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Rising up: Hierarchical Architectures of Metal–Organic Frameworks in Experiment and Simulation

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Abstract:

The controlled synthesis across several length scales, from the discrete molecular building blocks over size and morphology controlled nanoparticles towards two-dimensional sheets, thin films, and finally three-dimensional architectures is an advanced and highly active research field within the Metal-Organic Frameworks

(MOF) and also the overall material science community. Along with the synthetic progress the theoretical simulation of MOF material structures and properties has shown tremendous progress both in accuracy as well as system size.

Here, recent progress in the synthesis of hierarchically structured MOFs as well as the multi scale modelling and associated simulation techniques are reviewed, with a brief overview of the challenges and future perspectives associated with a simulation-based approach towards the development of advanced hierarchically structured MOF materials.

Further advancement in the field of hierarchically structured MOF materials will allow to optimize their performance, however it requires a deep understanding of the different synthesis and processing techniques as well as an enhanced implementation of material modeling. This will allow to select and synthesize the highest performing structures in a targeted rational manner.

1. Introduction

Hierarchical organization is a basic principle surrounding us in our daily life in many natural, technical, and social systems.[1] The human body, in fact, is a classic example of hierarchical organization. At the lowest level, simple molecular building blocks, such as amino acids or lipids, build up more complex self-assembling three-dimensional biomolecular machines being able to perform complex tasks including data-storage as genes on DNA, the control, readout and translation of genes into encoded proteins, catalytic functions, energy storage and consumption or signal transduction. These molecular components are then organized into sub-cellular and cellular compartments and domains. These are themselves then structured into different organs and organ systems, which ultimately, at the highest level, constitute the entire organism. These organisms then are able of self-replication and also part of more complex eco-systems.

Hierarchical synthetic materials contain structural elements at more than one length scale. This structural hierarchy can strongly influence the bulk material properties. Understanding the effects of hierarchical structure is essential for guiding the synthesis of new materials with desired properties that are tailored for specific applications. [2]The individual building blocks in the material--which are often grouped into different sub-domains and domains--are usually regarded as the structural elements in hierarchical materials. However, other features of the materials, such as porosity or chemical composition, can also be organized hierarchically, which is crucial for optimizing specific properties, such as diffusion within the material or directional energy transfer.[3] The hierarchical order of a material may be defined as the number (n) of levels of scale with a specific structure.[2] As in natural systems, such as proteins, one can categorize the structures at different length scales, starting from the smallest length scale, as primary structure, secondary structure, tertiary structure, and so on.[4]

MOFs are a class of functional crystalline materials that has grown immensely within the last 20 years.[5] MOFs have two components: metal ion or metal oxo clusters, which act as nodes, and organic molecules, which act as linkers between the nodes.

Due to the wide variety of suitable organic molecules and metal nodes, more than 70,000 different MOF crystal structures have already been reported.[6]

The large variability of MOFs in terms of their (i) framework architecture (ii) pore structure and (iii) incorporation of functional constituents permits MOF materials to be hierarchically structured using three approaches: according to architecture, according to porosity or according to the composition or distribution of functional constituents. The basic structure and composition of MOF materials and the different approaches to their hierarchical structuring are shown in **Figure 1**.

MOF materials with hierarchical architecture have a defined structure on multiple length scales. All MOFs have a defined framework structure on the molecular level (in the range several angstroms to several nm), which is largely defined by the choice of the molecular components. This represents the primary structure. To create secondary structures, one needs to structure the MOF material also at larger length-scales, from several 10th of nm, to µm and mm, and up to the macroscopic level.

Most MOF types are intrinsically porous, since the defined framework structure contains potential voids at the microporous (pore size below 2 nm) to mesoporous (pore size between 2 nm and 50 nm) length scales. This represents the primary porosity.[7] Introducing a secondary porosity at a larger length scale thus creates hierarchically porous materials. Here, one must keep in mind that the porosity of an MOF is closely linked to its framework topology.

The diversity of organic linkers and metal nodes suitable for synthesizing MOFs makes it possible to prepare numerous compounds, even for a single defined framework topology.[8] Since the molecular components have a defined organization at the molecular scale, one can hierarchically organize MOF materials by inserting different components on a larger length scale.[9, 10] **Table 1** summarizes the different types of hierarchies in MOFs, along with their characteristics and properties, and offers some related examples from natural systems.

An MOF's hierarchy type greatly influences the final properties of the bulk material, and the three types can provide complementary qualities. As evidenced in many biological materials, such as horn, wood or bone, hierarchical architecture provides materials with exceptional mechanical strength and unique material properties. [11] Hierarchical porosity, in contrast, enables fast transport and/or a high degree of flow distribution within a bulk material.[12] Compositional hierarchy can provide a protective layer or, if desired, promote the directional transport of ions or energy (e.g., in membranes or light-harvesting materials in solar cells).[13]

Further advances in creating hierarchically-structured MOF materials will require improved material modeling. Better models will help researchers select and synthesize the highest performing MOF material and structure in a targeted, rational manner. Given the almost unlimited possibilities offered by the numerous molecular components and 1D, 2D and 3D structures, this clearly represents an important step forward.

The experimental insight gained by developing more complex MOF-based materials has generated high demand for *in-silico* modeling of these materials. This demand stirs both from a desire to understand the basic principles leading to specific material properties and from the promise for accelerated development cycles by complementing the experimental insights. Multiple disciplines such as material science, physics, chemistry and the life-sciences have a long tradition of honing their specific simulation techniques to better understand and design their specific systems of interest. The on-going exponential growth of computational computing and data-storage powers accelerate the possible insight from such simulations, often by complementary experimental and simulation studies. [14, 15]

In the following sections we will provide an overview and analysis of the current status of hierarchically structured MOF materials as well as the multi scale modelling and associated simulation techniques employed in designing these molecular materials. After discussing the basic challenges and fundamental aspects in the synthesis of MOF materials associated with the introduction of hierarchical architectures, porosities and compositions, we want to give the readers a guideline into the simulation across different length scales, which will help to implement a simulation-based approach towards the design of hierarchically structured MOF materials with optimized properties.

2. Synthesis of hierarchical MOF materials

Introduction of hierarchy into MOF materials can be realized either by controlling the conditions during the MOF growth or by post-synthetic treatment of the material. In this regard, hierarchical MOF materials can be categorized into bottom-up and top-down approaches. The bottom-up approaches focus on the control of crystallization and growth processes, including utilizing templated crystallization, crystallization at interface, sol–gel processing[16] and transformation from metal template. Meanwhile, top-down approaches mainly including post-synthetic functionalization, chemical etching [17] and delamination processes. However, some processes, like surface-energy-driven process, can shape the MOF crystal and introduce structures into the MOF at different length scales, and are thus applied in both approaches.

2.1. MOFs with Hierarchical Architecture

2.1.1Production of MOF Secondary Architecture

The secondary architecture can span along different dimensions, leading to 0-D, 1-D, 2-D and 3-D architectures. Apart from 1-D MOF secondary architecture, bottom-up approaches and top-down approaches have been widely used in the construction of these hierarchical architectures. (**Figure 2**)

MOF 0-D Secondary Architecture: The major challenge in this field of 0-D architecture is to control the size of the MOF nanoparticles. Along with some cases where templates were employed, [18] most approaches focus on the control of nucleation rate and crystal growth rate. Both microwave and ultrasound can accelerate the nucleation rate and crystal growth rate and help to produce MOF 0-D architecture. [19] Modulators like water [20], methanol [21], acids [22, 23] and amine [24, 25] can also be added to adjust and control the growth of MOF 0-D architecture. [26]

It is rare to construct 0-D MOF architectures via top-down approaches. Avci et al. reported the shape modification of MOF via anisotropic etching. ZIF-8 crystals were etched with its shape change from rhombic dodecahedron to cubic. [27]

MOF 1-D Secondary Architecture: MOF 1-D secondary architectures include nanotubes, nanorods and nanowires, which are more challenging to produce compared to MOF 0-D secondary architectures.

Bottom-up approaches are widely used in the production, such as liquid-phase epitaxy methods, allowing rod-type MOF to be grown from gold surface.[28] Modulators can also control the growth of MOF to form nanorods in a solvothermal synthesis,[29] so is the reverse-phase microemulsion technique[30]. Apart from these methods that are subject to specific type of MOF, templates provide a more general approach. For instance MOFs can be coated on the surface of insoluble rod-type templates consisting of polymers,[31] metal oxides[32] or metal nanowires[33] to form 1-D structure. Upon template removal, MOF nanotube can be formed.[34]

When it comes to top-down approaches, there are only few reports on etching to from 1-D structure, since it is hard to control etching process or defects inside MOF.[35] However, it was shown that MOF tube can be transformed into MOF-shell-type tubes using etching.[36]

MOF 2-D Secondary Architecture: The production of MOF 2-D secondary architectures has been widely studied [35, 37] for both bottom-up and top-down approaches.

Bottom-up approaches include modulated synthesis and interfacial synthesis. By adding acid [25, 38], salt [39] or triethylamine [40] as modulator during MOF growth, MOF 2-D secondary architecture can be obtained. Interfacial synthesis has also been investigated using liquid/liquid interface [41] as well as gas/liquid interface (mainly

Langmuir–Blodgett method) [42, 43], of which production at liquid/gas interface can reach monolayer structure compared to those at liquid/gas interface with a minimum thickness of about 100nm. Apart from interfacial synthesis with two-liquid systems, interdiffusion of the metal ions and ligands in a mixed-solvent layer between two liquids for MOF showed to increase the yield substantially. [44]

Top-down approaches, such as exfoliating MOF crystal via different processes, are popular ways for production of 2-D secondary architectures: Sonication, [45, 46] mechanical exfoliation, [46, 47] chemical exfoliation [48] or simply solvent induced delamination, [49] taking advantage of the weak interactions or instability of linkers [48, 50] inside MOF structures, the crystal can be exfoliated into a 2-D secondary architecture. In most of these cases, the yield is the major challenge, as the thickness of the MOF sheets can vary within a certain range and be difficult to control.

Apart from the construction of nanosheet-type 2-D secondary architectures, methods were also developed for MOF films, layers and patterned layers [51], most of which have higher thickness and larger area, leading to 2-D hierarchy at a larger scale. Growth of MOF on the solid surface also often leads to MOF thin film. Different methods can be used to produce MOF film or layer, such as layer-by-layer (LbL) method [52], substrate-seeded heteroepitaxy (SSH) [53, 54], electrochemical deposition (ECD),[55] powder MOF-based deposition (PMD),[56] atomic layer deposition (ALD), [57] and chemical vapor deposition (CVD)[58, 59].

Along with the production of MOF layers on the surface, some methods were applied for MOF patterning on surfaces. [60] Examples are inkjet printing, [61] scanning-probe assisted patterning [62], and micro-contact printing (μCP) often combined with solvothermal [63] or LbL methods [64]. Light was also applied to structure MOF films, via photolithography of the substrate [65] or via electron beam lithography. [66] Applying an IR laser to locally heat a substrate to confine the MOF growth was also reported as a promising tool for direct laser writing of MOF.[67] Top-down approaches, which follow partial removal of the MOF layer, are also reported. [68]

MOF 3-D Secondary Architecture: 3-D secondary architectures mainly involve hollow or porous MOFs, which lead to the uneven distribution of MOF material in 3-D space. Porous MOFs will be discussed in more detail in section 2.2.

When it comes to the construction of hollow MOF architecture, one often applied bottom-up approach is to use sphere-like templates. [69] With hard template, like polystyrene [70], metal oxides particles [71], alumina beads [72], silica spheres [73] that are not easy to remove often give rise to the formation of particles with a MOF shell. By the partial removal of the hard template, so-called “yolk–shell” architecture can also be formed. [71, 74] Such structure are often used in batteries. [75] Soft templates, such as surfactants [70, 76] and even cell wall [77] can be used in production of shell-type MOF architecture.

MOF 3D secondary architectures can be also be produced by interfacial synthesis. [78] Spray-drying of a MOF precursor solution leads to the crystallization at the gas-liquid interface [79] and the formation of oil drop in aqueous solutions can template to the crystallization at such liquid-liquid interface.[80] Also gas bubbles can be used as template to produce hollow MOF architecture.[81]

Top-down approaches, mostly involving etching, were also used in the MOF production.[82] Taking advantage of surface-energy-driven mechanisms, MIL-101 growth and etching with acetic acid lead to the multi-shelled hollow MOF architecture.[83]

To build MOF 3-D architecture a larger length scales, one of the method is to construct the 3-D material mixed or coated with MOF. [84] By mixing UiO-66 or ZIF-8 with sodium alginate (SA), MOF hollow tube can be obtained. [85] Besides, 3-D printing was applied in the construction of acrylonitrile butadiene styrene (ABS) frameworks coated with Cu-BTC. [86]

2.1.2. Production of MOF with tertiary hierarchical architecture

Utilizing MOF 1-D secondary hierarchical architectures for the seeding process [87] or assembly into a line [88] leads to 1-D tertiary architecture. Similar strategies can be used for 3-D tertiary architectures. With applying soft template methods using colloidosomes, MOF with triple hierarchical architectures can be formed via Pickering emulsion. [89] In this hollow architecture, the levels different levels of hierarchical architecture can be easily observed. The Fe-soc-MOF lattices, as primary architecture, form defined cubic particles as secondary architecture, which then gather into shell-type tertiary architectures. Avci et al. recently reported the self-assembly of truncated rhombic dodecahedral particles of the ZIF-8 into even millimeter-sized superstructures. [90] **(Figure 3)**

Also, liquid-phase epitaxy methods on selected subtract can produce MOF with tertiary hierarchical architecture. Falcaro et al. [91] reported growing MOF on the substrate of crystalline copper hydroxide to get film-type tertiary hierarchical architecture with particle-type secondary hierarchical architecture.

By combining bottom-up and top-down approaches, tertiary hierarchical architecture can be made. By etching [92] or substitution [12], the shell-type structure or the MOF crystal can be further modified.**(Figure 4)** Also by anisotropically etching ZIF-8 and ZIF-67 with xylenol orange by pH control leads to hollow-box-shape or concave-tetrahedron-shape MOF nanoparticle.[93]

2.2. MOFs with Hierarchical Porosity

According to International Union of Pure and Applied Chemistry (IUPAC), pores within materials can be classified into 3 scales: micropores (with a pore diameter of less than 2 nm), mesopores (with a pore diameter between 2 nm to 50 nm) and macropores (with a pore diameter of more than 50 nm).[94] MOFs themselves usually intrinsically contain micropores originating from cavities within the framework structure.[95] These pores can reach the mesopore level in few reported cases.[96] Within a single MOF structure, there can be a coexistence of two or more pore types and sizes, all of which usually are within the same length scale. In constrast hierarchical porosity requires porosity at different length scales.

