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Biomimetic catalysis of metal–organic frameworks

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Metal–organic frameworks (MOFs) have attracted great attention as a new type of prospective material with various merits and functionalities. MOFs can either act as biomimetic catalysts to mimic enzymatic activities or serve as hosts to encapsulate bio-active species for biomimetic catalysis. However, in comparison with the dramatic development of MOFs in other catalytic fields, MOF-based biomimetic catalysis is still in its infancy and is yet to be systematically and comprehensively explored. Herein, the principles and strategies for the design and synthesis of MOF-based biomimetic catalysts, especially the structural features of representative MOFs that are related to biomimetic catalysis, are summarized and reviewed. In addition, recent advances in biomimetic catalysis of MOFs and the relationships between their catalytic performances and the structural specificities are discussed in detail as well.

Introduction

Enzymes are known to be among the most sophisticated materials in terms of catalysis due to their hallmarks such as high affinities towards substrates, substantial rate accelerations relative to un-catalyzed reactions, and unrivaled catalytic efficiency based on their high stereo-, chemo-, and regio-selectivities.[1,2] However, the high cost, mild reaction conditions, and the fragile nature of enzymes hinder their industrial applications.[3–6] One of the big challenges lies in how to successfully stabilize enzymes in what is often an unnatural environment while retaining their functions and activities. As one of the approaches that have been widely investigated to surmount these problems, enzyme immobilization can improve the thermal and environmental stability of enzymes and insolubilize them for easy recovery and recycling.[6–9] Solid supports often broaden the applicable pH range of enzymes, and protect them from denaturation by organic solvents, high temperatures or autolysis. Among the common porous materials (*e.g.* microporous zeolites,[10] mesoporous metal oxides[11,12] and silica,[13–15] macroporous polymers,[16,17]

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Yao Chen

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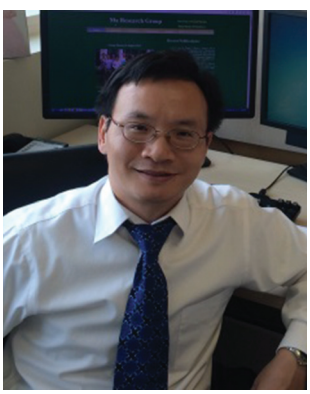

Shengqian Ma

Dr Shengqian Ma received his BS degree from Jilin University, China in 2003, and graduated from Miami University (Ohio) with a Ph.D. degree under the supervision of Hong-Cai Joe Zhou (currently at Texas A&M University) in 2008. After completing two years of Director's Postdoctoral Fellowship at Argonne National Laboratory, he joined the Department of Chemistry at the University of South Florida as an Assistant Professor in August 2010. He was promoted to an associate professor in 2015. His current research interests focus on the development of functional porous materials for energy-, biology-, and environment-related applications.

etc.), metal–organic frameworks (MOFs) meet most of the prerequisites for promising enzyme supporting materials: high surface area and porosity; structural versatility; amenability to be designed with specific functionalities.[18–21] On the other hand, the structural versatility allows metal–organic frameworks to mimic certain features of the functional active sites of enzymes, and perform as biomimetic catalysts. Just as in all other fields of scientific research, a lot of innovations in catalysis are inspired from nature. Generally, biomimetic catalysis refers to chemical catalysis that mimics certain key features of enzymes.[22–24] Biomimetic catalysts offer new perspectives and promising approaches to avoid those barriers, and provide opportunities for the design of materials to overcome the handicap of enzymes while retaining their beneficial features. Biomimetic catalysis is an important area in biomimetic chemistry, which is also encompassed by bio-inspired self-assembly of small molecules and biomimetic reactions in the total synthesis of natural products. By imitating the structural features and mechanisms of enzymes, biomimetic strategies can be used to develop catalysts with high turnover rate, efficiency and specificity, while possessing enhanced robustness that is easy to prepare and apply.[25,26] Biomimetic catalysts can often survive in various solvents (*e.g.* water, buffer, methanol, ethanol, dichloromethane and dimethylformide) and under harsh conditions (*e.g.* relatively strong acid or base, high temperatures, various organic solvents) with enhanced stability in comparison with their enzyme counterparts. In addition, biomimetic catalysts sometimes exhibit catalytic selectivity that is not observed in the native enzymes.[27]

Enzymes are capable of catalyzing myriad reactions, from the most fundamental reactions like simple oxidations of straight chain alkanes to reactions as complicated as C–C bond formation with exceptional selectivity. Some of the challenging transformations in organic synthesis can be easily achieved by enzymatic catalysis under mild conditions. By mimicking the active sites of native enzymes, many powerful catalysts can be generated for the synthesis and modification of fine chemicals and complicated drug molecules. In addition, with the continuous inspiration from nature, biomimetic catalysts can often be operated under mild and environment-friendly conditions with the reduction of energy consumption, waste generation and greenhouse gas emission, thus complying with the principles of green chemistry.[1,2]

Compared with traditional chemical catalysis, the knowledge of enzymatic catalysis is still relatively limited. The studies in biomimetic catalysis provide the platform for improved understanding of the mechanism and kinetics of enzymes. This fundamental understanding will in turn facilitate the design of biomimetic materials. In addition, biomimetic strategies can also provide guidance in the development of compounds (*e.g.* drugs or prodrugs) containing enzymatic structural motifs to catalyze reactions of biological interest.

In terms of uniformity, biomimetic catalysts can be divided into two catalogs: homogeneous and heterogeneous systems. Heterogeneous systems can offer great advantages in comparison with the homogeneous counterparts. One of the primary advantages of heterogeneous biomimetic catalysis is that the catalyst can be effectively recovered by straightforward methods, such as filtration, and such easy recovery and recycling is of paramount importance for large-scale industrial and commercial manufacturing processes. Moreover, solid supports improve the dispersion of catalytically active sites and thus enhance the catalytic efficiency. These features are of particular importance with regard to expensive catalysts, such as enzymes and precious metals. The facile separation of the catalyst can minimize or eliminate catalyst contamination and thereby lead to higher purity of the product, which will significantly reduce the cost of the purification process.

