Dynamic responsive porous crystals

Berichterstattung

Projektinformationen

DYNAPORE

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Projektwebsite

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Zusammenfassung vom Kontext und den Gesamtzielen des Projekts

The materials that society relies on to maintain and enhance living standards are produced by chemical manufacturing. Modern chemical manufacturing relies on solid porous materials for many key steps that involve the separation of molecules and/or their chemical transformations by catalytic processes. These solid porous materials, such as zeolites and carbons, have rigid solid state structures that are optimisable only for one chemical operation. This strongly contrasts with the natural manufacturing of chemicals in living systems, which perform complex processes at ambient conditions efficiently and selectively in single unit operations that combine multiple chemical steps. Nature can do this because it has access to dynamic, soft materials (such as proteins, DNA, polysaccharides etc.) that can respond to their chemical environments at each point in the process. For example, catalysis in biological systems is performed by the class of proteins known as enzymes. Proteins are chains of amino acids connected by peptide bonds. Many proteins are characterised by the potential availability of multiple structures, in strong contrast to the rigid porous materials used in current chemical manufacturing. These structures are related to each other by changes in single bond rotations of their polypeptide backbone. The appropriate structure for a particular chemical function, such as the binding or release of a specific molecule at a particular point in a more complex process, can then be selected by chemical stimulus provided by the environment, such as a change in the species interacting with the protein. This stimulus would change the protein structure by changing the rotations about the bonds that define the protein structure.

If we could design and produce porous materials that dynamically select the appropriate structure to carry out a desired chemical function in response to their environment, we would be able to manufacture, manipulate and deliver molecules in an entirely new way which builds in the efficiency of biological systems, reduces the operational cost of the chemical industry and improves its environmental footprint.

The overall objective of the project was to produce synthetic flexible porous materials that can adopt multiple structures, which are interconnected by the same single bond rotation pathway that proteins use, and to demonstrate the control of their function in chemical processes such as catalysis and separation by selecting the optimum structural configuration (Fig. 1).

(Figure 1 caption. A schematic representation of a flexible metal-organic framework, a porous material composed of metal nodes (yellow triangles) interconnected by flexible linkers (blue coils and ribbons). The conformation of the linkers can change depending on the guest molecules present in the pores. Thus, the pore shape and chemistry can be chemically controlled to produce a functional material. To achieve this objective, the project takes a multidisciplinary, experimental and computational, approach that is designed to maximize the understanding of the dynamics of flexible porous materials and to connect these dynamics to their crystal structures and chemical compositions. The project thus aims to establish structure – property – dynamics relationships to guide selection of the chemical components to build flexible porous materials that respond to changes in their environment by single bond rotation, and to enable understanding of the resulting properties. This is required to reveal the possibilities offered by porous materials that change their structures using the mechanisms adopted by biological systems.)

The project achieved the synthesis of many flexible porous materials that adopt multiple structures and it exploited the similarities of these materials with proteins, in terms of single bond rotation and sidechain functionality, in order to understand the dynamics of structural changes triggered by guest molecules. The degree of structural control of the conformation of flexible linkers and the arrangement of sidechain functional groups enabled the enhanced activity of these materials in the separation of isomers of important molecules, in line with the original objectives.

Arbeit, die ab Beginn des Projekts bis zum Ende des durch den Bericht erfassten Berichtszeitraums geleistet wurde, und die wichtigsten bis dahin erzielten Ergebnisse

The porous materials that were studied in this project belong to the category of metal organic frameworks (MOFs). Their structures consist of a framework of metal centres connected by organic linkers, which defines a porous structure consisting of cavities and channels that are occupied by guest molecules – by control of the interaction between the framework and the guests, we aim to change the structure of the MOF and allow it to perform specific chemical functions. The project targeted MOF that can adopt multiple structures and are thus flexible rather than rigid, with the flexibility arising from rotation about the single chemical bonds within the structure of the linker molecule – changes in the structure of the linker molecule due to changes in rotation about single bonds within it are referred to as changes in conformation. As the project progressed, the team were able to identify specific linker and metal combinations that allowed chemically tailored flexible response that improved performance in the separation of important molecules. They also identified the need to better understand in general which combinations of metal and flexible linkers were able to give the open frameworks required by the project, rather than closed structures with no space for guests, and thus developed a new digital tool for the research community to tackle this problem.