There are two kinds of MOF materials with hierarchical porosity. One is all-MOF material with multiple scales of porosity, this is mainly focused in this section. Another kind of hierarchically porous materials can be achieved by combining MOF with another, usually meso- or macroporous materials, creating hybrid structures, where MOFs usually provide the microporosity. Following this approach, several hierarchically porous materials have been constructed and applied. [59, 97]

In analogy to MOF hierarchical architectures, the primary porosity of hierarchically porous MOFs is its intrinsic microporosity originating from the framework. In order to generate hierarchically porous all-MOF materials, an additional secondary porosity has to be generated in/with MOFs within the mesoporous or macroporous range. For the secondary porosity both bottom-up and top-down approaches have been developed.

2.2.1. Bottom-up Approaches

Inspired by traditional zeolites with hierarchical structures, template strategies have become one of widely-used methods in the production of hierarchically porous MOFs, [98] with both soft and hard templates.

Soft template methods involve the self-assembly of structure-directing agents (SDAs) to form a template and the interaction of SDAs with metal ions or linkers to control the MOF growth. Different surfactants, which involve cationic structure-directing agents, anionic structure-directing agents and polymers have been used for soft template formation, such as cetyltrimethyl ammonium bromide (CTAB) [99], cetyltrimethylammonium chloride(CTAC) [100], amphiphilic dodecanoic acid[101] and non-ionic block copolymers [102]. Several small molecules, like 1,3,5-trimethylbenzene (TMB)[99] and citric acid (CA) [103], were applied to adjust the formation of the template and the nanocrystals. Recently, by combination of CTAB as template and electrochemically assisted self-assembly (EASA) technique, MOF thin films were grown on electrodes with 2-D honeycomb-like mesopores as secondary porosity in the walls of the cavities.[104]

Combining ionic liquids (ILs), supercritical carbon dioxide ($scCO_2$) and surfactant to form emulsion system can also produce hierarchically porous MOF with micro and mesopores as secondary porosity.[105] Also production of MOF with CO_2-expanded DMF can also introduce secondary porosity in the structure.[106]

For production of higher levels of hierarchical porosity, Reboul et al.[107] reported metal templates, such as hexagonal patterns and aerogels of alumina, can be transformed into hierarchically porous MOFs via reaction with likers, and the MOF have micropores, mesopores ae well as macropores.**(Figure 5)**

2.2.2. Top-down-approach

Top-down approaches mainly focus on introduction of structural defects and partial removal of metal nodes or linkers within the MOFs. Taking advantage of the complex structure inside MOFs, controlled treatment with water [108], acid [109] and H_2O_2[110], will partially destroy the MOF structure, leading to hierarchical porosity. **(Figure 6)** Controlling the partial removal of MOF segments form the structure, however, can be challenging and sometimes to total decomposition of the primary porosity. An alternative strategy is the introduction of unstable linkers to MOFs.[111] PCN-160 with AZDC (azobenzene-4, 40- dicarboxylate) as linker was synthesized and exchanged by CBAB (4-carboxybenzylidene-4-aminobenzate), which can be cleaved *via* a one-step hydrolysis reaction. After carefully choosing the condition in synthesis, exchange and acid treatment, hierarchical porous structures were obtained. **(Figure 7)**

2.3. MOFs with Hierarchical Composition

MOFs are composed of metal nodes connected by organic linkers, which are structured at a molecular level within the framework, which is regarded as the primary composition. Structuring different components within selected regions in one MOF crystal or within different layers of a MOF film at a microscopic or macroscopic length scale leads to a secondary composition. To produce MOFs with hierarchical composition, mostly liquid-phase epitaxy methods such as seeding or LbL processes were applied.

2.3.1. Seeding Processes

Seeding process is a classical bottom-up approach to produce layered crystalline materials, [112] through which block MOF and core-shell MOF structures can be obtained.

By using a MOF crystal as seed, an additional MOF of different composition can be grown on it to obtain core-shell-type hierarchically composed MOFs. (**Table 2**) The core-shell structures represents the secondary composition. By coating multiple shells, higher hierarchical composition can be obtained. [10] For characterization of this kind of the MOFs, XRD and SEM were used. In some cases, different levels of hierarchical composition can be directed observed by the optical microscope. [10]

By careful selection of the length of the linkers, the additional hierarchical composition can be selectively grown on the specific surface. Furukawa et al.[9] reported that, with the $[Zn_2(ndc)_2(dabco)]_n$ as the primary hierarchical composition, the growth of the $[Zn_2(ndc)_2(dpndi)]_n$ as the secondary hierarchical composition (ndc = 1,4-naphthalene dicarboxylate) is face-selective. **(Figure 8)**

After the formation of core-shell-type structures, several studies reported reduced crystallinity of the primary hierarchical composition, as confirmed by optical images and XRD data, which makes the block-type MOF of hierarchical composition more efficient than core-shell-type one in gas sorption and separation. [113]

2.3.2. Layer-by-Layer Processes

Layer-by-Layer processes have been widely used in deposition of MOF onto surface or nanoparticles using different techniques such as spin coating, dipping, spray and others[114] Surface-amounted MOF (SurMOF) with hierarchical composition was produced since 2011.[115, 116] Unlike seeding processes, MOFs with pcu topology is preferred in most of the production, such as $[Cu_2(ndc),(N\text{-ligand})]$ [115, 116, 117-119], $[Cu_2(bdc),(N\text{-ligand})]$ [117, 119, 120], $[Cu_2(BPDC),(N\text{-ligand})]$ [119, 121]. Recently, Chernikova et al. [181] reported a MOF-on-MOF thin films with hierarchical composition, where Cu-tbo-MOF-5 was grown on HKUST-1 *via* LbL process. (**Figure 9**)

As substrate for the LbL methods usually flat surfaces are used, but also nanoparticles have been utilized. With multiple growth on a single magnetic core particle with different types of MOF via LbL method, shell-on-shell-type hierarchical composition was obtained and can be further transformed into magGEL capsules, inside which cargo molecules can be released at different release kinetics depending on the pH of the environment. [122] **(Figure 10)** MOF crystal particles, can be used as surface for another MOF growth through LbL process, where UiO-66-NH_2 is surrounded by ZIF-8. [123]

2.3.3. Others

Besides these bottom-up approaches, MOF with hierarchical composition can be obtained via top-down approaches. Thorough post-synthetic modification on linkers, part of linkers in the crystal can be further transformed to form MOF with hierarchical composition.[124] Core–shell structure can be obtained from post-synthetic exchange (PSE) with linker exchange in MOF-5, UMCM-8, and UiO-66.[125] Also, MOFs can change their shape to obtain hierarchical composition by ligand exchange. MOF-5 in the treatment of 2-methylimidazole can be transformed into core-shell-type ZIF-8. [126] The hierarchically compositional component with amide group can be further functionalization. [115, 117, 120] Similarly, the hierarchically compositional component with azobenzene structure can change its spatial configuration in the appearance of light. [120]

Though epitaxy methods make it possible to construct many MOFs with hierarchical structure, it is hard to hybridize MOFs of which different crystallographic parameters. To overcome the disadvantage of epitaxy methods, Gu et al. report two MOFs with distinct morphologies and crystal structures, NH_2-UiO-66(Zr) and NH_2-MIL-125(Ti) were easily hybridized as MOF-on-MOF heterostructure through microwave heating in which NH_2-UiO-66(Zr) is exposed to NH_2-MIL-125(Ti) precursors with polyvinylpyrrolidone (PVP) as the structure-directing agent. [127]

3. Simulation of Hierarchical MOF

Advanced simulation techniques can complement experiments in variety of fields, ranging from, e.g. simulating biologically relevant molecules such as proteins or RNA[15, 128, 129] with atomic resolution over applications in molecular electronics[130] [131] to descriptions of material properties[132]. Common to all these applications is striking a good balance between the desired level of detail and the computational expenses. The involved methods can be broadly divided into methods based on quantum mechanics (QM), in particular on density functional theory (DFT), [133] and those based on molecular mechanics (MM). QM based methods tend to be computationally very involved as they calculate electronic densities around all involved atoms. In contrast, methods based on MM describe atoms as points in space that interact via computationally easy-to-calculate interactions such as simple harmonic ("spring") interactions with the surrounding atoms. Statistical mechanics allows to calculate ensemble properties such as free-energies from such simulations. [128]

3.1. Molecular Force Fields

The choice of an appropriate energy function to describe molecular-level energetics accurately is crucial. While quantum mechanics (QM)-based calculations would (in principle) allow to calculate molecular energies at arbitrary levels of accuracy, these calculations are computationally very demanding. Instead, one often resorts to condensing the QM-Hamiltonian into a simplified force field (technically a potential) composed by bead-like atoms. Effectively, one applies a classical Newtonian mechanics description to model atomic systems. The individual atoms are assigned properties such as mass, charge, size (van-der-Waals radius) and interactions strengths and types with neighboring atoms.

These interactions are divided into bonded and non-bonded terms. The bonded terms include bonds, angles and dihedrals (1-2, 1-3, and 1-4 interactions, **Figure 11**).The non-bonded terms are typically Van-der-Waals interactions and electrostatic interactions. (Equation 1)

Many of these force field have been developed for biomolecular applications such as, e.g., AMBER [134], CHARMM [135], GROMOS [136], or PFF01 [137].

3.1.1. Force-Field Challenges

The design of MOFs is tied to its purpose and realistic results of calculations and simulations are crucial for the prediction of their properties. In many cases the simulations use standard force-fields such as UFF (Universal Force-Field) [138] or DREIDING [139] and tune the parameters afterwards to achieve a good agreement with experimental data. A precise universal force-field, however, does not exist and especially for MOFs, where many different metals and organic linkers come together, it is very challenging to develop a general model. The more elements a force-fields tries to describe, the less precise is it for a large variety of systems. Trying to parametrize a MOF structure from scratch by doing *ab initio* DFT calculations is often time consuming and involved, yet still the best option to create and model a MOF topology. The downside of this approach is that the derived parameters are most likely no transferable to different MOFs except for cases of extremely highly chemical similarity.

3.1.2. UFF4MOF

Creating a force-field can be developed by *ab initio* calculations or fitting to experimental data, or by expanding an existing force-field to create a suitable description for MOFs. UFF4MOF[140] follows this approach and is based on the UFF force-field by Rappè.[140] While many force constants are derived via chemical similarity from the underlying UFF force-field, re-parametrization by additional, prior DFT calculations for parameters such as bond lengths and angles is recommended to significantly increase the accuracy of the subsequent simulation. In the case of UFF4MOF, the basic parametrization of UFF itself has remained unchanged but a small group of molecules was experimentally measured and the results were extrapolated to include almost every element in the periodic table. A consequence of this method is the necessity of correction terms for bond distances between two atoms. The bond order correction and the electronegativity correction have to be considered. The force field describes stretching, bending, torsion and inversion for bonded interactions and in case of non-bonded interactions there are terms for Van-der-Waals and electrostatic interaction. The stretching potential is expressed by a harmonic function or alternatively by a Morse potential, the bending, torsion and inversion potentials are expressed by cosine Fourier expansions. Van-der-Waals interactions are described traditionally by a 6-12 type Lennard-Jones potential and the electrostatic interactions keep their respective form from electrodynamics.

As UFF applied to MOF structures could not provide accurate results, UFF4MOF is solving this problem by adding new atom types with tuned parameters to achieve results which match well with the experimental data.[140] A particular challenge of UFF was the inconsistency within the metal node of the MOF and the reason to introduce fitting atom types specifically for the metal nodes in UFF4MOF.

A test parametrization of some MOF families such as IRMOF and HKUST with UFF4MOF showed decent consistency with experimental results. However, the attempt of covering almost every element in the force-field results in a rather rough parametrization. *Ab initio* methods are therefore still inevitable to achieve a more precise topology, with the downside that the parameters are not transferable to other structures.

3.2. Molecular Dynamics

In Molecular Dynamics (MD) one integrates the forces derived from a molecular modeling approach/ force field on each atom over time. This results in a trajectory which provides dynamic information about the investigated atomic system. MD is an approach finding wide application in the field of biomolecular simulations, where much insight can be transferred to simulations of MOFs about the involved methods and challenges [128, 141].

In short, the critical components are (1) choosing a good MM force field description for both the system of interest and solvent, which can be described explicitly or implicitly. In addition, the periodic boundary conditions need to be chosen. (2) Then, the forces are derived during the simulation from the MM force field for each particle. One particular challenge here the long-range nature of some interactions such as electrostatics, which make an efficient parallelization of computation on many-core architectures challenging due to the need for communication and data-exchange. (3) These forces are then integrated over time by a discrete time step typically on the order of *1-2fs*. While a large time-step is desired for efficient calculations, the time-step is limited by the fasted movements and oscillations within the system. As the dynamical trajectory is sequential in nature, different parts of the simulations cannot be easily computed in parallel, though advanced sampling approaches such as Parallel Tempering [142], Accelerated MD [143], or Markov Chain Models try to circumvent this challenge [144]. (4) Temperature and pressure need to be controlled for numerical drift via thermostat and barostat while maintaining the correct statistical ensemble.

3.3. Density Functional Theory

Density Functional Theory (DFT) calculates the local ground state electric charge density of an atom or a molecule by solving quantum mechanical equations. First there are two simplifications: (1) The nucleus of an atom is neglected in the calculations as its movement is too slow compared to that of the electrons (Born-Oppenheimer approximation). (2) Also the many-body Schrodinger's equation describing every electron will not be used to calculate the total energy but the wave function of single electrons will be used to calculate the local electron density (Kohn-Scham function). [145] The functionals in the total energy function can be adjusted for different purposes with B3LYP being the most popular. [146] Adding pseudopotentials to improve the DFT calculation is another possibility. Pseudopotentials describe the core set of electrons that have a negligible influence on the chemical properties and thus, are separated from the valence electrons. [147] However, the choice of the right pseudopotentials is crucial for the outcome of the calculation.

3.4. Software tools for simulation

There exist several tools for DFT and MD, some commercial and some commonly available open-source packages. An example for a freely available simulation package is GROMACS [136] (Groningen Machine for Chemical Simulations). Being optimized for protein structures it is a popular choice for biochemical simulations. The software has pre-implemented force-fields such as AMBER and CHARMM (with many variants) which are both used for biomolecular system and OPLS. [148] It is possible to add customized force-fields to extend the existing possibilities of simulations.

An alternative to GROMACS is LAMMPS [149] (Large-scale Atomic/Molecular Massively Parallel Simulator) which is also open-source and has the most commonly used force-fields implemented. LAMMPS focuses on material modeling but can also be used for other tasks e.g. biochemical systems. A commercial molecular simulation package for MD is DL-Poly [150]. However, the license is free for academic research only. Other popular choice for MD simulations include the NAMD [151], AMBER [152], and CHARMM [153] simulations suites.

