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The future of metal–organic frameworks and covalent organic frameworks: rational synthesis and customized applications

Xing Han,[b] Wenqiang Zhang,[b] Zhijie Chen,*[ac] Yan Liu*[b] and Yong Cui*[b]

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Metal–organic frameworks (MOFs) and covalent organic frameworks (COFs) are designable and tunable functional crystalline porous materials that have been explored for applications such as catalysis, chemical sensing, water harvesting, gas storage, and separation. On the basis of reticular chemistry, the rational design and synthesis of MOFs and COFs allows us to have unprecedented control over their structural features and functionalities. Given the vast number of possible MOF and COF structures and the flexibility of modifying them, it remains challenging to navigate the infinite chemical space solely through a trial-and-error process. This Opinion Article provides a brief perspective of the current state and future prospects of MOFs and COFs. We envision that emerging technologies based on machine learning and robotics, such as high-throughput computational screening and fully automatic synthesis, can potentially address some challenges facing this field, accelerating the discovery of porous framework materials and the development of rational synthetic strategies for customized applications.

Wider impact

The development and applications of metal–organic frameworks (MOFs) and covalent organic frameworks (COFs) are rapidly evolving fields. The exceptional, tailorable properties of these materials, along with their customizable applications, have attracted substantial interest and investment. Innovations in synthesis methodologies, such as fully automatic synthesis, high throughput screening, and machine learning, are opening new frontiers in the design, synthesis, and applications of MOFs and COFs. This Opinion article provides insights and predictions regarding the future trajectory of MOFs and COFs. By focusing on the principles of rational design and customized applications, we explore how these advancements shape the future of MOFs and COFs. We believe that the integration of advanced technologies can drive scientific advancement and potentially achieve significant societal and economic benefits.

Introduction

Metal–organic frameworks (MOFs) and covalent organic frameworks (COFs) are two promising classes of crystalline porous materials, that have tunable pore structures, high surface areas, and programmable functionalities.[1] These materials have been studied for applications, including heterogeneous catalysis,[2,3] water harvesting,[4,5] CO_2 capture,[6,7] molecular separation,[8–10] chemical sensing,[11] and ion batteries.[12]

MOFs are constructed from metal-containing nodes and organic ligands *via* coordination bonds while COFs are made from organic building units *via* covalent bonds. One of the most impressive characteristics of these porous framework materials is that they can be rationally designed and synthesized with customized applications at molecular level precision.[13–15]

This Opinion Article aims to offer readers a brief overview of MOFs and COFs, as well as our perspective about the future of this field. First, we will cover a few representative examples showing the application of reticular chemistry to the rational synthesis and customized applications of MOFs and COFs. We raise some questions and challenges in this field from an experimental perspective. Next, we envision how emerging techniques including high-throughput computational screening (HTCS) and fully automatic synthesis (FAS) coupled with machine learning (ML) can address some of these challenges. Finally, we conclude with a discussion on the future directions, particularly focusing on the importance and role of artificial

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[a] *Stoddart Institute of Molecular Science, Department of Chemistry, Zhejiang University, Hangzhou 310058, China. E-mail: zhijiechen@zju.edu.cn*

[b] *School of Chemistry and Chemical Engineering, Frontiers Science Center for Transformative Molecules and State Key Laboratory of Metal Matrix Composites, Shanghai Jiao Tong University, Shanghai 200240, China. E-mail: liuy@sjtu.edu.cn, yoncui@sjtu.edu.cn*

[c] *Zhejiang-Israel Joint Laboratory of Self-Assembling Functional Materials, ZJU-Hangzhou Global Scientific and Technological Innovation Center, Zhejiang University, Hangzhou 311215, China*

intelligence in empowering the field of reticular chemistry and functional framework materials.

Rational synthesis and targeted applications

Scientists can tune the framework materials with high precision, by judiciously selecting molecular building blocks with different compositions, sizes, geometrical shapes, linkages, and connectivities.[16–19] The initial step to make frameworks with desired topologies is the selection of molecular building blocks with specific geometry. It is possible to moderate the pore sizes of framework materials *via* varying the length of the organic structure without altering its connectivity and shape. In the case of COF materials, the linkage groups between the connected building units can be deployed to construct the framework backbone, onto which functional groups with desired chemical properties can be appended.