The project integrated experimental work, which involved synthesis, characterisation and property measurement of the new flexible MOFs, with computational work, which involved both the theoretical analysis and understanding of the properties associated with the new flexible MOFs, and the use of this knowledge to guide the design of the next set of MOF to be tackled experimentally by predicting which are the best linkers to choose to access the flexible structures. We went beyond the originally envisaged scope of the work by developing machine learning models to take advantage of data in guiding the experimental synthesis work in the project.

The selection of the organic linker is a crucial step for the design of a new flexible MOF because the linker must bring the capability to change its structure by rotating around single bonds and also the chemical functionality that is necessary for the desired application, in particular to allow the interaction with the chemical environment to drive the change in structure. The organic linkers that were used in the project included three classes of molecules (i) pure peptides, (ii) peptide-like molecules that were designed and synthesized for the purposes of this project and (iii) other commercially available linkers that can change their structures by rotation about single bonds. Each of these classes of molecules has different characteristics relevant to their MOF chemistry, which are their terminal groups that bind to the metal centres to form the solid state crystal structure of the MOF, the number of sp3 carbons (carbons with four other chemically bonded neighbours) that are responsible for the ability to change structure by rotation about single bonds (referred to as conformational flexibility), and the available chemical functionalities. As the project progressed, we were able to develop design understanding that allowed us to both select specific linkers and metals that would afford dynamic open frameworks and to chemically tune their response to guests by modifying the chemistry of the pores in a systematic manner.

New MOFs were successfully synthesized with organic linkers from every class and their crystal structures were determined by single crystal x-ray diffraction (SCXRD). The structural flexibility of the new MOFs was explored by exchanging the solvent molecules contained in their pores with a library of small molecules that was selected using methods from chemical informatics to cover a variety of properties such as polarity, size and functional groups (Fig. 2). The understanding from these experiments was used to guide the modification of materials to enhance their performance and their selection for evaluation in applications in the later stages of the project.

(Figure 2 caption. The structural flexibility of a new MOF for every class of linker, (a) ZnGGH with pure peptide linker, (b) ZnGlyPyr with peptide-like linker, and (c) ZnCSA with commercially available carboxylate linker, demonstrated by exchanging the solvent molecules in the pores. Distinct structures that differ by linker conformation were identified for each MOF by these exchange experiments and they were compared to each other. The purpose of these experiments is to understand the range of changes in the MOF features that are responsible for their properties (such as pore size, pore shape, position of functional groups, bonding interactions to the guest molecules in the pores) that can be accessed by changing the chemical species in their pores, ensuring that the full range of possible structures and associated functions are identified.)

The flexible MOFs that were synthesized by the project demonstrate the key features targeted at the outset. Their pore structures and shapes respond dynamically to the guests present within them by chemically-driven rotations about single chemical bonds of the organic linkers. This leads to substantial changes in pore size, up to 10 Å, and in the pore shape. These dynamic guest-responsive materials contain chemical functionalities accessible to the species in the pores, which allow specific chemical interactions with the guest molecules. In the final stages of the project, we were able to specifically chemically modify these classes of framework in order to direct and optimize their response to guests for high performance in applications.