Popular DFT codes licenses such as VASP [154], Turbomole [155] or GAUSSIAN [156] are commercial available. Unlike MD simulation packages, where in principal the biomolecular force field description and used software packages are similar to each other, DFT codes can differ quite substantially. The needed pseudopotentials and functionals are not always part of the program and have to be obtained in another way. There also exist different methods to describe the potentials, e.g. VASP uses planewave basis and is suited to calculate periodic structures. For molecular systems, GAUSSIAN or Turbomole tend to be the most popular choices.

3.5. Simulation methods

MD simulations in different areas have a long tradition. [157] Investigating physical properties of MOFs by performing MD simulations provide beneficial input for experimental groups. Analyzing simulation data allows to obtain promising predictions and improves the experiment and helps to save time and money. Typically such simulations are based on deposited structures of MOFs found in, e.g., the Cambridge Structural Database with its currently (2018) over 81,000 entries [158]

4.5.1. Stability of MOFs

An interesting physical property of MOFs is the stability under pressure or by adding different solvents to the simulated system. For example MOF-5 was simulated with water as solvent resulting in a stable MOF at a lower water content, however, distortions were already visible at slightly higher water content.[159] The simulation could also pinpoint the reason for the instability, namely the similarity between the oxygen atoms of the MOF metal node and water. This resulted in modifying MOF-5 to increase the water stability. [160] Another type of stability is the mechanical stability and elasticity. An indicator for structural stability is the shear modulus which is given in units of pressure. The higher the shear modulus the higher the ability of the material to withstand deformation. DFT calculations showed the weak point of MOF-5 allowing to take targeted countermeasures. [161] The stiffness of a material is expressed by the Young's modulus and can be calculated by DFT. Comparing the results allows to compare (not synthesized) MOFs with known materials, e.g. "MOF-5 behaving as a soft and ductile material with a Young's modulus of the order of Oak wood".[162]

4.5.2. Electric and Thermic Conductivity

As DFT calculates the electron density, thus, investigating the electronic structure and the electric conductivity of MOFs becomes plausible. Evaluating the band gap allows to determine the conducting type of the MOF. Further by modifying the MOF it is possible to change the band gap and find novel semiconductors [163]. For example the calculated band gap of MOF-5 amounts to 2.5 eV which would classify it between insulating and semiconducting materials [162]. Hence, using DFT calculations allows to design tailor-made (semi)-conductors or insulators for various applications.

Another interesting property of a material is the thermal conductivity. In MD simulations one can apply a thermostat to the system and define a temperature, hence it is then possible to investigate on the thermal conductivity. Simulations lead to a thermal conductivity of about 0.31 $Wm^{-1}K^{-1}$ for MOF-5 which is also weakly dependent on temperature [164]. Thus, MOF-5 qualifies as an insulating material. Being able to investigate these values may lead to novel thermal insulating materials.

4.5.3. Diffusion through MOFs

One of the most interesting aspects of a MOF is its effect on guest particle/molecules. MOFs are prime candidates for gas storage, gas separation or catalysis [165]. Atoms and other smaller molecular compounds are able to diffuse through the pores of a

MOF. The efficiency of the diffusion is determined by the structure and functionalization of the MOF. The simulated adsorption isotherms of Ar, CH_4 and H_2 for different MOFs were compared with experimental data and were within 10-15% error range [166]. Many MOFs (MOF-2. MOF-3, IRMOF-1, IRMOF-6, IRMOF-8) were found not suitable for hydrogen storage and even the more promising results were not derived by simulations at room temperature, which experimentalists want to achieve. It should be noted that the MD simulations used DREIDING and/or UFF as force-fields, which delivered decent results, are the first candidates for improvement in future simulations. The diffusivity of benzene into MOF-5 was found in good agreement with experimental results. [167] （**Figure 12**）

4.5.4. Gas Storage in MOFs

Closely related to the diffusion of guest molecules through the pores of a MOF is the storage (mainly of gases) in the MOFs via adsorption. Functionalizing the organic linkers allows to optimize the MOF for storage of different atoms or molecules. For example increasing the hydrogen uptake of a MOF would enable its use as batteries or energy storage in general. [168] Simulations could show that by increasing the aromatic content of the organic linker in Zn-MOF-C6 increases the hydrogen uptake and also changing the Zn to Mg is beneficial for the hydrogen storage.(**Figure 13**) [169] Another application for microporous materials such as MOFs is carbon dioxide capture. Positioning such MOFs at the exhaust of power plants with high CO_2 output results in a decrease of emission.[170] IL/IRMOF-1 composites were classified as good candidates for CO_2 capture by simulating the behavior of the material under the influence of the guest molecules [171].

4.5.5. Gas Separation by MOFs

Different types of gases in an environment can be separated through MOFs by having varying diffusion constants. A MOF sensible only to one type of molecule/atom filters the mixed gas by letting the fitting gas diffuse into the pores. Hence, a mixed gas can be separated by a MOF membrane where only the preferred gas is able to diffuse to the other side of the membrane. Depending on the MOFs and guest molecules, applying pressure on one side of the membrane may change the diffusivity to enable fine tuning of the separation process. [172] Some MOFs such as UiO-66 or HKUST-1 have different pore sizes and can be used for more complex storage or separation processes.[173] The simulation even predicted the dependence of the electrostatic interaction on the separation efficiency, thus, indicating further improvement suggestions for experiments.(**Figure 14**)

4.5.6. Interaction between guest molecules and MOFs

An interesting effect of MOFs related to diffusion is the ability to breath. Breathing in this context means the stretching and returning to the original state of the material. This effect can expand the materials' volume, thus, increasing the pore size. According to theory the effect originates from the interaction between metal node and organic linker. The flexible bond between both components and the effect of guest molecules on the MOF together makes the effect of breathing possible [174]. Further investigations showed that not only the type of the MOF is relevant for the breathing effect but also the interaction between guest molecules and MOF [175]. The two states of a breathing MOF are described by two energy minima in which the material is physically stable. Switching between these two energies results in different arrangements of the crystal structure and, thus in an increase or decrease of volume of the MOF.

4.5.7. MOFs as drug carriers

As MOFs are highly tunable by functionalizing the ligands they make prime candidates for drug delivery. Customizing the MOF to special needs allows precise medical treatment [176]. The MOF as a drug holder needs to be stable under certain conditions such as in a water environment and/or possess a particular temperature resistance. As mentioned above these properties can be explored via MD simulations. Also the controlled release of the drug is easier to achieve with MOFs. Ten different MOFs were tested via simulations as carrier for anticancer drug molecules whereby two MOFs showed a decent uptake of the drug. A strong relation between the pore size and drug uptake was indicated with MOF-74 materials as a good drug carrier candidate.

An important issue is the effect of the metal in the body. Chromium for example is highly toxic for the body and should not be used in the MOF for drug design. On the other side metals such as iron are already existent in the human body and do not affect the health negatively.[177] Hence, it is of vital importance to design a nontoxic MOF where scientists can greatly benefit from theoretical models. So called covalent organic frameworks (COFs) only consist of organic building blocks (two or more) that make up the crystalline structure. Here again computational calculations assist the experiments by providing theoretical values which then can be compared to experimental results.[178]

4.5.8. High Throughput Screening of MOFs

The many metal nodes for MOFs and even more organic linkers result in a huge amount of theoretically possible MOF structures. Not every combination is experimentally feasible and finding candidates for different applications would require to examine each and every MOF combination which would be too inefficient and time consuming. A high-throughput computational screening of MOFs support distinguishing between promising and unsuited candidates. [179] One presented approach is to gather a high number of MOFs from databases like the Cambridge Structural Database (CSD) and do a quick analysis of properties such as porosity and gas adsorption on the dataset. A great benefit is to be expected by correlations of various properties of MOFs, hence a classification of different structures would be possible. In case of methane a preferred pore size for MOF topologies could be determined at which the MOF would achieve an optimized storage capacity.[180]

4. Summary

MOFs offer an intriguing way for the controlled synthesis of functionalized structures across multiple length scales from nm to µm. Their basic molecular building blocks provide a large flexibility by permitting many desirable functionally and/or structurally relevant properties for assembly. These building blocks can be stacked hierarchically towards, e.g., one-dimensional rods, two-dimensional sheets, or three-dimensional architectures. Next to the architecture also other features of the materials, such as porosity or chemical composition, can also be organized hierarchically, which is crucial for optimizing specific properties, such as diffusion within the material or directional energy transfer. The resulting MOFs vary strongly across several length scales in terms of their framework architecture and pore structure and provide the material science community a powerful toolbox to tailor material properties towards many applications.

Efforts to design MOFs for specific applications can be supplemented by powerful simulation techniques based on Molecular Mechanics or Density Functional Theory. The tremendous growth of both raw computational power and large databases support both accuracy and applicability with first successes in simulating gas storage and diffusion, drug storage or high-throughput screening of existing MOF materials for particular applications. Still, further refinement of computational tools both in respect of accuracy and of transferability towards new systems is needed to allow rational *in-silico* design of novel MOFs towards broad real-world applications. Still, the prospect of accurate predictions of hypothetical new MOFs and their likely chemical and electronic features is daunting and hard to underestimate. The further advancement of hierarchically structured MOF materials will likely be guided by an interplay of optimized synthesis and processing techniques with enhanced implementation of material modelling. This will allow to first *de-novo* design and then synthesize high and highest performing structured materials by specific targeting of rationally selected candidates.

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References

[1] E. Ravasz, A.-L. Barabási, *Phys. Rev. E* **2003**, *67*, 026112.

[2] R. Lakes, *Nature* **1993**, *361*, 511.

[3] W. Schwieger, A. G. Machoke, B. Reiprich, T. Weissenberger, T. Selvam, M. Hartmann, in *Zeolites in Catalysis: Properties and Applications*, The Royal Society of Chemistry, 2017, 103.

[4] H. S. Stoker, *General, organic, and biological chemistry*, Nelson Education, 2012.

[5] a) H. Furukawa, K. E. Cordova, M. O'Keeffe, O. M. Yaghi, *Science* **2013**, *341*, 1230444; b) S. Kitagawa, R. Kitaura, S. i. Noro, *Angew. Chem., Int. Ed.* **2004**, *43*, 2334.

[6] P. Z. Moghadam, A. Li, S. B. Wiggin, A. Tao, A. G. Maloney, P. A. Wood, S. C. Ward, D. Fairen-Jimenez, *Chem. Mater.* **2017**, *29*, 2618.

[7] a) S. R. Batten, N. R. Champness, X.-M. Chen, J. Garcia-Martinez, S. Kitagawa, L. Öhrström, M. O'Keeffe, M. P. Suh, J. Reedijk, *Pure Appl. Chem.* **2013**, *85*, 1715; b) J. Rouquerol, D. Avnir, C. Fairbridge, D. Everett, J. Haynes, N. Pernicone, J. Ramsay, K. Sing, K. Unger, *Pure Appl. Chem.* **1994**, *66*, 1739.

[8] H. Deng, C. J. Doonan, H. Furukawa, R. B. Ferreira, J. Towne, C. B. Knobler, B. Wang, O. M. Yaghi, *Science* **2010**, *327*, 846.

[9] S. Furukawa, K. Hirai, Y. Takashima, K. Nakagawa, M. Kondo, T. Tsuruoka, O. Sakata, S. Kitagawa, *Chem. Commun.* **2009**, 5097.

[10] K. Koh, A. G. Wong-Foy, A. J. Matzger, *Chem. Commun.* **2009**, 6162.

[11] a) P. Fratzl, R. Weinkamer, *Prog. Mater Sci.* **2007**, *52*, 1263; b) M. A. Meyers, J. McKittrick, P.-Y. Chen, *Science* **2013**, *339*, 773.

[12] H. Xia, J. Zhang, Z. Yang, S. Guo, S. Guo, Q. Xu, *Nano-Micro Lett.* **2017**, *9*, 43.

[13] W. Schwieger, A. G. Machoke, T. Weissenberger, A. Inayat, T. Selvam, M. Klumpp, A. Inayat, *Chem. Soc. Rev.* **2016**, *45*, 3353.

[14] a) J. Heurich, J. Cuevas, W. Wenzel, G. Schön, *Phys. Rev. Lett.* **2002**, *88*, 256803; b) A. Schug, M. Weigt, J. N. Onuchic, T. Hwa, H. Szurmant, *Proc. Natl. Acad. Sci. U. S. A.* **2009**, *106*, 22124; c) K. Lindorff-Larsen, S. Piana, R. O. Dror, D. E. Shaw, *Science* **2011**, *334*, 517; d) B. Mattes, Y. Dang, G. Greicius, L. T. Kaufmann, B. Prunsche, J. Rosenbauer, J. Stegmaier, R. Mikut, S. Özbek, G. U. Nienhaus, *Elife* **2018**, *7*.

[15] G. Uguzzoni, S. J. Lovis, F. Oteri, A. Schug, H. Szurmant, M. Weigt, *Proc. Natl. Acad. Sci. U. S. A.* **2017**, *114*, E2662.

[16] K. Sumida, K. Liang, J. Reboul, I. A. Ibarra, S. Furukawa, P. Falcaro, *Chem. Mater.* **2017**, *29*, 2626.

[17] B. Tu, Q. Pang, D. Wu, Y. Song, L. Weng, Q. Li, *J. Am. Chem. Soc.* **2014**, *136*, 14465.

[18] a) M.-H. Pham, G.-T. Vuong, A.-T. Vu, T.-O. Do, *Langmuir* **2011**, *27*, 15261; b) W. J. Rieter, K. M. Taylor, H. An, W. Lin, W. Lin, *J. Am. Chem. Soc.* **2006**, *128*, 9024.

[19] a)P. Sarawade, H. Tan, D. Anjum, D. Cha, V. Polshettiwar, *ChemSusChem* **2014**, *7*, 529; b) N. A. Khan, S. H. Jhung, *Coord. Chem. Rev.* **2015**, *285*, 11.

[20] B. Ghalei, K. Sakurai, Y. Kinoshita, K. Wakimoto, A. P. Isfahani, Q. Song, K. Doitomi, S. Furukawa, H. Hirao, H. Kusuda, *Nat. Energy* **2017**, *2*, 17086.

[21] T.-H. Bae, J. S. Lee, W. Qiu, W. J. Koros, C. W. Jones, S. Nair, *Angew. Chem., Int. Ed.* **2010**, *49*, 9863.

[22] A. Umemura, S. Diring, S. Furukawa, H. Uehara, T. Tsuruoka, S. Kitagawa, *J. Am. Chem. Soc.* **2011**, *133*, 15506.