Several analogs of materials have been widely investigated for biomimetic catalysis, such as organic macrocycles, polymers, nanoparticles, porous aluminosilicates and mesoporous silicas,[23–26] among which porous polymers, aluminosilicates and silicas have been used as the support for the design of heterogeneous biomimetic catalysts. However, these traditional porous materials are composed of either inorganic or organic compounds and suffer from intrinsic limitations. Specifically, inorganic compounds lack structural flexibility, whereas organic compounds are usually amorphous without crystalline structures. MOFs, which are defined as 2D or 3D coordination polymers composed of metal moieties and organic linkers, have fueled intensive research over the past two decades in a variety of fields, such as gas separation and storage, heterogeneous catalysis, biocatalysis, sensors and biomedicine.[28] As an emerging family of highly porous crystalline materials, MOFs can be deliberately designed to combine the beneficial properties of organic and inorganic materials into one system by pre-selecting the appropriate inorganic (metals or metal clusters) and organic (organic ligands) building blocks and/or by post-synthetic modifications, and thus they largely expand the repertoire of porous materials. The unlimited choices of metals and organic building blocks give rise to enormous structural diversity yet various metrics and functionalities. Therefore, MOFs possess several extraordinary properties that are preferred for the design of biomimetic catalysts, such as high surface area (up to 10 000 $m^2 g^{-1}$), high and tunable porosity, structural versatility as well as the amenability to be designed with specific functionalities, and thus they are positioned in a unique place amongst traditional porous materials. Moreover, MOFs can be tailored to create the suitable environment around the catalytically active site, which can associate with the cages/channels of MOFs to demonstrate chemo-, regio-, stereo- and/or enantio-selectivities that cannot be expected from native enzymes. In addition, since the crystal structures of MOFs are more accessible than other porous materials, the pore environments in MOFs are clearer than ever before. The well-defined shape, size, and chemical environments of the cages or channels of MOFs offer excellent opportunities to design and control the morphology, composition, and distribution of the catalytically active site and the porous support, which will give rise to the improvements in catalytic performance and understanding of the basis of heterogeneous biomimetic design.[29] Last but not least, these

heterogeneous biomimetic catalysts can be created by a range of methodologies such as one-pot synthesis, post-synthetic modification, ship-into-a-bottle strategies, *etc*., and the different strategies used for the biomimetic design can also affect the catalytic performance of the catalysts. However, there are still challenges remaining in the MOF field, such as water instability. Several strategies have been pursued to address this issue, for instance, using building blocks with high connectivity (*e.g.* $[Zr_6O_4(OH)_4(COO)_{12}]$ and$[Cr_3O(COO)_6]$). Another strategy is to employ a hydrophobic polymer as the ligand to synthesize MOFs.[30]

Although the first biomimetic strategy reported for MOF application can be dated back to as early as 2006,[31] the biomimetic catalysis based on MOFs has rarely been explored, and the design and application of MOF-based biomimetic catalysts are yet to be systematically and comprehensively developed. Herein, the strategies for the design and synthesis of MOF-based biomimetic catalysts, especially the structural features of representative MOFs related to biomimetic catalysis are reviewed. Recent advances of biomimetic catalysis of MOFs and the relationship between their catalytic performances and the structural specificities are discussed in detail as well.

Design and synthesis of MOF-based biomimetic catalysts

Despite the tremendous progress achieved in the biomimetic field, the research of artificial enzymatic catalysis is still in its infancy. In a natural enzymatic system, the structure of the enzyme is elaborately constructed to precisely control the function. This fine-tuning between the structure and function leads to the excellent catalytic efficiency. Therefore, the performance of biomimetic catalysts can rarely keep up with their natural enzyme counterparts due to the low structural tunability and complexity. A solution to this problem may be offered by the emergence of MOFs, which can be fine-tuned and tailored to create the suitable environment around the catalytically active site. For less than one decade, the biomimetic catalyst toolbox was further broadened by MOF-based catalysts.

The approaches used for the synthesis of MOF-based biomimetic catalysts

In general, currently existing MOF-based biomimetic catalysts can be classified into two types:

I. The MOF frameworks themselves serve as the biomimetic catalysts (type I).

II. The catalytically active species or compounds/complexes containing catalytically active sites that mimic certain features of enzymes are encapsulated into MOFs to form heterogeneous biomimetic catalysts (type II).

For type I biomimetic catalysts, MOFs can be directly prepared by using catalytically active ligands such as Fe-porphyrins. A perfect example of this strategy is the synthesis and biomimetic catalysis of MMPF-6 (PCN-222(Fe)),[32,33] which is constructed using Fe-TCPP (TCPP-tetrakis(4-carboxyphenyl) porphyrin) as a heme-like ligand and highly stable Zr6 clusters as nodes, and demonstrated impressive peroxidase activities

Fig. 1 The 3D structure of MMPF-6 (PCN-222(Fe)) with mesopores. The figure is reproduced with the permission of the publisher from ref. 32.

(Fig. 1). In principle, bioactive organic ligands such as amino acids, hydroxyl carboxylic acids, nucleotide acids, cinchona alkaloids, peptides and biotin are good candidates to serve as the ligands for the synthesis of MOFs with potential favourable features for bio-functions, such as biocatalysis, chirality, and highly selective substrate-binding ability. In addition, type I MOFs can also be prepared by using non-catalytic ligands like free base porphyrins. After the preparation of MOFs, post-synthetic modification (PSM) can be performed to provide catalytically active sites to MOFs. For example, MOF-525 synthesized with free porphyrins can react with Fe^{3+} salts to produce Fe-porphyrin MOF-525 frameworks through postmetalation.[34]