The flexible MOFs containing linkers of the second class, peptide-like molecules, provided a new example of structural flexibility where a small change in the linker conformation produces large changes to guest accessible pore space. ZnGlyPyr and ZnL-AlaPyr demonstrate the most characteristic changes in the trefoil shaped pores, from interconnected to separated pore domains and they reposition the sidechain functionality to accommodate the guests and control the adsorption of gases (Fig. 3), including control of the capture of $CO2$. The family of peptide-like molecules was further expanded to include other amino acid residues such as serine and valine. This enabled the synthesis of flexible MOFs with different sidechain functionalities on the same framework structure, which is a significant advancement compared to the initially identified ZnGGH material, which is highly flexible but does not contain free functionalities and cannot be chemically tuned in this way. The response of this new family of materials to guest molecules in the pores is tuned by changing the amino acid residue, which is the way that the response of proteins is controlled in natural systems. Longer versions of these peptide-like linkers, with large conformational space, have been prepared by attaching dipeptides, which creates the challenge of how to assemble such large and adaptable molecules into a porous flexible MOF structure. This point was addressed in this specific case with the assistance of theoretical simulations that identified the specific linker structure and chemistry with the appropriate conformation to construct a large pore and very flexible MOF. The resulting response to guests was demonstrated and understood with extensive structural measurements, and showed that the expansion of the linker conformational space dramatically altered the guest response of the larger pore material. All new MOFs bring features such as bulky sidechain functionalities, the presence of multiple sidechains with distinct chemistries, and large pores, which were exploited in structural response experiments with an expanded set of guests and exemplify the vision of human-made materials with chemically tunable protein-like responses.

(Figure 3 caption. The presence methyl sidechain in ZnL-AlaPyr changes the response of the framework to benzene compared to ZnGlyPyr that has no sidechain functionality. In ZnL-AlaPyr the pores are smaller and structural position of benzene is very different compared to ZnGlyPyr. (b) The adsorption - desorption isotherms of benzene vapors to both frameworks have been measured at 25oC and they demonstrate not only different amounts of uptake but also different shapes of isotherms that correspond to different mechanisms of adsorption.)

The structural responses to a diverse library of guests of each flexible MOF were utilized to inform decisions about the potential application in separation or catalysis that they could be used in. Several of the flexible MOFs developed in the project were then evaluated in property tests relevant to separations and catalysis, which required their synthesis at sufficient scale to enable these tests. A set of materials displayed outstanding performance in the industrially important separation of hexane isomers, which was correlated with their crystal structural features and particularly the accessible space created in their pores from the different chemistries of the diverse range of functional groups that were located within the flexible porous scaffold. This maps a designed flexible porous structure onto high application performance.

Theoretical simulations on the flexible MOFs that were synthesized provided detailed understanding of the structural behaviour and the properties of these compounds. The range of flexibility for every experimentally obtained flexible MOF was evaluated by density functional theory (DFT) calculations. The purpose of this step is to identify the number of stable structures that each framework can produce and reveal the modifications, in terms of pore geometry and the location of functional groups, that a framework is subjected as it is transformed from one structure to another through its interactions with the guests in the pores. For each MOF host, we parameterize a bespoke force field model to model adsorption of guest molecules and understand the control mechanisms of the guest-host interactions changing the structure of the MOF. The contribution of the organic linker to the flexibility of the MOF is assessed comparing the conformation of the linker in all possible, experimentally observed and theoretically predicted, structures. In highly flexible MOFs, the range of potential linker conformations is large and requires the deployment of principal component analysis (PCA), a method that simplifies high dimensional data, to highlight the key rotational states of single bonds that drive the observed structural change of the MOFs.

The combination of the above calculations with the experimental data allowed the project team to construct the conformational energy landscape (CEL) of a flexible MOF. The CEL is a representation commonly used by protein scientists to depict the energy of a protein as a function of all possible conformations that can be accessed by single bond rotations within the protein. This advance is aligned with the project goal of understanding and controlling how mechanisms like those used in biology can be used to control flexible man-made MOF, because the CEL represents key progress in developing the structure-property-dynamics relationships that the project needs to understand and control flexible MOF behaviour. CELs can now be used to depict and understand the favourable states of flexible MOFs and the transition pathways between them versus the available conformational space of the organic linkers. Once this concept was established, the latter stages of the project focused on chemically controlling the CEL response by modifying the pore chemistry and pore geometry, requiring expansion of the classes of material displaying CEL response.