A widely used strategy to tailor a particular MOF/COF for a given application involves functionalizing the building blocks – for example, Mg_2(olz) (olz^{4-} = (*E*)-5,5′-(diazene-1,2-diyl)bis(2-oxidobenzoate)) could be post-modified by appending diamines on the open metal sites in the framework.[20] By changing the type of amine that was appended, Long and coworkers could control the single-step CO_2 adsorption profiles across a wide range of pressures or temperatures (Fig. 1). In another example, Cui and coworkers show that they can combine the merits of the two chiral COFs (CCOFs) containing only one type of metal, *i.e.* Mn-CCOF-4, which promotes epoxidation of alkenes, and Cr-CCOF-4, which promotes ring opening of epoxides, by introducing two different metals (*e.g.*, Mn, and Cr) *via* post-synthetic metal exchange in CCOF-4.[2] In addition, they reveal the dramatical enhancement of the chemical stability of CCOF-4 towards acidic (1 M HCl) and basic conditions (9 M NaOH) as compared to their non alkylated analogs, by incorporating *tert*-butyl groups on the pore walls. In a follow-up study, Cui and coworkers used a linker extension strategy to tune the enantioselective induction ability. By Incorporating BINOLs into conformationally rigid pores of three-dimensional (3D) COFs, high enantioselectivity could be achieved in the catalytic synthesis of the practically important dihydroquinazolinones, whereas the corresponding homogeneous controls displayed no enantioselectivity (Fig. 1).[21] Similarly, Yaghi *et al.* applied a linker extension strategy for generating MOFs with superior moisture-capturing properties to get MOF-LA2-1, which exhibits an approximately 50% improvement in water uptake capacity as compared to its isostructural counterpart MOF-303. This approach allows us to increase the pore volume while retaining the ability of the MOF to harvest water in arid environments for long-term uptake and release cycling, as well as affording a reduction in regeneration heat and temperature (Fig. 1).[22]

Another important phenomenon in the field of COF and MOF materials is the interpenetration of crystalline structures.