[23] a) G. Zahn, H. A. Schulze, J. Lippke, S. König, U. Sazama, M. Fröba, P. Behrens, *Microporous Mesoporous Mater.* **2015**, *203*, 186; b) A. Schaate, P. Roy, A. Godt, J. Lippke, F. Waltz, M. Wiebcke, P. Behrens, *Chem. - Eur. J.* **2011**, *17*, 6643.

[24] G. Wißmann, A. Schaate, S. Lilienthal, I. Bremer, A. M. Schneider, P. Behrens, *Microporous Mesoporous Mater.* **2012**, *152*, 64.

[25] M.-H. Pham, G.-T. Vuong, F. d. r.-G. Fontaine, T.-O. Do, *Cryst. Growth Des.* **2012**, *12*, 3091.

[26] T. Tsuruoka, S. Furukawa, Y. Takashima, K. Yoshida, S. Isoda, S. Kitagawa, *Angew. Chem., Int. Ed.* **2009**, *48*, 4739.

[27] C. Avci, J. Ariñez-Soriano, A. Carné-Sánchez, V. Guillerm, C. Carbonell, I. Imaz, D. Maspoch, *Angew. Chem., Int. Ed.* **2015**, *54*, 14417.

[28] A. Kojtari, P. J. Carroll, H.-F. Ji, *CrystEngComm* **2014**, *16*, 2885.

[29] M.-H. Pham, G.-T. Vuong, F.-G. Fontaine, T.-O. Do, *Cryst. Growth Des.* **2012**, *12*, 3091.

[30] K. M. L. Taylor, W. J. Rieter, W. Lin, *J. Am. Chem. Soc.* **2008**, *130*, 14358.

[31] M. Gao, L. Zeng, J. Nie, G. Ma, *RSC Adv.***2016**, *6*, 7078.

[32] a) M. S. Yao, W. X. Tang, G. E. Wang, B. Nath, G. Xu, *Adv. Mater.* **2016**, *28*, 5229; b) W.-w. Zhan, Q. Kuang, J.-z. Zhou, X.-j. Kong, Z.-x. Xie, L.-s. Zheng, *J. Am. Chem. Soc.* **2013**, *135*, 1926.

[33] W. Zhang, Z.-Y. Wu, H.-L. Jiang, S.-H. Yu, *J. Am. Chem. Soc.* **2014**, *136*, 14385.

[34] H. Yu, X. Qiu, P. Neelakanda, L. Deng, N. M. Khashab, S. P. Nunes, K.-V. Peinemann, *Sci. Rep.* **2015**, *5*, 15275.

[35] A. Kondo, C. C. Tiew, F. Moriguchi, K. Maeda, *Dalton Trans.* **2013**, *42*, 15267.

[36] H. Li, F. Yue, H. Xie, C. Yang, Y. Zhang, L. Zhang, J. Wang, *CrystEngComm* **2018**, *20*, 889.

[37] L. Cao, T. Wang, C. Wang, *Chin. J. Chem* . **2018**, *36*, 754.

[38] L. Cao, Z. Lin, W. Shi, Z. Wang, C. Zhang, X. Hu, C. Wang, W. Lin, *J. Am. Chem. Soc.* **2017**, *139*, 7020.

[39] M. Hu, S. Ishihara, Y. Yamauchi, *Angew. Chem., Int. Ed.* **2013**, *52*, 1235.

[40] S. Zhao, Y. Wang, J. Dong, C.-T. He, H. Yin, P. An, K. Zhao, X. Zhang, C. Gao, L. Zhang, *Nat. Energy* **2016**, *1*, 16184.

[41] a) X. Sun, K.-H. Wu, R. Sakamoto, T. Kusamoto, H. Maeda, H. Nishihara, *Chem. Lett.* **2017**, *46*, 1072; b) T. Pal, T. Kambe, T. Kusamoto, M. L. Foo, R. Matsuoka, R. Sakamoto, H. Nishihara, *ChemPlusChem* **2015**, *80*, 1255; c) N. Lahiri, N. Lotfizadeh, R. Tsuchikawa, V. V. Deshpande, J. Louie, *J. Am. Chem. Soc.* **2016**, *139*, 19; d) X. Huang, P. Sheng, Z. Tu, F. Zhang, J. Wang, H. Geng, Y. Zou, C.-a. Di, Y. Yi, Y. Sun, W. Xu, D. Zhu, *Nat. Commun.* **2015**, *6*, 7408; e) A. J. Clough, J. M. Skelton, C. A. Downes, A. A. De La Rosa, J. W. Yoo, A. Walsh, B. C. Melot, S. C. Marinescu, *J. Am. Chem. Soc.* **2017**, *139*, 10863.

[42] a) V. c. Rubio-Giménez, S. Tatay, F. Volatron, F. J. Martínez-Casado, C. Martí-Gastaldo, E. Coronado, *J. Am. Chem. Soc.* **2016**, *138*, 2576; b) R. Makiura, S. Motoyama, Y. Umemura, H. Yamanaka, O. Sakata, H. Kitagawa, *Nat. Mater.* **2010**, *9*, 565; c) R. Dong, M. Pfeffermann, H. Liang, Z. Zheng, X. Zhu, J. Zhang, X. Feng, *Angew. Chem., Int. Ed.* **2015**, *54*, 12058; d) R. Dong, Z. Zheng, D. C. Tranca, J. Zhang, N. Chandrasekhar, S. Liu, X. Zhuang, G. Seifert, X. Feng, *C Chem. - Eur. J.* **2017**, *23*, 2255; e) R. Makiura, R. Usui, Y. Sakai, A. Nomoto, A. Ogawa, O. Sakata, A. Fujiwara, *ChemPlusChem* **2014**, *79*, 1352; f) R. Makiura, O. Konovalov, *Sci. Rep.* **2013**, *3*, 2506; g) V. Rubio-Giménez, S. Tatay, F. Volatron, F. J. Martínez-Casado, C. Martí-Gastaldo, E. Coronado, *J. Am. Chem. Soc.* **2016**, *138*, 2576.

[43] S. Motoyama, R. Makiura, O. Sakata, H. Kitagawa, *J. Am. Chem. Soc.* **2011**, *133*, 5640.

[44] T. Rodenas, I. Luz, G. Prieto, B. Seoane, H. Miro, A. Corma, F. Kapteijn, F. X. L. i Xamena, J. Gascon, *Nat. Mater.* **2015**, *14*, 48.

[45] a) G. E. Gomez, M. C. Bernini, E. V. Brusau, G. E. Narda, D. Vega, A. M. Kaczmarek, R. Van Deun, M. Nazzarro, *Dalton Trans.* **2015**, *44*, 3417; b) P.-Z. Li, Y. Maeda, Q. Xu, *Chem. Commun.* **2011**, *47*, 8436; c) P. Amo-Ochoa, L. Welte, R. González-Prieto, P. J. Sanz Miguel, C. J. Gómez-García, E. Mateo-Martí, S. Delgado, J. Gómez-Herrero, F. Zamora, *Chem. Commun.* **2010**, *46*, 3262; d) P. Chandrasekhar, A. Mukhopadhyay, G. Savitha, J. N. Moorthy, *J. Mater. Chem. A* **2017**, *5*, 5402.

[46] X. Wang, C. Chi, K. Zhang, Y. Qian, K. M. Gupta, Z. Kang, J. Jiang, D. Zhao, *Nat. Commun.* **2017**, *8*, 14460.

[47] A. Abhervé, S. Mañas-Valero, M. Clemente-León, E. Coronado, *Chem. Sci.* **2015**, *6*, 4665.

[48] Y. Ding, Y.-P. Chen, X. Zhang, L. Chen, Z. Dong, H.-L. Jiang, H. Xu, H.-C. Zhou, *J. Am. Chem. Soc.* **2017**, *139*, 9136.

[49] a) T. Araki, A. Kondo, K. Maeda, *Chem. Commun.* **2013**, *49*, 552; b) Y. Peng, Y. Li, Y. Ban, W. Yang, *Angew. Chem., Int. Ed.* **2017**, *56*, 9757; c) A. Gallego, C. Hermosa, O. Castillo, I. Berlanga, C. J. Gómez-García, E. Mateo-Martí, J. I. Martínez, F. Flores, C. Gómez-Navarro, J. Gómez-Herrero, S. Delgado, F. Zamora, *Adv. Mater.* **2013**, *25*, 2141.

[50] M. J. Cliffe, E. Castillo-Martínez, Y. Wu, J. Lee, A. C. Forse, F. C. N. Firth, P. Z. Moghadam, D. Fairen-Jimenez, M. W. Gaultois, J. A. Hill, O. V. Magdysyuk, B. Slater, A. L. Goodwin, C. P. Grey, *J. Am. Chem. Soc.* **2017**, *139*, 5397.

[51] a) P. Falcaro, D. Buso, A. J. Hill, C. M. Doherty, *Adv. Mater.* **2012**, *24*, 3153; b) I. Stassen, N. Burtch, A. Talin, P. Falcaro, M. Allendorf, R. Ameloot, *Chem. Soc. Rev.* **2017**, *46*, 3185.

[52] a) J. Liu, B. Lukose, O. Shekhah, H. K. Arslan, P. Weidler, H. Gliemann, S. Bräse, S. Grosjean, A. Godt, X. Feng, K. Müllen, I.-B. Magdau, T. Heine, C. Wöll, *Sci. Rep.* **2012**, *2*, 921; b) S. Sakaida, K. Otsubo, O. Sakata, C. Song, A. Fujiwara, M. Takata, H. Kitagawa, *Nat. Chem.* **2016**, *8*, 377.

[53] Y. Zhao, N. Kornienko, Z. Liu, C. Zhu, S. Asahina, T.-R. Kuo, W. Bao, C. Xie, A. Hexemer, O. Terasaki, P. Yang, O. M. Yaghi, *J. Am. Chem. Soc.* **2015**, *137*, 2199.

[54] J. Reboul, S. Furukawa, N. Horike, M. Tsotsalas, K. Hirai, H. Uehara, M. Kondo, N. Louvain, O. Sakata, S. Kitagawa, *Nat. Mater.* **2012**, *11*, 717.

[55] a) N. Campagnol, T. Van Assche, T. Boudewijns, J. Denayer, K. Binnemans, D. De Vos, J. Fransaer, *J. Mater. Chem. A* **2013**, *1*, 5827; b) W.-J. Li, J. Lü, S.-Y. Gao, Q.-H. Li, R. Cao, *J. Mater. Chem. A* **2014**, *2*, 19473; c) W.-J. Li, J. Liu, Z.-H. Sun, T.-F. Liu, J. Lü, S.-Y. Gao, C. He, R. Cao, J.-H. Luo, *Nat. Commun.* **2016**, *7*, 11830.

[56] a) Y. Chen, S. Li, X. Pei, J. Zhou, X. Feng, S. Zhang, Y. Cheng, H. Li, R. Han, B. Wang, *Angew. Chem., Int. Ed.* **2016**, *55*, 3419; b) V. M. Aceituno Melgar, H. T. Kwon, J. Kim, *J. Membr. Sci.* **2014**, *459*, 190; c) L. Fan, M. Xue, Z. Kang, H. Li, S. Qiu, *J. Mater. Chem.* **2012**, *22*, 25272.

[57] a) E. Ahvenniemi, M. Karppinen, *Chem. Commun.* **2016**, *52*, 1139; b) K. B. Lausund, O. Nilsen, *Nat. Commun.* **2016**, *7*, 13578.

[58] a) H. Walch, J. Dienstmaier, G. Eder, R. Gutzler, S. Schlögl, T. Sirtl, K. Das, M. Schmittel, M. Lackinger, *J. Am. Chem. Soc.* **2011**, *133*, 7909; b) Y. Li, J. Xiao, T. E. Shubina, M. Chen, Z. Shi, M. Schmid, H.-P. Steinrück, J. M. Gottfried, N. Lin, *J. Am. Chem. Soc.* **2012**, *134*, 6401; c) B. Wurster, D. Grumelli, D. Hötger, R. Gutzler, K. Kern, *J. Am. Chem. Soc.* **2016**, *138*, 3623.

[59] I. Stassen, M. Styles, G. Grenci, H. Van Gorp, W. Vanderlinden, S. De Feyter, P. Falcaro, D. De Vos, P. Vereecken, R. Ameloot, *Nat. Mater.* **2016**, *15*, 304.

[60] P. Falcaro, R. Ricco, C. M. Doherty, K. Liang, A. J. Hill, M. J. Styles, *Chem. Soc. Rev.* **2014**, *43*, 5513.

[61] a) M. Hou, H. Zhao, Y. Feng, J. Ge, *Bioresources and Bioprocessing* **2017**, *4*, 40; b) J.-L. Zhuang, D. Ar, X.-J. Yu, J.-X. Liu, A. Terfort, *Adv. Mater.* **2013**, *25*, 4631.

[62] C. Carbonell, I. Imaz, D. Maspoch, *J. Am. Chem. Soc.* **2011**, *133*, 2144.

[63] a) J. J. Gassensmith, P. M. Erne, W. F. Paxton, C. Valente, J. F. Stoddart, *Langmuir* **2011**, *27*, 1341; b) J.-L. Zhuang, D. Ceglarek, S. Pethuraj, A. Terfort, *Adv. Funct. Mater.* **2011**, *21*, 1442.

[64] J. L. Zhuang, D. Ceglarek, S. Pethuraj, A. Terfort, *Adv. Funct. Mater.* **2011**, *21*, 1442.

[65] a) A. Schaller, A. Ullrich, S. Horn, D. Volkmer, *Chem. Commun.* **2015**, *51*, 12494; b) B. K. Keitz, C. J. Yu, J. R. Long, R. Ameloot, *Angew. Chem., Int. Ed.* **2014**, *53*, 5561.

[66] J. Zhuang, J. Friedel, A. Terfort, *Beilstein journal of nanotechnology* **2012**, *3*, 570.

[67] K. Hirai, K. Sada, *Chem. Commun.* **2017**, *53*, 5275.

[68] G. Lu, O. K. Farha, W. Zhang, F. Huo, J. T. Hupp, *Adv. Mater.* **2012**, *24*, 3970.

[69] a) H. Kim, M. S. Lah, *Dalton Trans.* **2017**, *46*, 6146; b) V. Valtchev, *Chem. Mater.* **2002**, *14*, 4371.

[70] H. J. Lee, W. Cho, M. Oh, *Chem. Commun.* **2012**, *48*, 221.

[71] C.-H. Kuo, Y. Tang, L.-Y. Chou, B. T. Sneed, C. N. Brodsky, Z. Zhao, C.-K. Tsung, *J. Am. Chem. Soc.* **2012**, *134*, 14345.

[72] S. Aguado, J. Canivet, D. Farrusseng, *Chem. Commun.* **2010**, *46*, 7999.