Following the ideas developed in Nature 2019, the flexibility of several new MOFs from the ZnXPyr family was studied using Density Functional Theory to identify the relative stability of open and closed pore forms of these MOFs. The DFT data were also used to fit a set of molecular mechanics force filed models to study adsorption of small molecules. Specifically, for chiral MOFs, we compiled a dataset containing 26 groups of chiral molecular pairs and computationally investigated adsorptive selectivity for representative pairs. The map of the chemical space of chiral molecules and the developed protocol for identifying promising separation targets for a given MOF are new tools for materials screening developed in this project. To rationalise the experimental data, we applied this protocol to assess the relative strength of adsorption of hexane isomers and evaluate differences in their packing in several MOFs from the ZnXPyr family.

The selection of the components, organic linker and metal, to construct a flexible MOF that has the appropriate pore size to interact with different guests is not a straightforward process and it requires for the researchers to navigate through and understand large amounts of published data. Although we were able to understand how to access and expand the specific families of materials discovered and studied in the project, throughout the activity the team faced the challenge of not being able to pin down a general set of rules for designing and selecting the components that would guarantee the successful synthesis a flexible and porous MOF. Many of the organic linkers prepared during the project did not yield the expected flexible MOF structures, even though they had large enough conformational space and other characteristic features that seemed appropriate based on the teams understanding at the time (Fig. 4). This is because of the intrinsic challenge of constructing an open structure when the organic linker is able to change its shape, and thus fill space, in contrast to when a linker is rigid and can be directed to a well-defined arrangement in space by coordination to a metal. To address this issue the project team developed a machine learning tool that the predicts the porosity of a MOF based solely on its components. This method leverages the data of the crystal structure for thousands of MOFs available in Cambridge Structural Database to assess whether a particular combination of metal and linker will provide a porous material, in order to support the most efficient selection of components for porous materials, taking into account the potential flexibility of the linker. As the model requires only the chemical identity of the metal and the linker, it is able to advise the experimental researcher based on the information that they have at the point of synthesis when exploring new materials, by taking advantage of learning from vast arrays of data at a scale beyond that which humans can manage. The scope of this tool goes beyond the activities of this research project, as it can be used to guide the synthesis of porous materials related to separation, catalysis and any other application tuned by the size of pores. The tool is freely available to the research community and can be easily modified to target different pore sizes.
(Figure 4 caption. (a) The molecule H2GSA was designed as a very good candidate linker to produce a flexible porous MOF because it has three sp3 carbons on its backbone to produce large conformational space. Many synthetic experimental conditions were tested with this molecule and transition metals but the only MOF yielded was the non-porous and non-flexible ZnGSA. This reflects the difficulty faced by the synthetic chemist in selecting metals and linkers to access porous MOF. (b) To assess potential porosity of MOF materials before their synthesis, we developed a machine-learning tool based solely on the chemical properties of the MOF constituents, the metal and the organic linker. This allows the synthetic researcher to judge the consequences to choosing a particular linker, including but not limited to the linker classes covered in this project, for the likely porosity of the resulting material.

The results of those experimental and computational studies were published in four research articles, with further articles in preparation for submission.

Nature 565, 2019, 213-217
Crystal Growth and Design 19, 2019, 5604-5618
Journal of the American Chemical Society 142, 2020, 14903-14913
Angewandte Chemie International Edition 61, 2022, e202114573

Fortschritte, die über den aktuellen Stand der Technik hinausgehen und voraussichtliche potenzielle Auswirkungen (einschließlich der bis dato erzielten sozioökonomischen Auswirkungen und weiter gefassten gesellschaftlichen Auswirkungen des Projekts)

