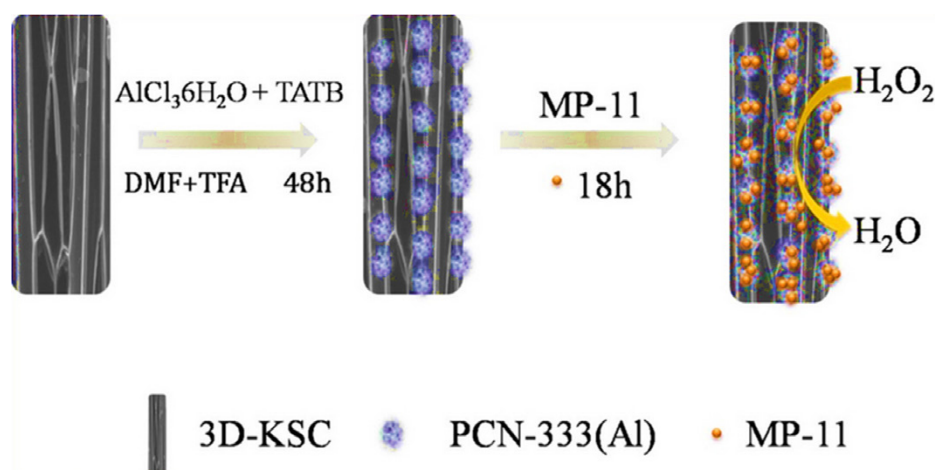
Fig. 6. Schematic illustration of the stepwise fabrication process and the testing principle of the novel H_2O_2 electrochemical biosensor. Reproduced with permission from reference [53], copyright (2016) Royal Society of Chemistry.

derived) to prepare a hydrogen peroxide biosensor. The MP-11 molecules that were encapsulated showed better catalytic performance in comparison to pristine ones. The mesoporous structure of PCN-333 (Al) was a suitable cavity size for encapsulating MP-11 ($1.1\times 1.7 \times 3.3$ nm). UA, glucose, and AA didn't greatly affect the H_2O_2 detection (less than 5%), and also other components like K^+, Na^+, Cl^-, and cysteine did not exhibit obvious interference (Fig. 6) [53].

A biosensor based on GOx-AuNPs-Cu(BTC) MOF-3D KSCs (three-dimensional microporous carbon) integrated electrode has been introduced newly for glucose sensing [54]. The procedure of preparing composite electrodes is described below. First, scientists grew Cu-BTC on a 3D KSCs integrated electrode. Then, the electrodeposited AuNPs onto Cu (BTC) MOF-3D KSCs integrated electrode. In the end, GOx was deposited on AuNPs-Cu (BTC)MOF-3D KSCs integrated electrode to produce a ratiometric sensor for glucose. The sensitivity, accuracy, and selectivity of the mentioned sensor were extremely high in glucose detection. For detecting Pb^{2+}, the AuNPs based electrochemical biosensor was developed on a paper working electrode (PWE) and this occurred by using iron-porphyrinic MOF ((Fe-P) n-MOF-Au-GR) hybrids modified with DNA, as signal probes. Among all other competing metal ions, this sensor was selective toward Pb^{2+}. Simple construction, high sensitivity/selectivity, and economical fabrication are just some of the advantages of the AuNPs-MOF based sensing platform. According to these features, it is an ideal sensor that has the potential for detecting Pb^{2+} in biological and also environmental samples.

CONCLUSION

As a conclusion in this review, properties of different MOF–biomolecule composites in the field of electrochemical sensing were studied and their excellent performance toward each specific analyte was deduced. The presence of MOFs in biosensors resulted in enhanced sensitivity during the electrochemical sensing process. Holding a large number of enzyme molecules through diverse interactions, and effectively adsorbing analytes from the bulk solution through the π-π interactions between the aromatic groups of analytes and organic linkers of MOFs were some of the reasons for this enhanced sensitivity caused by MOFs. In addition, due to the particular pore size of the MOFs, their selectivity toward particular analytes was increased remarkably. In a bulk solution, the pore size of MOFs can help the catalytic process by adsorbing analysts that fit their pore and it is proof for increasing selectivity by MOFs. In addition, even pristine MOFs can act as catalysts owing to the presence of acid/basic sites and redox groups on organic linkers. Higher sensitivity can be reached by choosing MOFs as host materials. This might reflect the synergistic effect made by both the MOF and enzymes that exist in the composites.

CONFLICTS OF INTEREST

The authors declare that there are no conflicts

of interest regarding the publication of this paper.

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