For type II biomimetic catalysts, catalytic species can be encapsulated into MOFs either during the synthesis of MOFs (one-pot strategies) or through PSM. For the one-pot strategy, all the starting materials and the catalytically active components are combined in one reaction system. The catalytic component will be encapsulated into the MOF structure during the crystal formation process. For example, to synthesize a biomimetic catalyst Co-BBP@Tb-MOF, Lee *et al.* prepared the terbium-MOF through a solvothermal reaction according to the procedure reported by Park *et al.*[35] To encapsulate the catalytically active Co-BBP complex into terbium-MOF, $Tb(NO_3)_3{\cdot}5H_2O$ (0.03 g), triazine-1,3,5-tribenzoic acid (0.01 g) and Co-BBP (0.005 g) were dissolved in 2.0 mL of DMA, 0.4 mL of methanol and 0.1 mL of H_2O. The mixture was sealed and heated at 105 °C. After 2 days, Co-BBP@Tb-MOF was harvested and washed at room temperature.[36] Larsen *et al.* reported the synthesis of MOMzyme-1, a class of metal organic materials that mimic the enzymatic activity of heme proteins, by the encapsulation of metalloporphyrin during the formation of HKUST-1 crystals.[37] Sometimes, the bioactive species can also serve as the templates to facilitate the formation of porous MOFs during the synthesis. Zhang and Zaworotko reported the adoption of porphyrins as a structure-directing template to prepare a series of porphyrin encapsulated metal organic materials (porph@MOMs).[38] These porph@MOMs can serve as efficient heterogeneous catalysts towards oxidation of olefins. For the PSM strategy, the catalytically active species can be loaded into the MOFs through various encapsulation strategies. A common example is to

encapsulate the active species in the "ship-in-a-bottle" fashion. To load catalytically active compounds or complexes into the cages/channels within the MOF framework, the active species and the MOF are mixed and incubated in a certain solution for a certain period. Sometimes, heating is required to facilitate the ingression of guest molecules into the framework. In 2010, Volkmer *et al.* immobilized *N*-hydroxyphthalimide (NHPI) in the pores of MFU-1.[39] The pre-synthesized MFU-1 (15 mg) was suspended for 3 days in a solution of NHPI (50 mg) dissolved in acetonitrile (5 mL). Afterwards, the NHPI@MFU-1 materials were filtered off and dried under vacuum.

The design of MOF-based biomimetic catalysts

In terms of the design of MOF-based biomimetic catalysts, several critical factors need to be taken into cautious consideration for both types of biomimetic catalysts, such as (1) the diffusion of substrates/products, (2) the dispersion of catalytically active sites and (3) the affinity of biomimetic catalyst towards certain substrates. Generally, the diffusion of the reactant to the catalyst surface can often be the rate-limiting step in heterogeneous catalysis. In order to initialize catalysis, the substrate has to diffuse into the framework and interact with the catalytically active sites embedded in the MOF structures. Therefore, the quick diffusion of substrates into the framework will accelerate the catalytic process, and is crucial for the high initial rate and catalytic efficiency. On the other hand, the products need to diffuse out of the framework, so the removal of the products from the framework will change the chemical equilibrium and facilitate the reaction to proceed in the forward direction. In addition, the accessible space of the biomimetic catalyst will potentially limit the number of available active sites, which will also affect the reaction rates. Therefore, the high porosity, high surface area, and large pore sizes are favorable for the design of MOF-based biomimetic catalysts. In this context, mesoporous MOFs (mesoMOFs) can largely expand the utility of MOFs in catalysis due to their enlarged pore sizes (2–50 nm) as well as the special characteristics of the mesoporous cages or channels, such as the shape and chemical environments. Some beneficial features of MOFs such as the tunable pore sizes and high surface areas can be utilized to improve the dispersion of catalytically active sites, and thus to enhance the catalytic efficiency. The unlimited choices of metals and organic building blocks provide the opportunity to deliberately design the MOFs with specific functional motifs to interact with certain substrates and improve the affinity of the biomimetic system. In order to achieve the optimal affinity towards the target substrate in a biocatalysis system, the shape and charge distribution of the active site in enzyme is often complementary to that of the target substrate. This feature can inspire the design of biomimetic catalysts. For example, for a hydrophobic substrate, the hydrophobic catalytically active sites can provide favorable hydrophobic interactions in the polar aqueous buffer, which further enhances the binding affinity. In addition, for enzymatic reactions, the enzyme active sites usually prefer a hydrophobic environment compared to an aqueous system to achieve higher initial rates. This rate acceleration is due to the fact that many mechanisms of enzymatic catalysis are based on general acids or bases. In aqueous systems, these highly soluble reagents need to undergo the desolvation process, so that they can interact with the substrate and catalyze the reaction. The design of a biomimetic catalyst involving a hydrophobic pocket can provide the favorable hydrophobic environment, and enhance the hydrophobic binding to the target substrate.

Representative MOFs used in biomimetic applications

Incorporation of porphyrins or metalloporphyrins

Metalloporphyrins or related metalloproteins, such as heme-based enzymes (cytochromes, peroxidases, myoglobins, and hemoglobins), have attracted enormous attention from scientists due to their critical functions and catalytic activities in many important biological processes.[40,41] The single iron porphyrin active site of hemoprotein is often embedded within the evolutionarily designed protein pockets, and serves as the catalytic center for the efficient synthesis and manipulation of many complex molecules that are crucial for essential life processes. It is known that heme can undergo self-destruction in oxidizing environments or self-assembly to form catalytically inactive dimers in aqueous solution, which hinders the direct application of heme as oxidation catalysts. In terms of both biocatalytic and biomimetic catalysis, various strategies and approaches have been investigated to search for the catalysts with comparable or superior peroxidase activities compared with native hemoproteins.