[73] S. Sorribas, B. Zornoza, C. Téllez, J. Coronas, *Chem. Commun.* **2012**, *48*, 9388.

[74] Y. Liu, W. Zhang, S. Li, C. Cui, J. Wu, H. Chen, F. Huo, *Chem. Mater.* **2014**, *26*, 1119.

[75] a) G. Zhang, S. Hou, H. Zhang, W. Zeng, F. Yan, C. C. Li, H. Duan, *Adv. Mater.* **2015**, *27*, 2400; b) Z. Wei Seh, W. Li, J. J. Cha, G. Zheng, Y. Yang, M. T. McDowell, P.-C. Hsu, Y. Cui, *Nat. Commun.* **2013**, *4*, 1331; c) Y. Zhao, X. Li, J. Liu, C. Wang, Y. Zhao, G. Yue, *ACS Appl. Mater. Interfaces* **2016**, *8*, 6472.

[76] a) G. Liang, J. Xu, X. Wang, *J. Am. Chem. Soc.* **2009**, *131*, 5378; b) X. Cao, L. Dai, L. Wang, J. Liu, J. Lei, *Mater. Lett.* **2015**, *161*, 682.

[77] W. Li, Y. Zhang, Z. Xu, Q. Meng, Z. Fan, S. Ye, G. Zhang, *Angew. Chem., Int. Ed.* **2016**, *55*, 955.

[78] a) Y. Yang, F. Wang, Q. Yang, Y. Hu, H. Yan, Y.-Z. Chen, H. Liu, G. Zhang, J. Lu, H.-L. Jiang, H. Xu, *ACS Appl. Mater. Interfaces* **2014**, *6*, 18163; b) G.-Y. Jeong,

R. Ricco, K. Liang, J. Ludwig, J.-O. Kim, P. Falcaro, D.-P. Kim, *Chem. Mater.* **2015**, *27*, 7903.

[79] A. Carné-Sánchez, I. Imaz, M. Cano-Sarabia, D. Maspoch, *Nat. Chem.* **2013**, *5*, 203.

[80] a) J. Huo, J. Aguilera-Sigalat, S. El-Hankari, D. Bradshaw, *Chem. Sci.* **2015**, *6*, 1938; b) R. Ameloot, F. Vermoortele, W. Vanhove, M. B. J. Roeffaers, B. F. Sels, D. E. De Vos, *Nat. Chem.* **2011**, *3*, 382.

[81] L. Peng, J. Zhang, J. Li, B. Han, Z. Xue, B. Zhang, J. Shi, G. Yang, *J. Colloid Interface Sci.* **2014**, *416*, 198.

[82] a) W. Zhang, X. Jiang, Y. Zhao, A. Carné-Sánchez, V. Malgras, J. Kim, J. H. Kim, S. Wang, J. Liu, J.-S. Jiang, Y. Yamauchi, M. Hu, *Chem. Sci.* **2017**, *8*, 3538; b) C. Avci, J. Ariñez-Soriano, A. Carné-Sánchez, V. Guillerm, C. Carbonell, I. Imaz, D. Maspoch, *Angew. Chem., Int. Ed.* **2015**, *54*, 14417.

[83] W. Liu, J. Huang, Q. Yang, S. Wang, X. Sun, W. Zhang, J. Liu, F. Huo, *Angew. Chem., Int. Ed.* **2017**, *56*, 5512.

[84] Z. Wang, J. Wang, M. Li, K. Sun, C.-j. Liu, *Sci. Rep.* **2014**, *4*, 5939.

[85] Y. Chen, F. Chen, S. Zhang, Y. Cai, S. Cao, S. Li, W. Zhao, S. Yuan, X. Feng, A. Cao, X. Ma, B. Wang, *J. Am. Chem. Soc.* **2017**, *139*, 16482.

[86] O. Halevi, J. M. R. Tan, P. S. Lee, S. Magdassi, *Adv. Sustainable Syst.* **2018**, *2*, 1700150.

[87] S. Choi, T. Kim, H. Ji, H. J. Lee, M. Oh, *J. Am. Chem. Soc.* **2016**, *138*, 14434.

[88] N. Yanai, M. Sindoro, J. Yan, S. Granick, *J. Am. Chem. Soc.* **2013**, *135*, 34.

[89] M. Pang, A. J. Cairns, Y. Liu, Y. Belmabkhout, H. C. Zeng, M. Eddaoudi, *J. Am. Chem. Soc.* **2013**, *135*, 10234.

[90] C. Avci, I. Imaz, A. Carné-Sánchez, J. A. Pariente, N. Tasios, J. Pérez-Carvajal, M. I. Alonso, A. Blanco, M. Dijkstra, C. López, D. Maspoch, *Nat. Chem.* **2017**, *10*, 78.

[91] P. Falcaro, K. Okada, T. Hara, K. Ikigaki, Y. Tokudome, A. W. Thornton, A. J. Hill, T. Williams, C. Doonan, M. Takahashi, *Nat. Mater.* **2017**, *16*, 342.

[92] L. Lupica-Spagnolo, D. J. Ward, J.-J. Marie, S. Lymperopoulou, D. Bradshaw, *Chem. Commun.* **2018**, *54*, 8506.

[93] C. Avci, J. Ariñez-Soriano, A. Carné-Sánchez, V. Guillerm, C. Carbonell, I. Imaz, D. Maspoch, *Angew. Chem. Int. Ed.* **2015**, *54*, 14417.

[94] J. Haber, *Pure Appl. Chem.* **1991**, *63*, 1227.

[95] A. Schoedel, O. M. Yaghi, *Macrocyclic and Supramolecular Chemistry: How Izatt-Christensen Award Winners Shaped the Field* **2016**, 200.

[96] X. Lian, Y.-P. Chen, T.-F. Liu, H.-C. Zhou, *Chem. Sci.* **2016**, *7*, 6969.

[97] J. Caro, *Chem. Soc. Rev.* **2016**, *45*, 3468.

[98] X.-Y. Yang, L.-H. Chen, Y. Li, J. C. Rooke, C. Sanchez, B.-L. Su, *Chem. Soc. Rev.* **2017**, *46*, 481.

[99] a) X.-X. Huang, L.-G. Qiu, W. Zhang, Y.-P. Yuan, X. Jiang, A.-J. Xie, Y.-H. Shen, J.-F. Zhu, *CrystEngComm* **2012**, *14*, 1613; b) L.-G. Qiu, T. Xu, Z.-Q. Li, W. Wang, Y. Wu, X. Jiang, X.-Y. Tian, L.-D. Zhang, *Angew. Chem., Int. Ed.* **2008**, *47*, 9487.

[100] a) L. H. Wee, C. Wiktor, S. Turner, W. Vanderlinden, N. Janssens, S. R. Bajpe, K. Houthoofd, G. Van Tendeloo, S. De Feyter, C. E. Kirschhock, *J. Am. Chem. Soc.* **2012**, *134*, 10911; b) Y. Li, D. Zhang, Y.-N. Guo, B. Guan, D. Tang, Y. Liu, Q. Huo, *Chem. Commun.* **2011**, *47*, 7809.

[101] S. Diring, S. Furukawa, Y. Takashima, T. Tsuruoka, S. Kitagawa, *Chem. Mater.* **2010**, *22*, 4531.

[102] S. Cao, G. Gody, W. Zhao, S. Perrier, X. Peng, C. Ducati, D. Zhao, A. K. Cheetham, *Chem. Sci.* **2013**, *4*, 3573.

[103] L.-B. Sun, J.-R. Li, J. Park, H.-C. Zhou, *J. Am. Chem. Soc.* **2011**, *134*, 126.

[104] S. Alizadeh, D. Nematollahi, *J. Am. Chem. Soc.* **2017**, *139*, 4753.

[105] Y. Zhao, J. Zhang, B. Han, J. Song, J. Li, Q. Wang, *Angew. Chem., Int. Ed.* **2011**, *50*, 636.

[106] L. Peng, J. Zhang, Z. Xue, B. Han, X. Sang, C. Liu, G. Yang, *Nat. Commun.* **2014**, *5*, 4465.

[107] J. Reboul, S. Furukawa, N. Horike, M. Tsotsalas, K. Hirai, H. Uehara, M. Kondo, N. Louvain, O. Sakata, S. Kitagawa, *Nat. Mater.* **2012**, *11*, 717.

[108] Y. Kim, T. Yang, G. Yun, M. B. Ghasemian, J. Koo, E. Lee, S. J. Cho, K. Kim, *Angew. Chem., Int. Ed.* **2015**, *54*, 13273.

[109] P. Yang, F. Mao, Y. Li, Q. Zhuang, J. Gu, *Chem. - Eur. J.* **2018**, *24*, 2962.

[110] X. Yang, S. Wu, P. Wang, L. Yang, *J. Solid State Chem.* **2018**, *258*, 220.

[111] S. Yuan, L. Zou, J.-S. Qin, J. Li, L. Huang, L. Feng, X. Wang, M. Bosch, A. Alsalme, T. Cagin, *Nat. Commun.* **2017**, *8*, 15356.

[112] a) J. C. Noveron, M. S. Lah, R. E. Del Sesto, A. M. Arif, J. S. Miller, P. J. Stang, *J. Am. Chem. Soc.* **2002**, *124*, 6613; b) J. C. MacDonald, P. C. Dorrestein, M. M. Pilley, M. M. Foote, J. L. Lundburg, R. W. Henning, A. J. Schultz, J. L. Manson, *J. Am. Chem. Soc.* **2000**, *122*, 11692.

[113] P. Á. Szilágyi, M. Lutz, J. Gascon, J. Juan-Alcaniz, J. van Esch, F. Kapteijn, H. Geerlings, B. Dam, R. van de Krol, *CrystEngComm* **2013**, *15*, 6003.

[114] a) V. Chernikova, O. Shekhah, M. Eddaoudi, *ACS Appl. Mater. Interfaces* **2016**, *8*, 20459; b) J.-L. Zhuang, A. Terfort, C. Wöll, *Coord. Chem. Rev.* **2016**, *307*, 391.

[115] B. Liu, M. Ma, D. Zacher, A. Bétard, K. Yusenko, N. Metzler-Nolte, C. Wöll, R. A. Fischer, *J. Am. Chem. Soc.* **2011**, *133*, 1734.

[116] a) D. Zacher, K. Yusenko, A. Bétard, S. Henke, M. Molon, T. Ladnorg, O. Shekhah, B. Schüpbach, T. de los Arcos, M. Krasnopolski, *Chem. - Eur. J.* **2011**, *17*, 1448; b) O. Shekhah, K. Hirai, H. Wang, H. Uehara, M. Kondo, S. Diring, D. Zacher, R. A. Fischer, O. Sakata, S. Kitagawa, *Dalton Trans.* **2011**, *40*, 4954.

[117] M. Meilikhov, S. Furukawa, K. Hirai, R. A. Fischer, S. Kitagawa, *Angew., Chem. Int. Ed.* **2013**, *52*, 341.

[118] M. Tu, R. A. Fischer, *J. Mater. Chem. A* **2014**, *2*, 2018.

[119] Z. Wang, J. Liu, B. Lukose, Z. Gu, P. G. Weidler, H. Gliemann, T. Heine, C. Wöll, *Nano Lett.* **2014**, *14*, 1526.

[120] M. Tu, S. Wannapaiboon, R. A. Fischer, *Dalton Trans.* **2013**, *42*, 16029.

[121] L. Heinke, M. Cakici, M. Dommaschk, S. Grosjean, R. Herges, S. Bräse, C. Wöll, *Acs Nano* **2014**, *8*, 1463.

[122] S. Schmitt, M. Silvestre, M. Tsotsalas, A.-L. Winkler, A. Shahnas, S. Grosjean, F. Laye, H. Gliemann, J. Lahann, S. Bräse, *ACS nano* **2015**, *9*, 4219.

[123] Z. Song, F. Qiu, E. W. Zaia, Z. Wang, M. Kunz, J. Guo, M. Brady, B. Mi, J. J. Urban, *Nano Lett.* **2017**, *17*, 6752.

[124] I. Stassen, I. Boldog, C. Steuwe, D. De Vos, M. Roeffaers, S. Furukawa, R. Ameloot, *Chem. Commun.* **2017**, *53*, 7222.

[125] J. A. Boissonnault, A. G. Wong-Foy, A. J. Matzger, *J. Am. Chem. Soc.* **2017**, *139*, 14841.

[126] X. Xu, Y. Sun, Q. Zhang, S. Wang, L. Zhang, Z. Wu, G. Lu, *ChemistrySelect* **2016**, *1*, 1763.

[127] Y. Gu, Y.-n. Wu, L. Li, W. Chen, F. Li, S. Kitagawa, *Angew. Chem., Int. Ed.* **2017**, *56*, 15658.

[128] S. A. Adcock, J. A. McCammon, *Chem. Rev.* **2006**, *106*, 1589.

[129] A. Schug, J. N. Onuchic, *Curr. Opin. Pharmacol.* **2010**, *10*, 709.

[130] J. C. Cuevas, J. Heurich, F. Pauly, W. Wenzel, G. Schön, *Nanotechnology* **2003**, *14*, R29.

[131] M. Elbing, R. Ochs, M. Koentopp, M. Fischer, C. von Hänisch, F. Weigend, F. Evers, H. B. Weber, M. Mayor, *Proc. Natl. Acad. Sci. U. S. A.* **2005**, *102*, 8815.

[132] a) L. Pastewka, M. O. Robbins, *Proc. Natl. Acad. Sci. U. S. A.* **2014**, 201320846; b) N. Riley, *J. Fluid Mech.* **1996**, *310*, 378.

[133] P. Hohenberg, W. Kohn, *Physical review* **1964**, *136*, B864.

[134] R. Salomon- Ferrer, D. A. Case, R. C. Walker, *Wiley Interdiscip. Rev.: Comput. Mol. Sci.* **2013**, *3*, 198.

[135] B. R. Brooks, C. L. Brooks III, A. D. Mackerell Jr, L. Nilsson, R. J. Petrella, B. Roux, Y. Won, G. Archontis, C. Bartels, S. Boresch, *J. Comput. Chem.* **2009**, *30*, 1545.

[136] H. J. Berendsen, D. van der Spoel, R. van Drunen, *Comput. Phys. Commun.* **1995**, *91*, 43.

[137] T. Herges, W. Wenzel, *Biophys. J.* **2004**, *87*, 3100.

[138] A. K. Rappé, C. J. Casewit, K. Colwell, W. A. Goddard III, W. Skiff, *J. Am. Chem. Soc.* **1992**, *114*, 10024.

[139] S. L. Mayo, B. D. Olafson, W. A. Goddard, *J. Phys. Chem.* **1990**, *94*, 8897.

[140] D. E. Coupry, M. A. Addicoat, T. Heine, *J. Chem. Theory Comput.* **2016**, *12*, 5215.