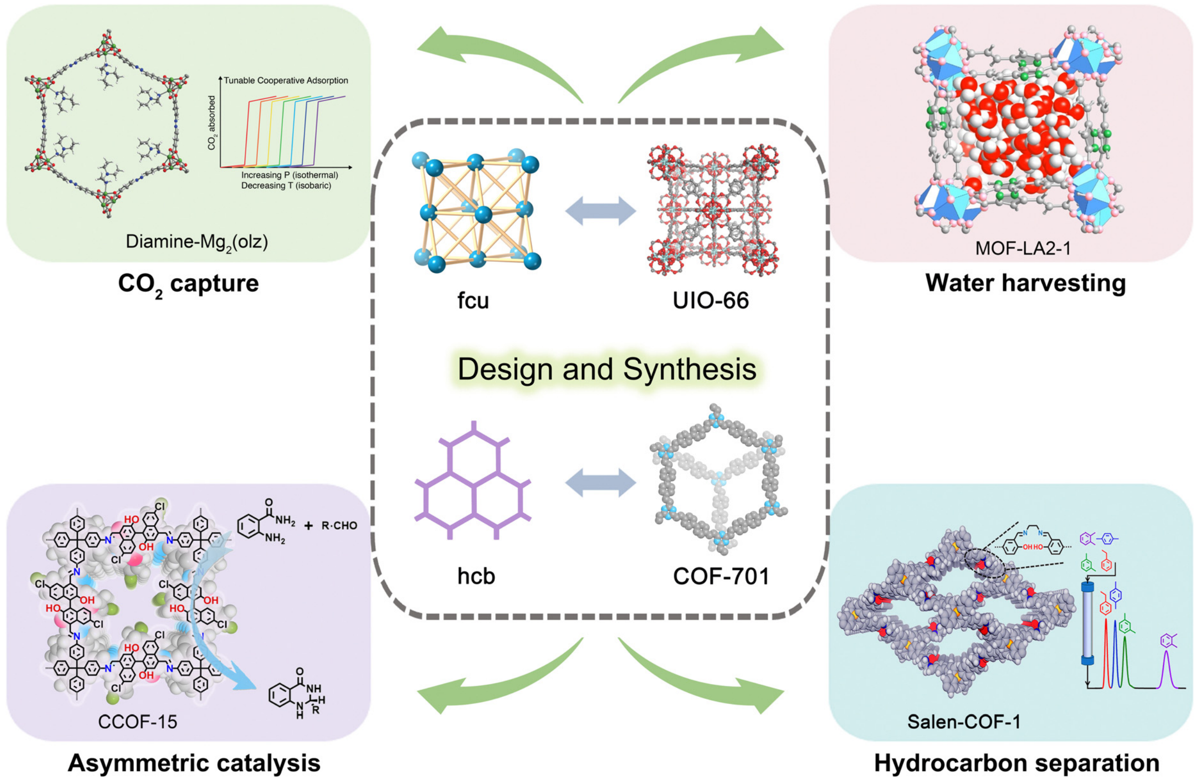

Fig. 1 Illustration of rational synthesis and customized applications for MOFs and COFs. Reproduced with permission from ref. 20 (Copyright 2022, American Chemical Society), ref. 21 (Copyright 2020, John Wiley and Sons), ref. 22 (Copyright 2022, American Chemical Society), and ref. 23 (Copyright 2019, American Chemical Society).

The reticulation of interpenetration serves as an effective approach to tune the pore structures and functionalities of these framework materials. The microporous 3D salen-COFs work as stationary phases of HPLC for baseline separation of xylene isomers and ethylbenzene with excellent column efficiencies and repeatability (Fig. 1).[23] In addition, increasing the number of different kinds of building units and functionalities incorporated into the frameworks will significantly expand the reticular chemical space and result in multivariate structures. Preliminary evidence suggests that these multivariable MOFs surpass their homogeneous counterparts in enabling programmed drug release, achieving highly selective separations, and facilitating enzyme-like catalysis.[24]

MOFs and COFs offer promising solutions to pressing global concerns related to environmental and energy issues over the last two decades. However, the research workflow remains dependent on manual experimentation, a process that can be complex, time consuming, and resource-intensive. The diverse arrangement of organic linkers and metal nodes, as well as the combination of topological structures, makes reticular chemistry a discipline that operates in an infinite space of compositions, structures, properties, and applications. So far, we've only tapped into a tiny portion of this infinite space, the immense potential of reticular chemistry still awaits exploration. Addressing such a vast problem using manual experimentation sounds like a seemingly impossible task.[25]

In addition, it is also challenging to predict the outcome of the self-assembly of different building blocks. For instance, the 3D pyrene-based covalent organic framework (3D-Py-COF) is synthesized by linking tetrahedral and rectangular building blocks through imine condensation reactions.[26] According to the reticular chemistry structure resource (RCSR) database,[27] several nets (*e.g.*, pth, pti, pts, *etc.*) are possible for 3D-Py-COFs. In addition, these nets can include multiple interpenetrations, making it challenging to predict the final structure and the degree of interpenetration. In the case of MOFs, the complex variability of metal nodes can cause some structures to deviate considerably from the intended design. Furthermore, soft porous crystals like dynamic MOFs, COFs, hydrogen-bonded organic frameworks (HOFs), and molecular crystals can undergo structural changes when subjected to stimuli such as heat, gas/vapor, or light.[28–32] The structural degree of freedom is related to the mutual displacement of frameworks such as layers and cubic grids and the flexibility of the framework itself. As a result, these materials often exhibit a range of remarkable properties, including storage, separation, guest molecule exchange within their cavities, magnetism, conductivity, and catalysis.[33–36] It is important to note that understanding such a unique system can uncover new mechanisms that can be utilized in designing new materials with enhanced performance. This raises a question regarding which of the possible structures, resulting from a combination of building unit geometries, will form in the synthesis. And what are the specific conditions required for the formation of various structures?

Predicting the performance of these materials poses another challenge. While a researcher can introduce various functional groups into framework materials, it remains challenging to construct materials with optimal performance. The process often involves a cyclical routine of material synthesis, performance testing, and structural optimization until a satisfactory outcome is reached. However, this result may not necessarily reflect the material's optimal performance.