It is one of the hot trends to incorporate porphyrins/metalloporphyrins into MOFs for biomimetic applications. Several groups encapsulated hemin into porous MOFs to mimic heme-proteins' stunning functions in catalysis and molecular recognition.[42–44] Liu and co-workers reported the immobilization of hemin molecule into an amino-containing MOF (MIL-101(Al)-NH_2).[42] MIL-101 possesses a MTN zeolitic topology constructed from two kinds of polyhedral cages. The small cage has an internal diameter of ~29 Å while the larger cage has an internal diameter of ~34 Å. The formed Hemin@MIL-101 exhibited peroxidase-like activity toward catalytic oxidation of the substrate 3,3,5,5-tetramethylbenzidine (TMB) in the presence of H_2O_2 (Fig. 2). They developed sensitive and selective methods for the detection of glucose by using Hemin@MIL-101 and Hemin@HKUST-1. The analytical platform for glucose detection was observed to have a linear range from 1.0×10^{-5} mol L^{-1} to 3.0×10^{-4} mol L^{-1} ($R_2 = 0.993$). Recently, Yuan and coworkers built an electrochemical aptasensor for thrombin (TB) detection by the encapsulation of hemin into Fe-MIL-88 MOFs.[43] Their work points out the advantages of MOFs in the preparation of biomimetic catalysts, and extends the application of MOFs to biosensor applications.

MOFs consist of iron metal or a metal cluster and ligands including porphyrins as the major component can form the metalloporphyrin motifs within the framework to mimic the

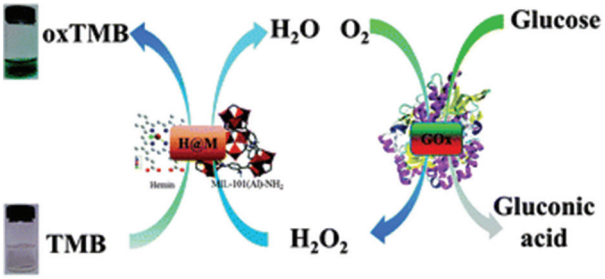

Fig. 2 Illumination of the catalytic oxidation of the substrate TMB in the presence of H_2O_2 by Hemin@MIL-101. The figure is reproduced with the permission of the publisher from ref. 42.

heme active center of heme-enzyme in terms of both structure and reactivity, and are capable of performing peroxidation of organic substrates by the use of hydrogen peroxide.

Larsen's group synthesized a class of biomimetic catalysts, MOMzyme-1, by selective encapsulation of catalytically active metalloporphyrins within one of the three nanoscale cages that exist in HKUST-1 using a "ship-in-a-bottle" approach.[37] In this approach, metalloporphyrins were encapsulated into the MOM frameworks during the solvothermal synthesis of MOMzyme-1 (Fig. 3) with up to ~66% (cavity) porphyrin loading. The benzenesulfonic acid groups of the porphyrin ligand further penetrate into the adjacent cages and thus form the orientation-specific proximal and distal heme pocket, which is crucial for the catalytic functions associated with heme enzymes. The peroxidase activity of Fe4SP@HKUST-1 towards monooxygenation of organic substrates was investigated using 2,2′-azinodi(3-ethylbenzthiazoline)-6-sulfonate (ABTS) as a redox indicator and compared with the homogenous systems, such as microperoxidase-11(MP-11), horse heart myoglobin (hhMb), and Fe4SP. Notably, the maximum yield in this biomimetic system is comparable to its MP-11 and Fe4SP counterpart in solution. However, due to the diffusion of the substrate molecules into the HKUST (Cu) frameworks, the product formation is slower in this heterogeneous Fe4SP@HKUST-1 system compared with the homogeneous systems. In addition, Fe4SP@HKUST-1 retained ~66% of the initial catalytic activity after three recovery cycles.

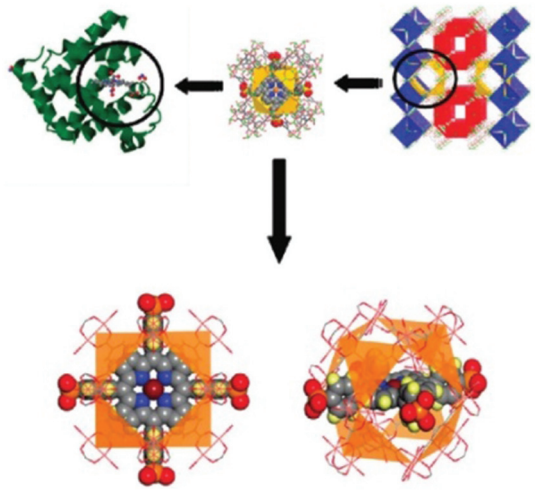

Fig. 3 (Top) Illustration of the similarities in the overall structural paradigm between heme proteins (left) and the porphyrin encapsulated HKUST-1 MOMzyme-1 (right). The diagram of HKUST-1 highlights the three distinct polyhedral cages that make up its structures. (Bottom) Diagram showing two equivalent orientations of the Mn(III)4SP within the octahemioctahedral cage of HKUST-1(Cu, Zn). The figure is reproduced with the permission of the publisher from ref. 37.

Instead of being encapsulated into MOFs, the metalloporphyrins can directly serve as the ligands to construct the MOFs. In 2012, Ma's group reported the biomimetic catalytic activities of a highly stable mesoporous MOF, MMPF-6, which is obtained by self-assembly of the iron(III) *meso*-tetrakis(4-carboxyphenyl)porphyrin chloride ligands with the *in situ* generated $Zr_6O_8(CO_2)_8(H_2O)_8$ SBUs under solvothermal conditions (Fig. 4).[32] The mesoporous MMPF-6 exhibited a Brunauer–Emmett–Teller (BET) surface area of 2100 $m^2\ g^{-1}$, and the pore sizes are predominantly around 11 Å and 33 Å. MMPF-6 demonstrated interesting peroxidase activity towards substrates such as 1,2,3-trihydroxybenzene (THB) and 2,2′-azinodi(3-ethylbenzothiazoline)-6-sulfonate (ABTS). The catalytic activity of MMPF-6 is comparable to that of a hemoprotein, myoglobin (Fig. 4a and 5), in terms of the initial reaction rates in buffer solutions. In addition, the biomimetic catalyst MMPF-6 exhibited solvent adaptability of retaining the peroxidase activity in ethanol (Fig. 5), while the native enzyme (myoglobin) quickly lost its catalytic activity in organic solvents. By investigating the oxidation of two different substrates (THB and ABTS), it was demonstrated that the peroxidase activity of MMPF-6 can involve both oxygen transfer and electron transfer mechanisms. Their recycling studies revealed that MMPF-6 can be reused for ten cycles without a significant drop in its peroxidase activity, which highlighted the heterogeneous feature of this biomimetic catalyst.