[141] A. Schug, C. Hyeon, J. N. Onuchic, *Coarse-Graining Condens. Phase Biomol. Syst.* **2008**, 123.

[142] U. H. Hansmann, Y. Okamoto, F. Eisenmenger, *Chem. Phys. Lett.* **1996**, *259*, 321.

[143] B. J. Grant, A. A. Gorfe, J. A. McCammon, *PLoS Comput. Biol.* **2009**, *5*, e1000325.

[144] a) G. Jayachandran, V. Vishal, V. S. Pande, *The Journal of chemical physics* **2006**, *124*, 164902; b) F. Noé, C. Schütte, E. Vanden-Eijnden, L. Reich, T. R. Weikl, *Proc. Natl. Acad. Sci. U. S. A.* **2009**, *106*, 19011.

[145] T. Ziegler, *Chem. Rev.* **1991**, *91*, 651.

[146] J. Tirado-Rives, W. L. Jorgensen, *J. Chem. Theory Comput.* **2008**, *4*, 297.

[147] V. Milman, B. Winkler, J. White, C. Pickard, M. Payne, E. Akhmatskaya, R. Nobes, *Int. J. Quantum Chem* **2000**, *77*, 895.

[148] W. L. Jorgensen, J. Tirado-Rives, *J. Am. Chem. Soc.* **1988**, *110*, 1657.

[149] S. Plimpton, *Journal of computational physics* **1995**, *117*, 1.

[150] I. T. Todorov, W. Smith, K. Trachenko, M. T. Dove, *J. Mater. Chem.* **2006**, *16*, 1911.

[151] J. C. Phillips, R. Braun, W. Wang, J. Gumbart, E. Tajkhorshid, E. Villa, C. Chipot, R. D. Skeel, L. Kale, K. Schulten, *J. Comput. Chem.* **2005**, *26*, 1781.

[152] D. A. Case, T. E. Cheatham, T. Darden, H. Gohlke, R. Luo, K. M. Merz, A. Onufriev, C. Simmerling, B. Wang, R. J. Woods, *J. Comput. Chem.* **2005**, *26*, 1668.

[153] B. R. Brooks, R. E. Bruccoleri, B. D. Olafson, D. J. States, S. a. Swaminathan, M. Karplus, *J. Comput. Chem.* **1983**, *4*, 187.

[154] G. Kresse, J. Furthmüller, *Phys. Rev. B* **1996**, *54*, 11169.

[155] University of Karlsruhe and Forschungszentrum Karlsruhe GmbH, How to Quote Usage of TURBOMOLE, http://www.turbomole-gmbh.com/manuals/version_6_2/DOK_HTML/node5.html, accessed: 10, 2018.

[156] M. Frisch, G. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. Petersson, *Inc., Wallingford, CT* **2009**, *200*.

[157] B. J. Alder, T. E. Wainwright, *The Journal of Chemical Physics* **1959**, *31*, 459.

[158] F. H. Allen, *Acta Crystallogr. Sect. B: Struct. Sci.* **2002**, *58*, 380.

[159] J. A. Greathouse, M. D. Allendorf, *J. Am. Chem. Soc.* **2006**, *128*, 10678.

[160] J. Yang, A. Grzech, F. M. Mulder, T. J. Dingemans, *Chem. Commun.* **2011**, *47*, 5244.

[161] A. Samanta, T. Furuta, J. Li, *J. Chem. Phys.***2006**, *125*, 084714.

[162] M. Mattesini, J. Soler, F. Yndurain, *Phys. Rev. B* **2006**, *73*, 094111.

[163] H. Q. Pham, T. Mai, N.-N. Pham-Tran, Y. Kawazoe, H. Mizuseki, D. Nguyen-Manh, *J. Chem. Phys. C* **2014**, *118*, 4567.

[164] B. Huang, A. McGaughey, M. Kaviany, *Int. J. Heat Mass Transfer* **2007**, *50*, 393.

[165] U. Mueller, M. Schubert, F. Teich, H. Puetter, K. Schierle-Arndt, J. Pastre, *J. Mater. Chem.* **2006**, *16*, 626.

[166] a) G. Garberoglio, A. I. Skoulidas, J. K. Johnson, *J. Chem. Phys. B* **2005**, *109*, 13094; b) Q. Yang, C. Zhong, *J. Chem. Phys. B* **2005**, *109*, 11862.

[167] S. Amirjalayer, M. Tafipolsky, R. Schmid, *Angew. Chem., Int. Ed.* **2007**, *46*, 463.

[168] H. Wang, Q.-L. Zhu, R. Zou, Q. Xu, *Chem* **2017**, *2*, 52.

[169] S. S. Han, W.-Q. Deng, W. A. Goddard, *Angew. Chem., Int. Ed.* **2007**, *46*, 6289.

[170] K. Sumida, D. L. Rogow, J. A. Mason, T. M. McDonald, E. D. Bloch, Z. R. Herm, T.-H. Bae, J. R. Long, *Chem. Rev.* **2011**, *112*, 724.

[171] Y. Chen, Z. Hu, K. M. Gupta, J. Jiang, *J. Chem. Phys. C* **2011**, *115*, 21736.

[172] S. Qiu, M. Xue, G. Zhu, *Chem. Soc. Rev.* **2014**, *43*, 6116.

[173] Q. Yang, C. Zhong, *J. Chem. Phys. B* **2006**, *110*, 17776.

[174] M. Alhamami, H. Doan, C.-H. Cheng, *Materials* **2014**, *7*, 3198.

[175] A. V. Neimark, F.-X. Coudert, C. Triguero, A. Boutin, A. H. Fuchs, I. Beurroies, R. Denoyel, *Langmuir* **2011**, *27*, 4734.

[176] J. Della Rocca, D. Liu, W. Lin, *Acc. Chem. Res.* **2011**, *44*, 957.

[177] R. C. Huxford, J. Della Rocca, W. Lin, *Curr. Opin. Chem. Biol.* **2010**, *14*, 262.

[178] N. Huang, L. Zhai, D. E. Coupry, M. A. Addicoat, K. Okushita, K. Nishimura, T. Heine, D. Jiang, *Nat. Commun.* **2016**, *7*, 12325.

[179] a) C. E. Wilmer, M. Leaf, C. Y. Lee, O. K. Farha, B. G. Hauser, J. T. Hupp, R. Q. Snurr, *Nat. Chem.* **2012**, *4*, 83; b) Y. J. Colón, R. Q. Snurr, *Chem. Soc. Rev.* **2014**, *43*, 5735.

[180] Y. G. Chung, J. Camp, M. Haranczyk, B. J. Sikora, W. Bury, V. Krungleviciute, T. Yildirim, O. K. Farha, D. S. Sholl, R. Q. Snurr, *Chem. Mater.* **2014**, *26*, 6185.

[181] V. Chernikova, O. Shekhah, I. Spanopoulos, P. N. Trikalitis, M. Eddaoudi, *Chem. Commun.* **2017**, *53*, 6191.

[182] a) J. Ren, N. M. Musyoka, H. W. Langmi, B. C. North, M. Mathe, X. Kang, *Int. J. Hydrogen Energy* **2014**, *39*, 14912; b) J. Ren, H. W. Langmi, N. M. Musyoka, M. Mathe, X. Kang, S. Liao, *Materials Today: Proceedings* **2015**, *2*, 3964.

[183] K. A. McDonald, J. I. Feldblyum, K. Koh, A. G. Wong-Foy, A. J. Matzger, *Chem. Commun.* **2015**, *51*, 11994.

[184] T. Li, J. E. Sullivan, N. L. Rosi, *J. Am. Chem. Soc.* **2013**, *135*, 9984.

[185] T. Ishiwata, A. Michibata, K. Kokado, S. Ferlay, M. W. Hosseini, K. Sada, *Chem. Commun.* **2018**, *54*, 1437.

[186] L.-W. Yin, C. Li, S. Dong, R. Tang, X. Ge, C. Wang, Z. Zhang, Y.-p. Lu, *Energy Environ. Sci.* **2018**.

[187] K. Hirai, S. Furukawa, M. Kondo, M. Meilikhov, Y. Sakata, O. Sakata, S. Kitagawa, *Chem. Commun.* **2012**, *48*, 6472.

[188] J. Zhuang, L. Y. Chou, B. T. Sneed, Y. Cao, P. Hu, L. Feng, C. K. Tsung, *Small* **2015**, *11*, 5551.

[189] Y. Yoo, H.-K. Jeong, *Cryst. Growth Des.* **2010**, *10*, 1283.

[190] a) J. Tang, R. R. Salunkhe, J. Liu, N. L. Torad, M. Imura, S. Furukawa, Y. Yamauchi, *J. Am. Chem. Soc.* **2015**, *137*, 1572; b) J. Xu, S. Liu, Y. Liu, *RSC Adv.***2016**, *6*, 52137.

[191] L. Peng, J. Zhang, J. Li, B. Han, Z. Xue, B. Zhang, J. Shi, G. Yang, *J. Colloid Interface Sci.* **2014**, *416*, 198

[192] M. Tsotsalas, A. Umemura, F. Kim, Y. Sakata, J. Reboul, S. Kitagawa, S. Furukawa, *J. Mater. Chem.* **2012**, *22*, 10159.

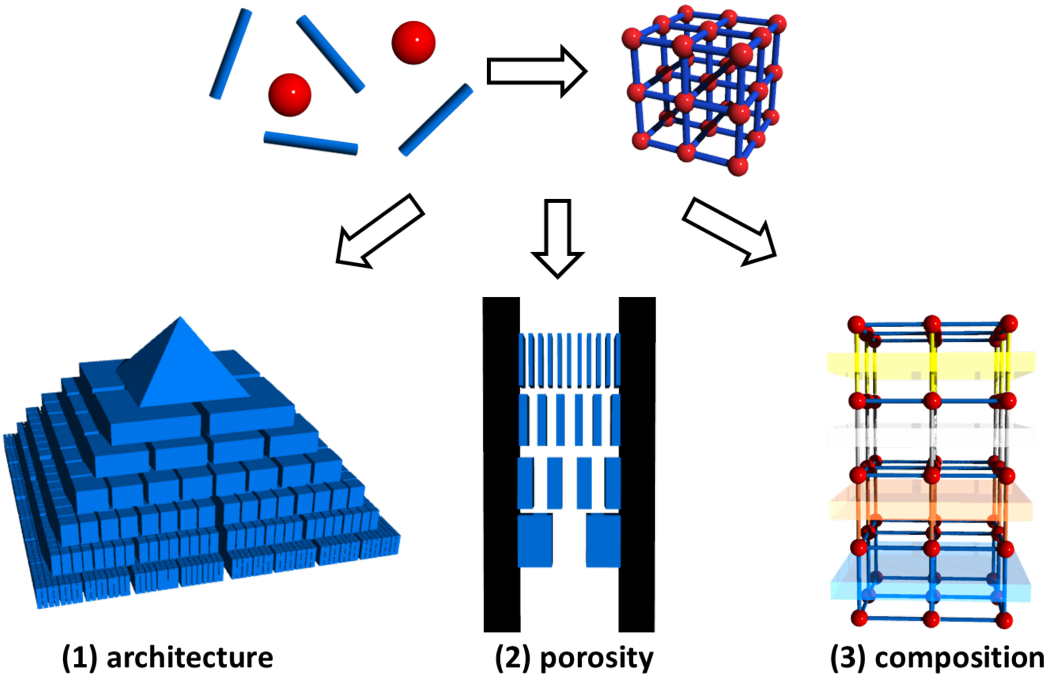

Figure 1. Top: Metal-Organic Frameworks prepared by self-assembly of metal nodes and organic linkers. Bottom: Different perspectives of hierarchical structuring in metal-organic frameworks (1) hierarchical architecture, (2) hierarchical porosity and (3) hierarchical composition.

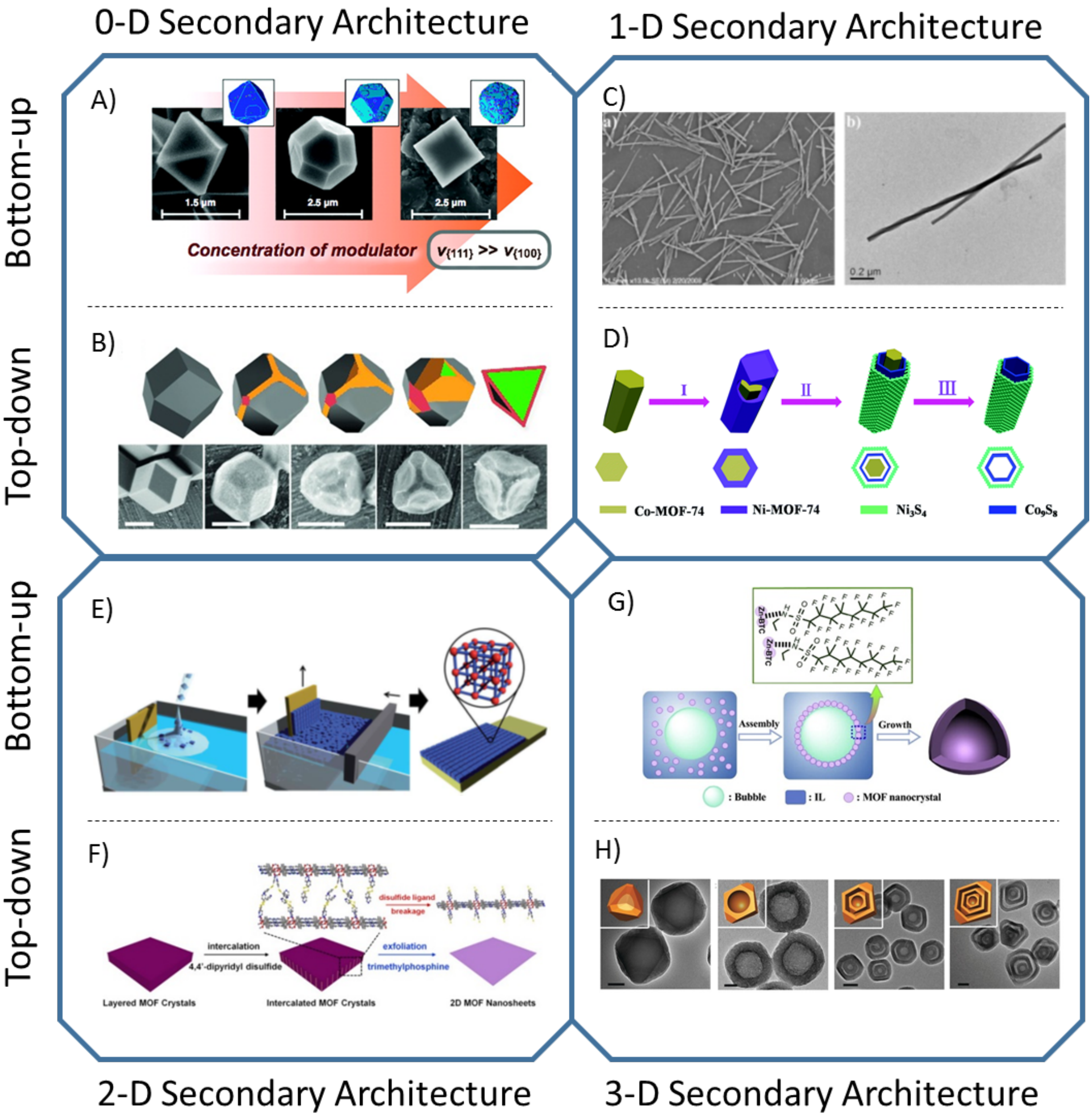

Figure 2. Production of MOFs with secondary hierarchical architecture using top-down or bottom-up approaches. A) Reprinted with permission. [22] Copyright 2011, American Chemical Society. B) Reproduced with permission. [27] Copyright 2016, Wiley-VCH. C) Reprinted with permission. [30] Copyright 2011, American Chemical Society. D) Reprinted with permission. [36] Copyright 2018, The Royal Society of Chemistry. E) Reprinted with permission. [192] Copyright 2013. Elsevier Inc. F) Reprinted with permission. [48] Copyright 2017, American Chemical Society. G) Reprinted with permission. [191] Copyright 2011, The Royal Society of Chemistry. H) Reproduced with permission.[83] Copyright 2017, Wiley-VCH.