The next question then is how we can rapidly design a structure to achieve a specific target performance metric? In light of recent advancements in robotic technology and digital computation, turning to integrating artificial intelligence (AI) for rational synthesis and customized applications is emerging as a promising solution to the aforementioned challenges (Fig. 2).

AI assisted discovery and experimentation

HTCS, which is based on molecular simulation, has become an efficient method to screen and estimate the performance limits of MOFs in recent decades.[37–40] Currently, there are experimental databases such as the CoRE MOF 2019,[41] as well as hypothetical structural databases like hMOFs[42] and hypothetical COFs,[43] which have been developed using various geometry-based tools and algorithms, including RCSR, ToposPro,[44] and ToBaCCo.[45] These databases enable researchers to investigate and determine energy landscapes, charge transport, gas adsorption and separation, guest–host interactions, and thermodynamic properties using methodologies such as molecular dynamics, density functional theory, and grand canonical Monte Carlo simulations.[46] Furthermore, the vast amount of data generated from these simulations can then be used to analyze structure–property relationships. Recently, data mining technology and ML have been starting to find widespread application in deriving design heuristics that otherwise would be difficult to identify. A number of different ML algorithms, like random forest, support vector machine, *k*-nearest neighbors, artificial neural networks, and other higher-level models, are currently being used.[47,48]

Reticular chemistry's complexity necessitates algorithms that can navigate vast design spaces and uncover novel structures or behaviors. Algorithms, powered by AI, can rapidly parse through numerous permutations and combinations, identifying optimal solutions that might be infeasible through manual efforts. In addition, predictive modeling can forecast the properties of a novel structure before its synthesis.[49]

After having identified the ideal material for a particular application, the next question that naturally comes up is, how can that material be synthesized? Often, here too, the synthesis procedure involves multiple steps with a variety of different variables that need to be optimized individually. For a typical optimization, a human may often need to perform a couple of hundred different synthesis conditions before arriving at one that meets the performance requirements. This process is often time consuming and cumbersome. In addition, any work performed by a human may lead to the introduction of small errors at each step of the process, which over time can accumulate, leading to issues with reproducibility.