Coincidently, Zhou's group also reported the biomimetic catalysis of the same mesoMOF (PCN-222(Fe)) and conducted related kinetics studies and compared its peroxidase activity with horseradish peroxidase (HRP).[33] The stability studies (powder X-ray diffraction and N_2 adsorption at 77 K) demonstrated the extraordinary stability of this biomimetic catalyst in

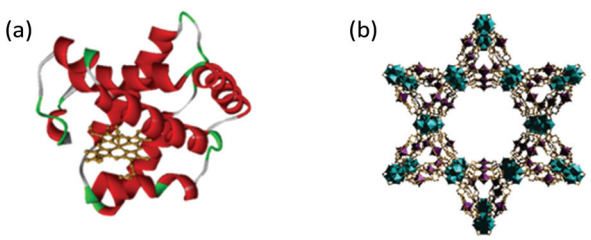

Fig. 4 (a) The structure of myoglobin; (b) hexagonal and triangular 1D channels of MMPF-6 (color scheme: C, grey; O, red; N, blue; Cl, green; Zr, turquoise; Fe, purple). The figure is reproduced with the permission of the publisher from ref. 32.

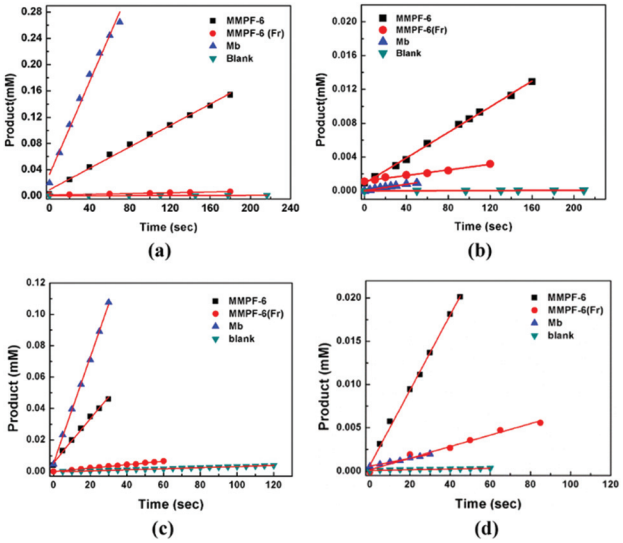

Fig. 5 Kinetic traces for oxidation of THB in (a) HEPES buffer and (b) an ethanol solution and oxidation of ABTS in (c) HEPES buffer and (d) ethanol solution. The figure is reproduced with the permission of the publisher from ref. 32.

water, boiling water, and concentrated aqueous HCl solutions (Fig. 6). By using the Michaelis Menten model, the kinetics parameters of PCN-222(Fe) in the biomimetic catalysis of the oxidation of three different substrates (pyrogallol, 3,3′,5,5′-tetra-methyl-benzidine, and *o*-phenylene diamine) were compared with the literature values of hemin and HRP (Table 1). The PCN-222(Fe) biomimetic catalyst was reported to exhibit superior peroxidase activity over hemin and even the real enzyme, HRP.

Incorporation of biomolecules

There are several remarkable developments in the encapsulation of a series of heme-based enzymes into MOFs. Ma's group first successfully encapsulated Microperoxidase-11 (MP-11) into a mesoporous MOF, Tb-mesoMOF.[45] The Tb-mesoMOF served as the host matrix due to its water stability and nanoscopic cages (3.9 and 4.7 nm in diameters) (Fig. 7b and c), and a loading of 19.1 μmol g^{-1} was achieved after ~50 h. The complex (MP-11@Tb-mesoMOF) demonstrated superior catalytic activity and recyclability in both 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid (HEPES) buffer and organic solvent (methanol), surpassing the free MP-11 counterpart. The same group also encapsulated a series of other heme-based proteins (myoglobin and cytochrome c) into mesoporous MOFs, and systematically investigated the catalysis and mechanisms of those biocatalysts.[27,46]

Recently, Zhou's group synthesized mesoporous water-stable MOFs (PCN-333 series) with ultra large cavities (large cage ~5.5 nm), which provided the single-molecule traps for enzyme encapsulation.[47] Three heme-proteins (horseradish peroxidase, cytochrome c and MP-11) were encapsulated in PCN-333. The characterization and biocatalysis demonstrated

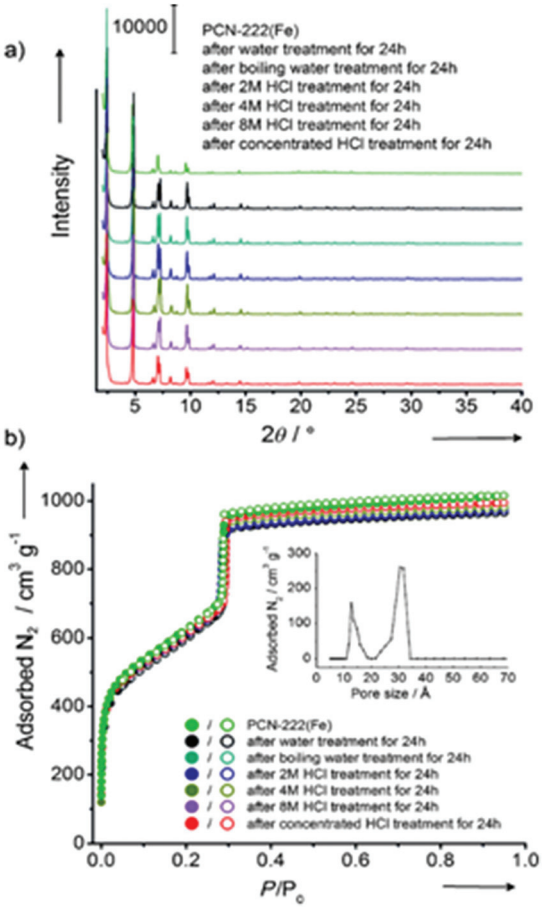

Fig. 6 (a) Powder X-ray diffraction patterns and (b) N_2 adsorption isotherms for PCN-222(Fe). The inset shows DFT pore size distribution for original PCN-222(Fe). The figure is reproduced with the permission of the publisher from ref. 33.