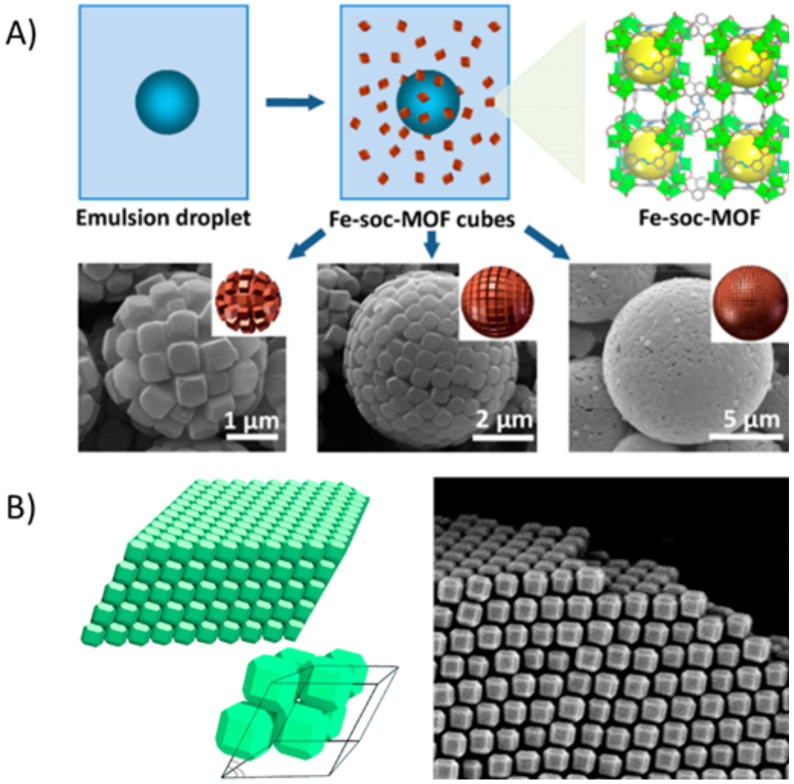

Figure 3. A) Schematic illustrations and SEM images of hollow colloidosomes of Fe-soc-MOF cubes. Reprinted with permission.[89] Copyright 2013, American Chemical Society. B) FE-SEM image and simulation of ZIF-8 superstructure. Reproduced with permission.[90] Copyright 2017, Nature Publishing Group

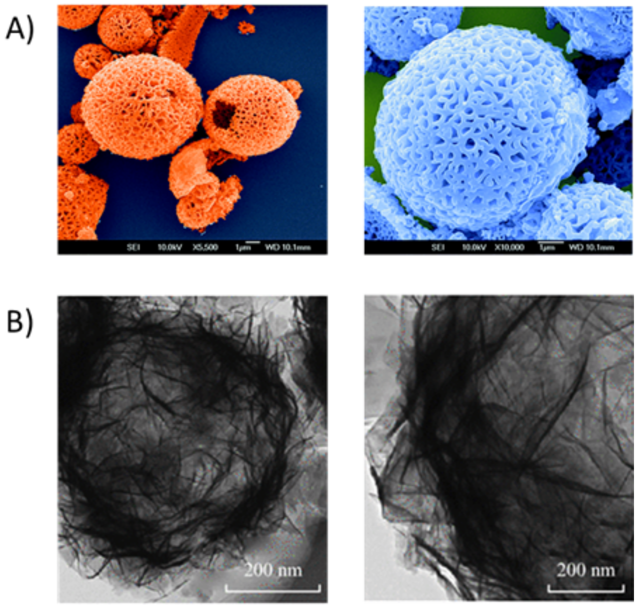

Figure 4. A) Etching for ZIF-8 hollow structure for the creation of MOF with tertiary hierarchical architecture. Reprinted with permission.[92] Copyright 2018, The Royal Society of Chemistry. B) Transformation and substitution of ZIF-8 lead to the 2D hollow spherical microstructures made of MOF nanoflakes.

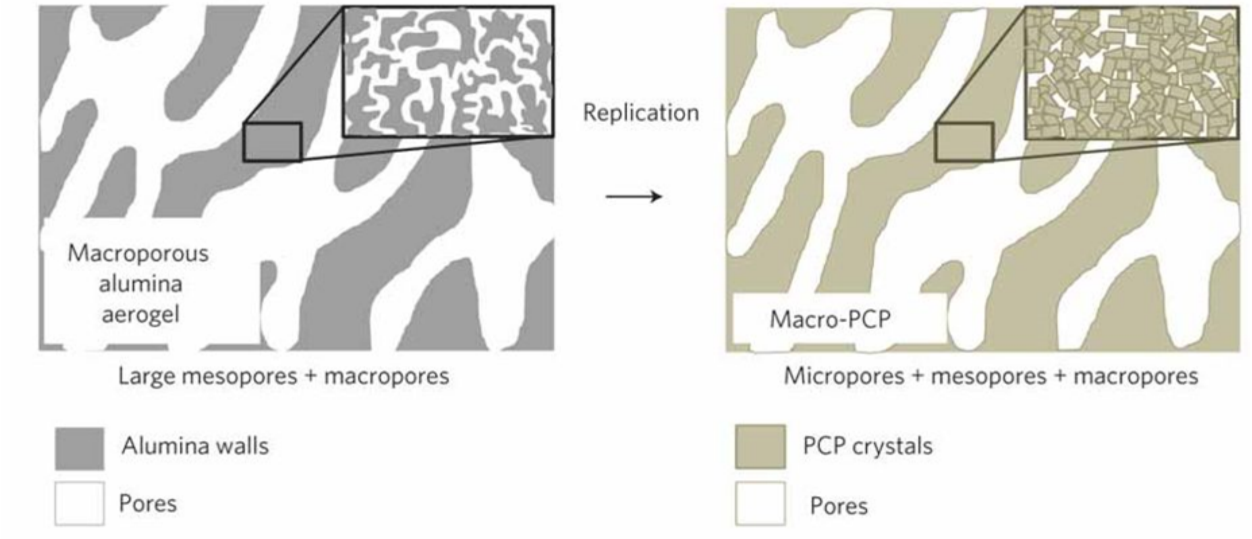

Figure 5. Hierarchically porous MOF materials with three levels of porosity. Reproduced with permission.[54] Copyright 2012, Nature Publishing Group.

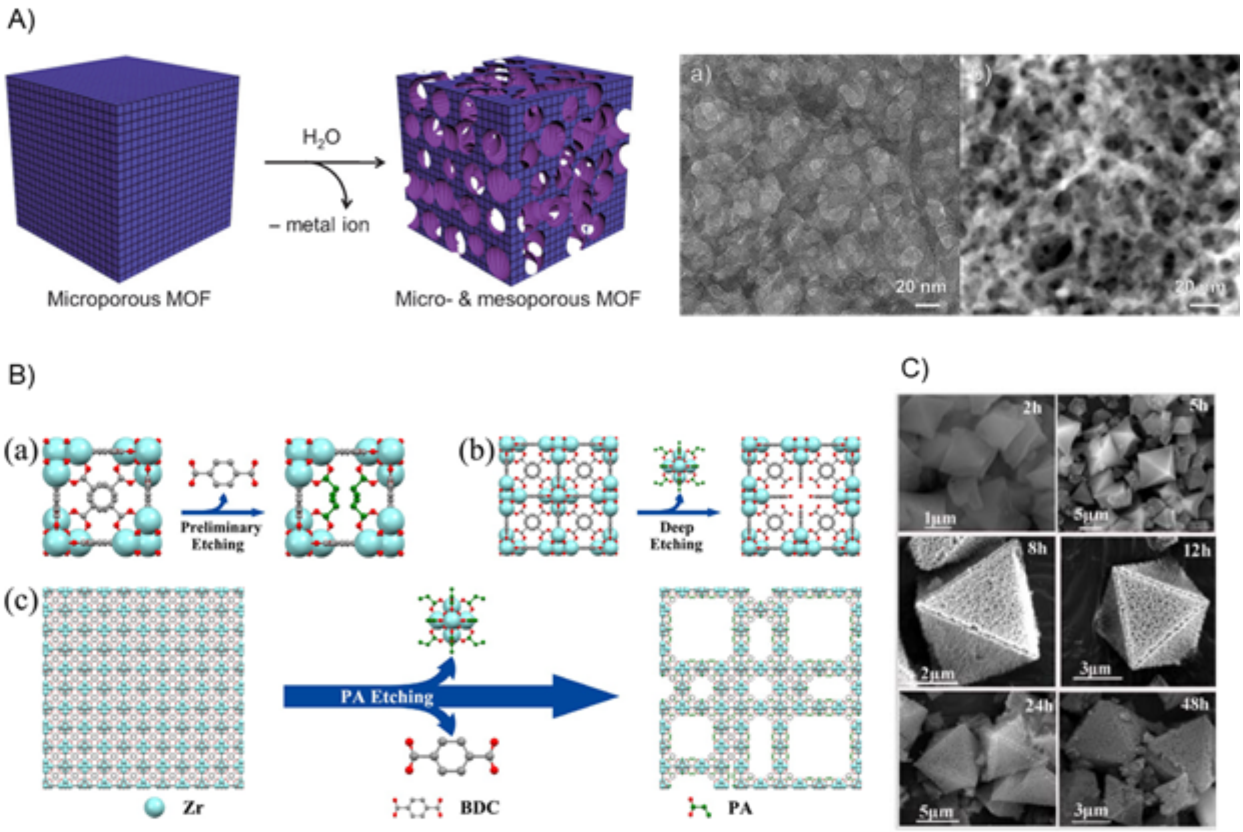

Figure 6. A) Creation of hierarchically porous POST-66(Y) MOF by treatment with water. Reproduced with permission.[108] Copyright 2015, Wiley-VCH. B) Creation of hierarchically porous UiO-66 by treatment with acid. Reproduced with permission.[109] Copyright 2018, Wiley-VCH. C) Creation of hierarchically porous

Cu-TATAB framework by treatment with H_2O_2. Reproduced with permission.[110] Copyright 2018, Elsevier.

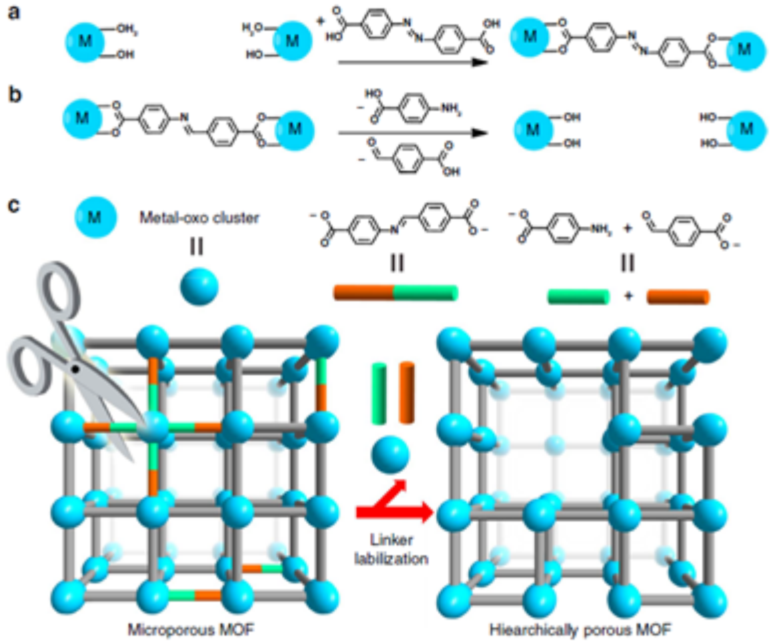

Figure 7. Formation of secondary porosity through instability of MOF linkers. Reproduced with permission.[111] Copyright 2017, Nature Publishing Group.

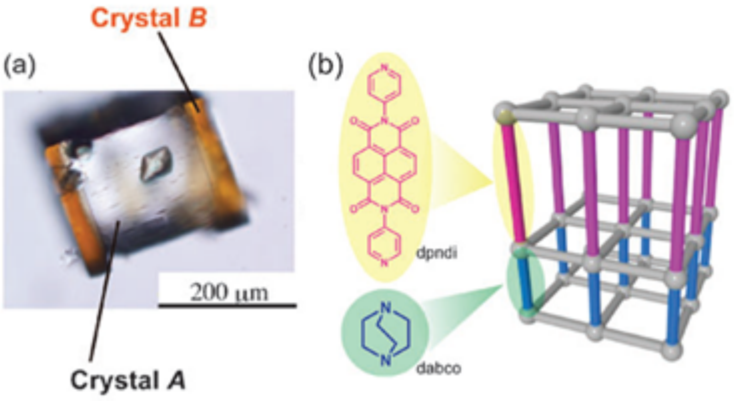

Figure 8. a) Face-selective epitaxial growth of MOFs with hierarchical composition, b) Schematic representation and chemical structure of the different linkers in the hierarchical composition. Reprinted with permission.[9] Copyright 2009,The Royal Society of Chemistry.