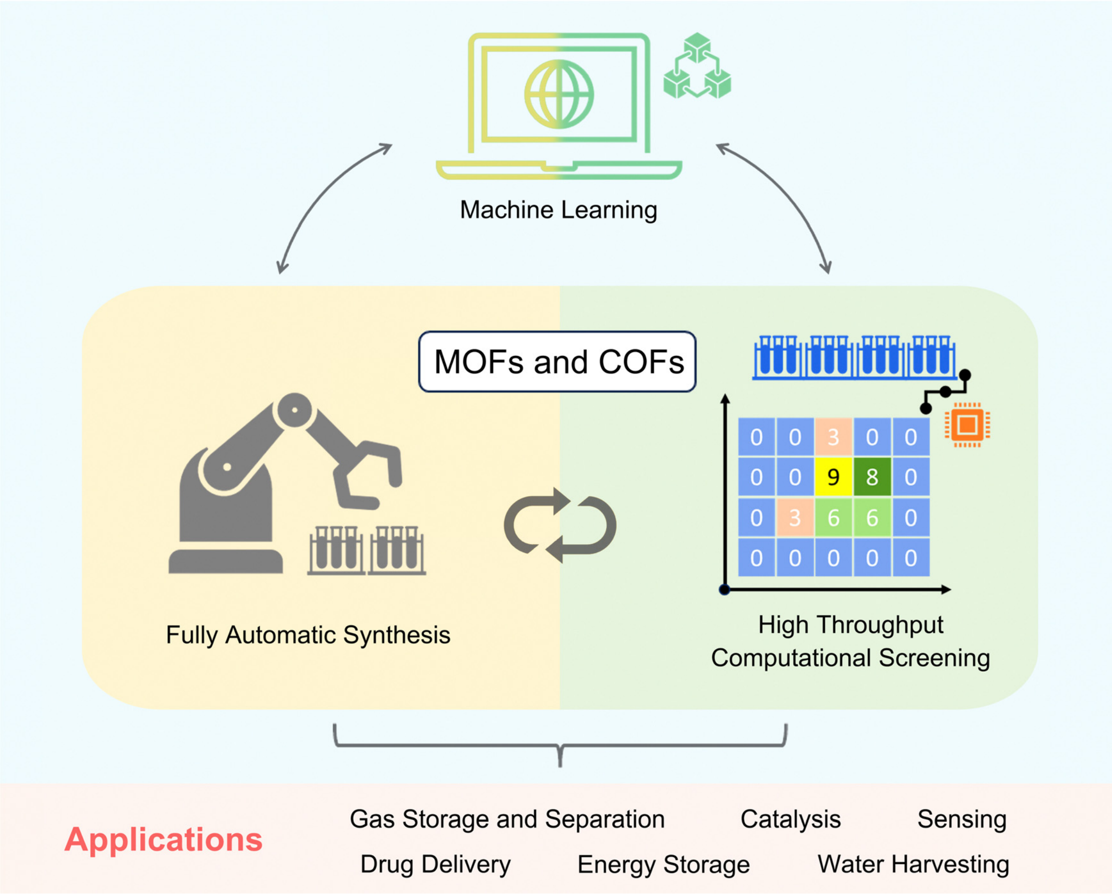

Fig. 2 The proposed future exploration on MOFs and COFs.

Given the recent advances in robotics and machine learning, and the development of state-of-the-art characterization techniques, FAS is gradually becoming a reality (Fig. 2).[50,51] FAS refers to a process that is capable of autonomously generating new reaction pathways, synthesis protocols, and optimization schemes to help realize the creation of a target material.[52] It normally involves both a software and hardware component which work in tandem. Since most of the human labor is eliminated in such a system, FAS can significantly enhance the reproducibility of the synthetic process by minimizing the impact of human errors and variability inherent in manual operations. Thus, it would contribute to the consistent production of high-quality materials.[53–55] Additionally, automation can facilitate the synthetic scale-up process of the related MOF or COF materials, and this is in turn vital for their implementation in industrial applications.

Here, it is also relevant to take note of some of the drawbacks associated with the application of AI in discovery and experimentation. Much of the source data that these models run on are databases created by human scientists and it is natural that any implicit/explicit biases inherent in the scientific process of the human scientist will also spill over into the models learning from this data. At the end, it is essential to acknowledge that AI operates within the chemical space in which it is trained and does not reliably extrapolate beyond that space.

To address this, we believe that there is a need to (i) generate more data and more importantly (ii) make sure that the data is well structured and standardized – this requires the development of standardized operating procedures for data reporting and curation and (iii) standardized protocols for the operation of different characterization techniques often used in the synthesis of different porous materials. Combined, this will help ensure that the data generated by the community is free of implicit human error and help reduce the sources of error in experimentation and data reporting. The development of a robust FAS platform requires reliable planning tools for synthesis and retrosynthesis,[56,57] but often the models that are used have limited scope leading to inaccurate results, much of it because of the insufficient domain knowledge encoded in these models. In addition, existing FAS platforms are often inflexible with limited functionalities due to limitations in the hardware – this problem is particularly acute when the synthesis procedure involves multiple steps, with each step often requiring its own specialized equipment. To address this issue, it would require the development of modular platforms that permit the rapid and easy exchange of equipment allowing the platform to be reconfigured for different applications. Given that currently, many different suppliers make different characterization equipment, integration of these devices becomes a critical bottleneck for the widespread adoption of FAS platforms.

Outlook

To accelerate the rational synthesis of new functional MOF and COF materials, it would require a multi-disciplinary (as shown and described above using different examples from literature) development approach that promotes integration of the different sub disciplines of robotics, ML, chemistry, and engineering. As we have discussed in this perspective, this will require the community to adopt common data sharing and reporting standards. When reporting data, we should not restrict ourselves to data that is positive, as is often done in the literature, but may also start to document failed reactions – we believe that there is a lot to learn from such data too. Although these automated methods are still in their infancy, and there is significant room for improvement, we believe that in the future, automation combined with ML and robotics will greatly accelerate the discovery, design and synthesis of new porous framework materials to address urgent challenges from clean energy and water to climate change.

Author contributions

X. H., Z. C, and Y. C. conceived the idea and led the project. X. H., Z. C, and Y. C. wrote the manuscript. All authors discussed and revised the manuscript.

Conflicts of interest

There are no conflicts to declare.

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