Table 1 Kinetics parameters for the oxidation of substrates by different catalysts. The table is reproduced with the permission of the publisher from ref. 33

Substrate	Catalyst	K_m [mM]	K_{cat} [min^{-1}]	k_{cat}/K_m [M^{-1} min^{-1}]
Pyrogallol	PCN-222(Fe)	0.33	16.1	4.85×10^4
	Hemin	N/A	2.4	N/A
	HRP	0.81	1.8×10^3	2.20×10^6
3,3,5,5-Tetra-methyl-benzidine	PCN-222(Fe)	1.63	14.0	8.59×10^3
	Hemin	0.78	0.1	1.26×10^2
	HRP	0.43	2.4×10^5	5.58×10^8
o-Phenylene-diamine	PCN-222(Fe)	8.92	7.3	8.18×10^2
	Hemin	N/A	0.8	N/A
	HRP	0.14	3.2×10^4	2.37×10^8

N/A = data not available.

high loading and reusability of the afforded hybrid materials (Fig. 8), which is probably due to the conjugated organic linkers and the concentrated metal sites provided many interaction sites between the guest protein molecules and the frameworks.

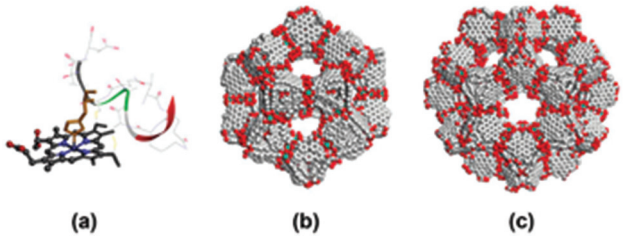

Fig. 7 (a) Molecular structure of MP-11, (b) 3.9 nm-diameter cage, and (c) 4.7 nm-diameter cage in Tb-mesoMOF. The figure is reproduced with the permission of the publisher from ref. 45.

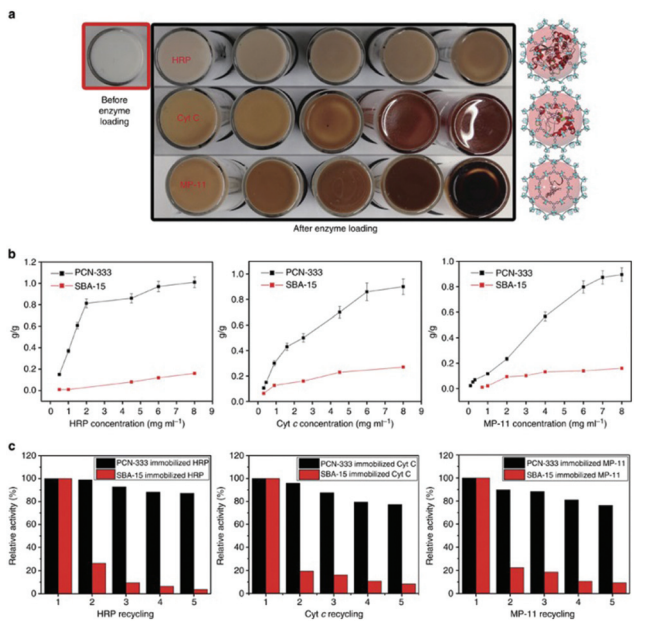

Fig. 8 (a) Color variations of PCN-333(Al) when loaded with different enzymes at different concentrations. (b) Plots of the loading capacities of different enzymes in PCN-333(Al). (c) Catalytic activity of immobilized enzymes in each recycle test. The figure is reproduced with the permission of the publisher from ref. 47.

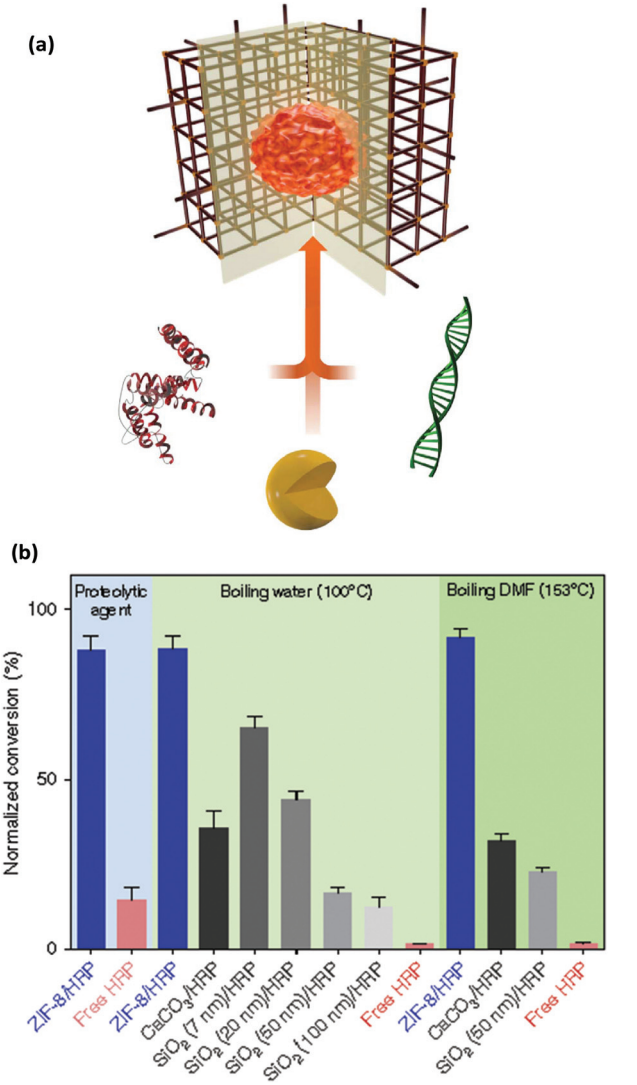

Fig. 9 (a) Schematic of a MOF biocomposite showing a biomacromolecule encapsulated within the porous, crystalline shell; (b) protective performance of ZIF-8 coatings on HRP. The figure is reproduced with the permission of the publisher from ref. 48.