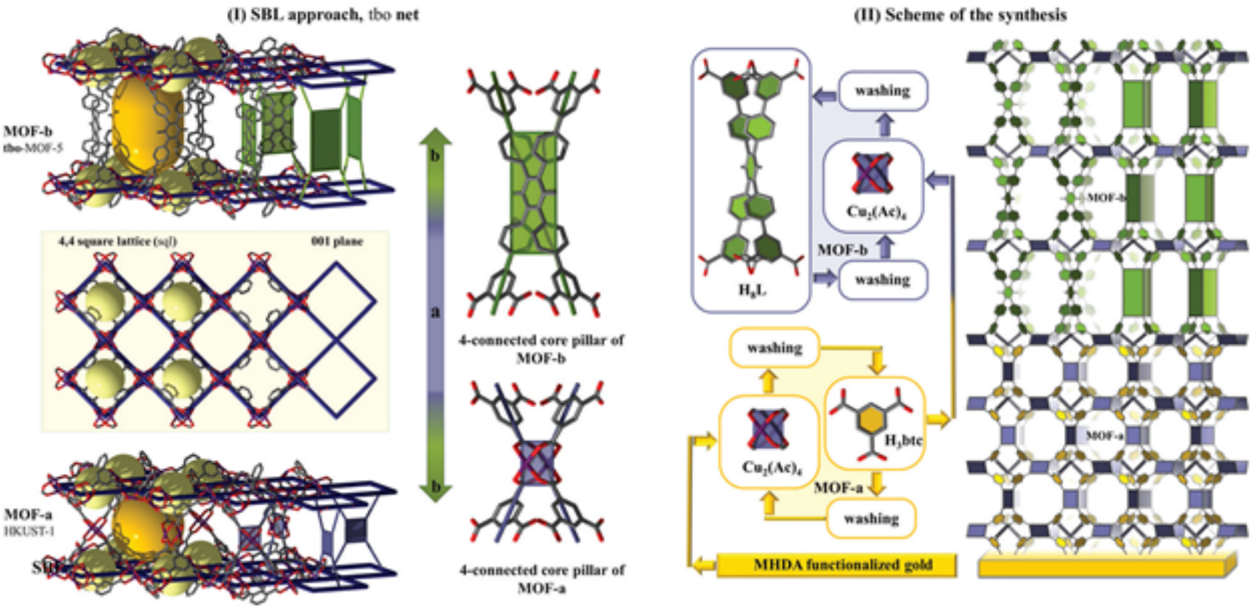

Figure 9. MOFs with hierarchical composition by combining Cu-tbo-MOF-5 grown on HKUST-1. Reprinted with permission.[181] Copyright 2017, The Royal Society of Chemistry.

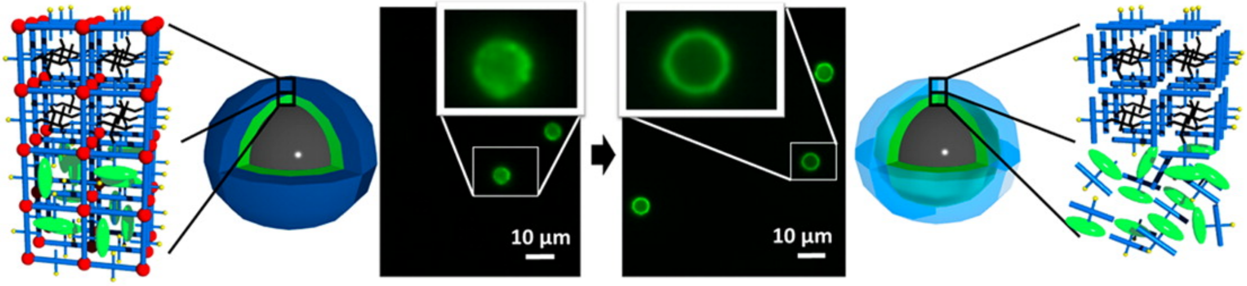

Figure 10. Hierarchically structured shell-on-shell MOF particles and their transformation into magGEL capsules. Reprinted with permission.[122] Copyright 2015, American Chemical Society.

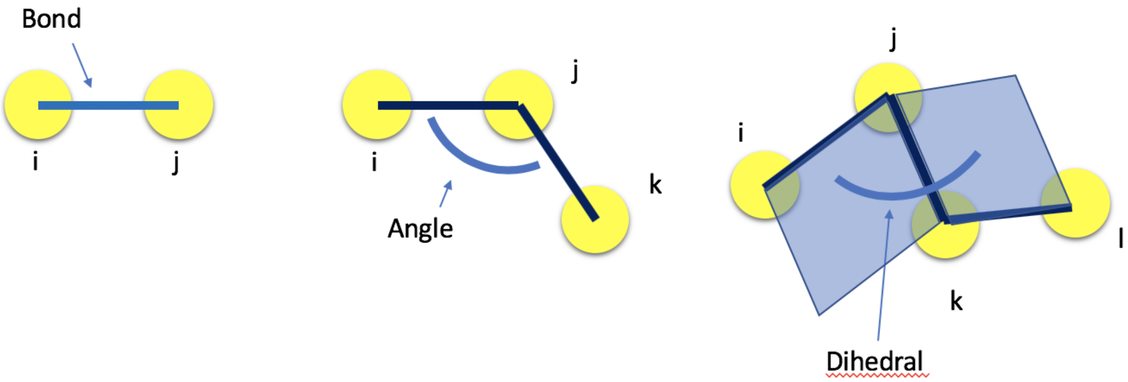

Figure 11. Bonds are formed between two atoms i and j, angles are between two bonds ij and jk and (proper) dihedrals are the angle between the planes formed by the vectors ij, jk and jk, kl, respectively. Improper dihedrals are not shown.

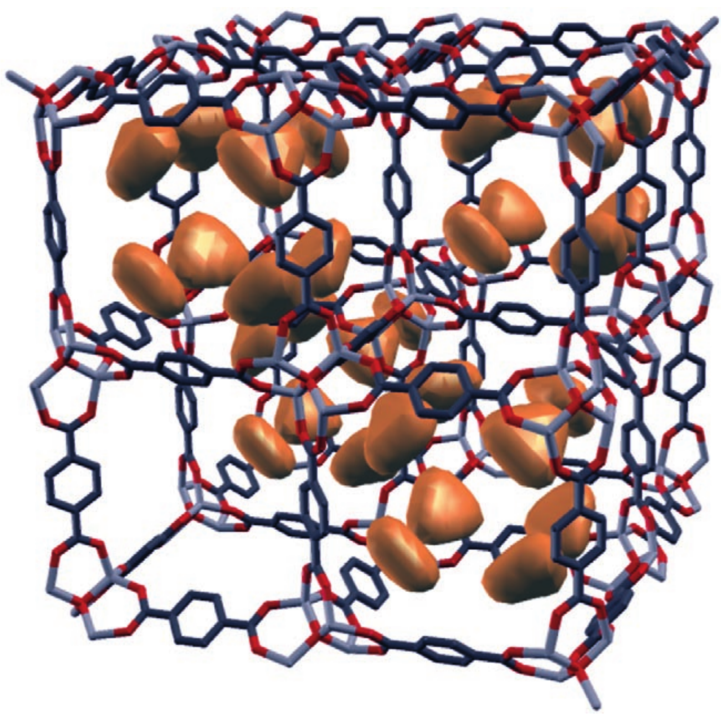

Figure 12. Probability distribution of the center of mass of benzene in MOF-5 at 300K. Reprinted with permission.[167] Copyright 2006, Wiley-VCH.

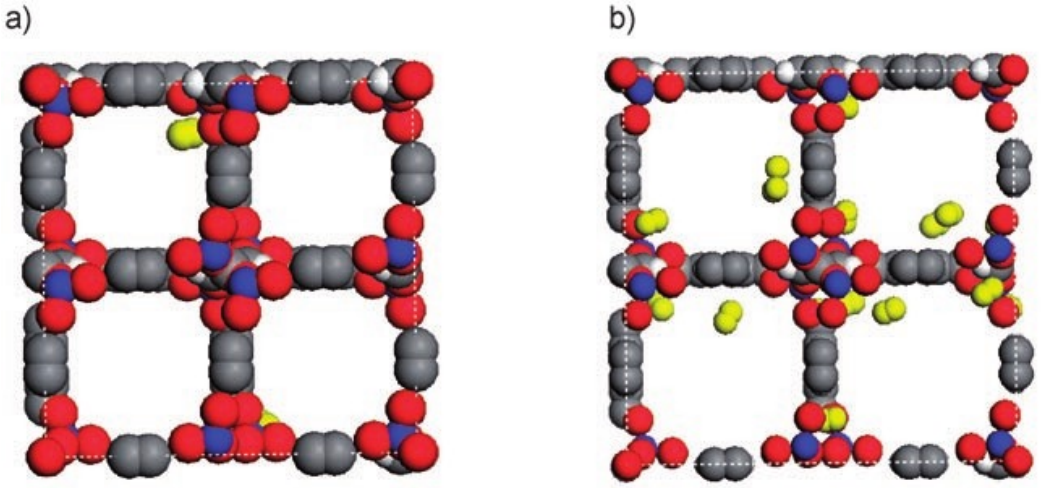

Figure 13. Zn-MOF-C6 at different pressures (a:p=0.05barm, b:p=0.5bar), hydrogen is adsorbed near the metal nodes. Zn = blue, O = red, C = gray, H=White and Yellow. Reproduced with permission.[169] Copyright 2007, Wiley-VCH.

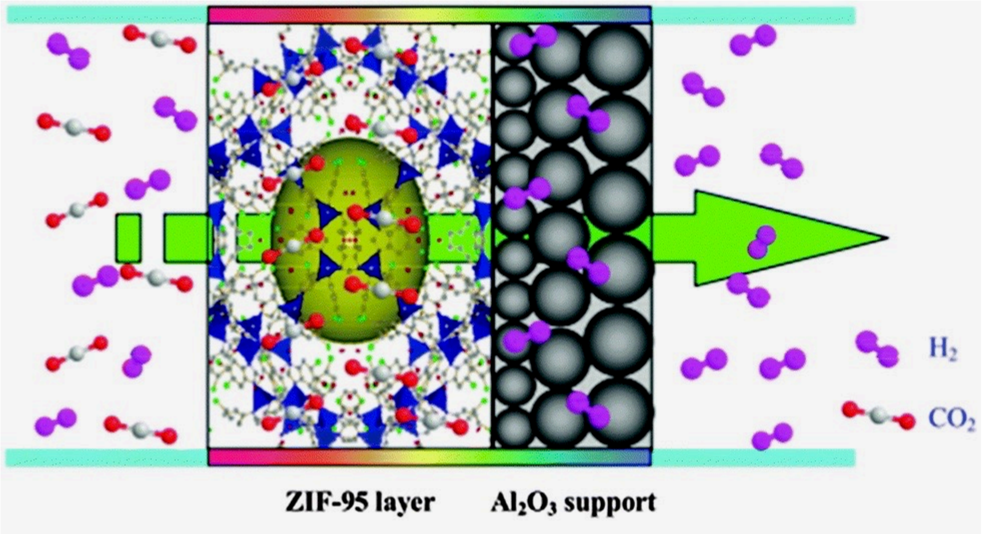

Figure 14. Zeolitic-Imidazolate Frameworks (ZIF) are similar to MOFs as they also possess a porous structure. This figure shows a ZIF-95 membrane separating carbondioxide from hydrogen. Reprinted with permission.[172] Copyright 2014, The Royal Society of Chemistry.

$$V(\vec{r}) = \sum_{bonds} K_b(x-x_0)^2 + \sum_{angles} K_a(\theta-\theta_0)^2 + \sum_{torsions} V_t(1-\cos(n\phi-\phi_0)) + \sum_{atoms} V_{ij}\left[\left(\frac{\varepsilon_{ij}}{r_{ij}}\right)^{12} - 2\left(\frac{\varepsilon_{ij}}{r_{ij}}\right)^{6}\right] + \sum_{atoms} \frac{q_i q_j}{4\pi\varepsilon_0\varepsilon_R r_{ij}} \qquad (1)$$

Equation 1. x are distances between neighboring atoms, θ are the angles formed between two neighboring bonds; ϕ is the dihedral between the planes formed by two neighboring sets of three atoms; r_{ij} are the distances between two atoms i and j; K_b, K_a are interactions strengths for bonds and angles; V_t, V_{ij} are interactions strengths for dihedrals and Van-der-Waals interactions; x_0 and θ_0, ϕ_0, ε_{ij} are equilibrium values for bonds, angles, dihedrals and Van-der-Waals interactions, respectively; q_i are charges of individual atoms; ε_R are a material specific dielectric constant.

Table 1. Different types of hierarchies in MOFs, their characteristics, properties and related examples in natural systems.

Type of hierarchy	Characteristics	Properties	Examples in natural systems
Architecture	Structural elements on more than one length scale	Optimized mechanical strength and rupture resistance	Tree
Porosity	Porosity on more than one length scale	Optimized mass flow combined with high surface area and accessibility	Lung
Composition	Organization of functional units on more than one length scale	Protective coatings/layers or optimized energy transfer	Skin

Table 2. Core-shell-type MOFs with hierarchical composition

Primary Composition (Seed)	Secondary Composition (Shell)	References	Remark
MIL-101(Cr)	UiO-66(Zr)	ref[182]	-
IRMOF-3; IRMOF-3	MOF-5; IRMOF-3	ref[10, 183]	MOF-5(2nd layer)@IRMOF-3(1st layer)@MOF-5(core), IRMOF-3(2nd layer)@MOF-5(1st layer)@IRMOF-3(core) was also produced
bio-MOF-11/14	bio-MOF-14	ref[184]	-
IRMOF-9	$[Zn_4O(Az BPDC)_3]$	ref[185]	(Azbpdc: azide-tagged BPDC)
UiO-66	NH_2-UiO-66	ref[186]	-
$[Zn_2(adc)_2(dabco)]$	$[Zn_2(NH_2\text{-bdc}),(dabco)]$	ref[187]	(adc: 9,10-anthracene dicarboxylate; dabco: dabco = 1,4-diazabicyclo[2.2.2]octane; NH_2-bdc = 2-amino-1,4-benzenedicarboxylate)
Co-MOF-74	Ni-MOF-74	ref[36]	-
UiO-66, Pd-UiO-NH_2	ZIF-8	ref[188]	-
IRMOF-1	IRMOF-3	ref[189]	-
ZIF-8	ZIF-67	ref[190]	-

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Hierarchical synthetic materials contain structural elements at more than one length scale. This structural hierarchy can strongly influence the bulk material properties. Recent progress in the synthesis of hierarchically structured MOFs as well as the multi scale modelling and associated simulation techniques are reviewed.

Keyword: Metal-Organic Framework, Hierarchical architectures, Molecular Dynamics

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Rising up: Hierarchical Architectures of Metal–Organic Frameworks in Experiment and Simulation