Liang *et al.* encapsulated proteins (*e.g.* horseradish peroxidase, HRP) and DNA into ZIF-8 through an interesting 'one-pot' biomimetic mineralization strategy (Fig. 9a).[48] In the typical biomimetic mineralization of ZIF-8/proteins, the proteins (*e.g.* BSA) and enzymes (*e.g.* HRP) were firstly dissolved in 2-methylimidazole (160 mM, 20 ml, pH 10.3) and then combined with a separate solution of zinc acetate, agitated for 10 s, and left in room temperature for 12 h. After recovery and washing, the encapsulation efficiency reached 90% for most of the tested proteins. The MOF-coated biomolecules maintained enzymatic activity in extreme harsh conditions (*e.g.* boiled dimethylformamide at 153 °C), which demonstrated the excellent performance of MOFs as protective coatings for biomacromolecules (Fig. 9b). Later, the same group encapsulated urease into ZIF-8 by biomimetic mineralization, and observed a significantly enhanced thermal stability (from 40 °C to ~60 °C) of urease upon encapsulation.[49]

Very recently, proteins finally became a structural component of MOFs. For the first time, Tezcan and coworkers successfully used ferritin protein building blocks to form a novel three-dimensional porous metal–organic framework.[50] Ferritin acts as spherical protein nodes and self-assembles into a ternary protein–metal–organic crystalline framework through metal–organic linker-directed interactions. The T112H ferritin molecules can be immobilized by Zn^{2+} to assemble into fcc packing, but eventually they form a bcc lattice upon complexation with the ditopic organic linkers (Fig. 10). This example of proteinaceous MOFs opened a new window in the synthesis of biomimetic MOFs, and may overcome some major drawbacks of conventional proteinaceous materials, such as the enhanced stability. The incorporated protein in the MOF structure may provide this catalog of hybrid materials with the benefit of

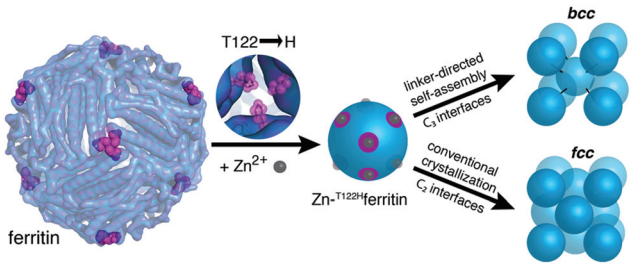

Fig. 10 Scheme for the metal–linker-directed assembly of ferritin into a 3D crystal lattice. The T112H ferritin molecules can be immobilized by Zn^{2+} (gray spheres) to assemble into fcc packing, but eventually they form a bcc lattice upon complexation with the ditopic organic linkers. The figure is reproduced with the permission of the publisher from ref. 50.

proteins' inherent functions in catalysis, electron transfer and sensing.

Other examples

In 2010, Volkmer *et al.* reported two pyrazolate-based cobalt(II)-containing MOFs, MFU-1 and MFU-2 using 1,4-bis[(3,5-dimethyl)pyrazol-4-yl] as ligands.[39] These two compounds exhibit similar structures as MOF-5 of pcu nets and demonstrated excellent stability against hydrolytic decomposition. Solution impregnation of MFU-1 with *N*-hydroxyphthalimide as a co-catalyst led to NHPI@MFU-1, which can oxidize a range of organic substrates under ambient conditions by employing O_2 in air. For example, NHPI@MFU-1 can catalyze the oxidation of cyclohexene at 35 °C without any additional solvent (Fig. 11). Notably, the activity of this heterogeneous system was only slightly reduced compared with the homogeneous NHPI acetonitrile solution. A suspension of NHPI@MFU-1 in the organic substrate was used to carry out the oxidation of cyclohexene, thus avoiding the use of additional solvents, simplifying workup procedures and reducing waste. The oxidation of cyclohexene was usually performed under harsh conditions such as high oxygen pressure and high temperatures. By contrast, this catalysis system was carried out under more cost-saving and environment-friendly conditions (35 °C, atmospheric oxygen).

In 2013, Lee *et al.* synthesized a new biomimetic complex (designated as Co-BBP) by the coordination of cobalt(II) with 2,6-bis(2-benzimidazolyl)pyridine (Fig. 12), which mimics the

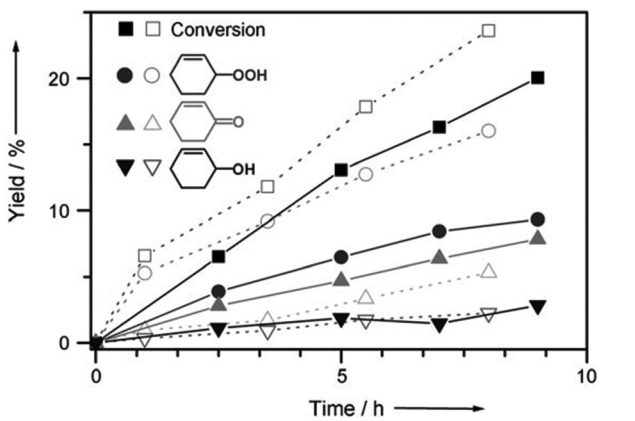

Fig. 11 Conversions [%] and yields [%] *versus* time for the reaction of cyclohexene with molecular oxygen at 35 °C. Filled symbols and solid lines: solvent-free catalysis employing NHPI@MFU-1; open symbols and dotted lines: catalysis employing MFU-1 suspended in NHPI-containing acetonitrile. The figure is reproduced with the permission of the publisher from ref. 39.

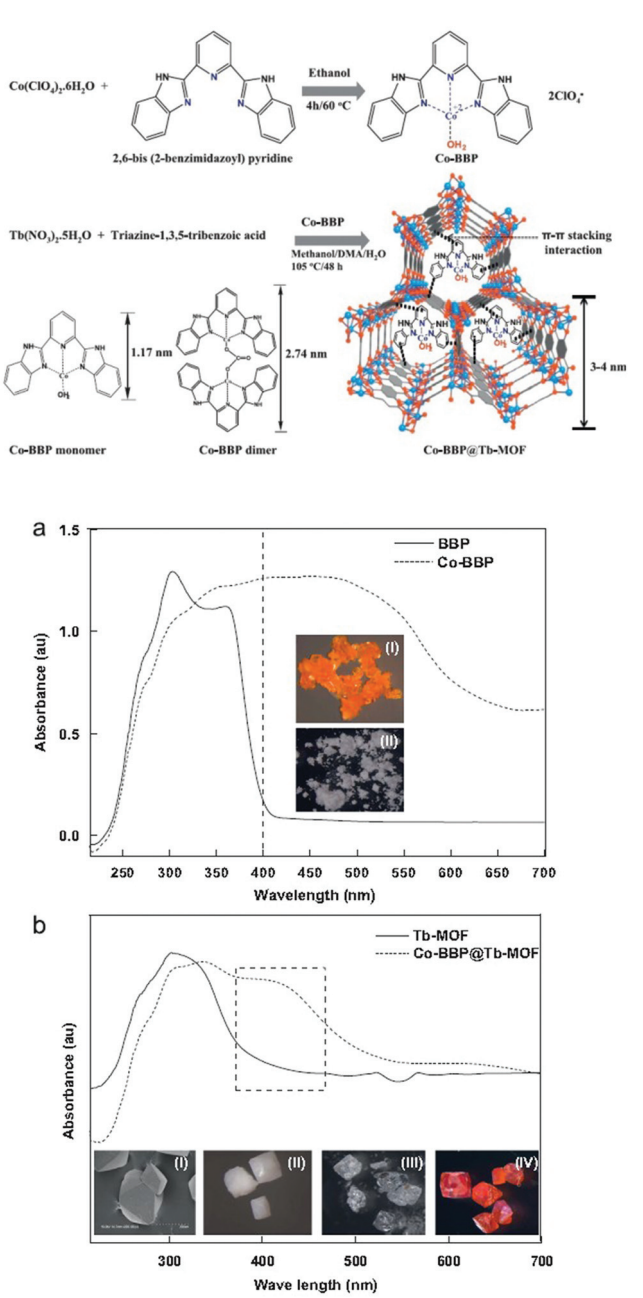

Fig. 12 Up: Schematic illustration of the preparation of Co-BBP and its encapsulation in Tb-MOF; bottom: (a) UV–vis DRS spectra of BBP and Co-BBP. (I) and (II) represent the optical images of Co BBP (orange color) and BBP (white color), respectively; (b) UV–vis DRS spectra of Tb-MOF and Co-BBP@Tb MOF. The figure is reproduced with the permission of the publisher from ref. 36.

active site of carbonic anhydrase (CA).[36] The synthesized Co-BBP was then encapsulated into the nanocages of a mesoporous terbium-MOF to form the Co-BBP@Tb-MOF complex using the "ship in a bottle" strategy (Fig. 12), and was confirmed by elemental analysis, UV–vis, DRS and FTIR spectroscopic analysis (Fig. 12). The biomimetic catalytic performance of Co-BBP@Tb-MOF in the sequestration of carbon dioxide (CO_2) was evaluated *via* an *in vitro* mineralization approach. The results from p-NPA hydrolysis indicated that the activity of Co-BBP increased by 14.39% after the encapsulation in Tb-MOF. In addition, it was reported that Co-BBP@Tb-MOF facilitated the formation of well-defined circular plates, and played the critical roles in the determination of the $CaCO_3$ morphology during the crystallization. Although it was observed that the conditions of CO_2 hydration in Co-BBP@Tb-MOF are different from those in carbonic anhydrase ($pK_a \sim 7$), the authors also proposed that the biomimetic catalysts were expected to enhance CO_2 hydration and calcium carbonate ($CaCO_3$) crystallization based on similar mechanisms to that of CA.

Li *et al.* reported the hydrolysis activity of HKUST-1 and its excellent catalytic reusability.[51] In this experiment, HKUST-1 demonstrated intrinsic enzymatic activity that mimic hydrolysis of bovine serum albumin (BSA) by trypsin. Compared to free trypsin, the MOF crystals possess much higher stability and reusability. In addition, HKUST-1 was also used to simulate trypsin and successfully detached A549 cells in cell culture experiments without the addition of EDTA. These interesting findings open an avenue for 'artificial enzyme' applications of MOFs, and also give rise to new possibilities for the exploitations of biomimetic applications of MOFs.

Conclusions

Biomimetic catalysis is still in need of in-depth and extensive studies. Due to the transformation from homogeneous to heterogeneous systems and the significant structural differences between the mimic materials and the enzyme, there are usually some differences between biomimetic catalysis and its native (proto) enzymatic catalysis in terms of mechanisms and catalytic kinetics. Therefore, the kinetic and mechanistic studies of biomimetic catalysis are of fundamental importance for the understanding and development in this field. The beneficial features of MOFs make them a promising candidate for the development of biomimetic materials. However, although many remarkable and exciting developments have been achieved in MOF-based catalysis over the past 20 years, biomimetic catalysis based on MOFs is still in an immature phase and much more remains to be explored. The systematic and comprehensive studies of the principles in the synthesis and design of MOF-based biomimetic catalysts are essential for further development and applications. Although remarkable progress has been achieved in MOF-related biomimetic studies, bio-inspired catalytic studies in this field are still dominated by immobilized enzymes and the related biocatalysis. Along with this, as the understanding of biocatalysis continues to advance, more efficient and various biomimetic catalysts will be rationally designed, thus facilitating the enhancement of the fundamental understanding of biocatalysis.

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