The team has been able to demonstrate (Nature 565, 2019, 213-217) that chemical control of the exact conformation adopted by a flexible linker through the rotation about its single bonds can trigger a specific chemical function by changing the crystal structure of the MOF, in line with the project aim of controlling chemical properties of flexible porous materials via single bond rotation and guest interaction. This was achieved by the development of the peptide-based crystalline porous material, with the code name ZnGGH, which is able to dynamically adapt its structure in the presence of different guests by reconfiguring the conformation of the flexible peptide chain through rotation about single chemical bonds. ZnGGH adopts nine distinct crystal structures. These structures display different pore sizes, pore geometries and internal surface chemistry because the peptide linker conformations change to give access to these different structures driven by their exact chemical interactions with the guest molecules, all of which were identified by the SCXRD structure determination. These structural changes were understood using the PCA method to analyse the observed linker conformations, which clustered the observed structures into three groups (Fig. 5).
(Figure 5 caption. Dihedral angle principal component analysis (dPCA) of linker conformations observed in 9 experimental structures of ZnGGH. The black circles marked with the number X for each ZnGGH-X structure denote the experimentally observed linker conformations while coloured solid circles correspond to the three pictured linker conformations observed in the calculated empty host structures S-ZnGGH, T-ZnGGH and F-ZnGGH, colour-coded according to their energy per linker. The calculated transition paths between these minima represent the conformational energy landscape of ZnGGH. The solid arrows indicate the positions of energy barriers on the conformational energy landscape and the dashed arrows show the largest change in linker torsions between the calculated structures shown.)
Computational analysis of these three groups revealed they led to three distinct groups of structures that were characteristic of low-energy arrangements of the entire framework. Thus, a conformational energy landscape for ZnGGH was constructed using the computationally optimised structures as minima that were connected by the simulated transition pathways. By controlling the structures adopted through the guest molecules selected to interact with the framework, it was possible to navigate through this landscape and produce behaviour in the crystalline porous material that was analogous to both the conformational selection (the selection of one of the three distinct groups of structures) and induced fit (the small change in the host structure due to the specific guest-host interactions) modes of guest response that are seen in proteins.
The liquid adsorption properties of the three different groups of ZnGGH structures were tested with

dioxane as probe molecule, in order to evaluate how the change in structure driven by chemical bond rotation through guest interaction can change the functional behaviour of a flexible porous material. The structures varied from highly active for dioxane uptake to completely inactive for dioxane uptake, according to their linker conformations. By changing the chemical environment of ZnGGH to transform its structure from an inactive to an active minimum, it was possible to chemically trigger the uptake of the dioxane molecules. The project thus understood the structural transformability of a crystalline porous material in terms of the conformational energy landscape picture used in protein science and controlled the activity of the material for the uptake of a chemical by selecting the appropriate minimum on the landscape by determining the conformation adopted by the linker through interaction with the guests (Fig. 6).

(Figure 6 caption. The demonstration of conformational selection and chemical triggering in ZnGGH: the calculated relative energies per linker are plotted for ZnGGH with DMSO and dioxane in the pores when their positions are optimised in a flexible host close to either the S-ZnGGH or T-ZnGGH minima i.e. with either straight or twisted linkers. For DMSO the T-ZnGGH minimum has the lower energy, in agreement with the experimentally observed structure. Dioxane prefers the S-ZnGGH minimum, however experiment shows that it cannot alone drive the transformation from T-ZnGGH to S-ZnGGH. The addition of DMF is required to select this minimum and allow dioxane uptake.)

To assist a MOF chemist with prioritisation of synthetic targets, we developed a machine-learning tool (Angewandte Chemie International Edition 61, 2022, e202114573) that predicts the porosity of MOF materials based solely on chemical properties of their constituents: the metal and the organic linker. This was developed to address specific challenges that arose in our project, but is generally useful across the metal-organic framework field. Our method leverages data available for thousands of synthesised MOF to predict properties of interest in potential synthetic targets without requiring knowledge of their structure but only requiring the knowledge of their constituents. This approach opens up a new line of research as it has a different objective compared to the typical ML tools for MOFs that focus on the structure-property relationship in known materials. Instead, we focus on the chemistry-property relationship which allows our model to make a prediction with over 80% accuracy as to whether the new synthesised material is going to be porous before the material is synthesised.

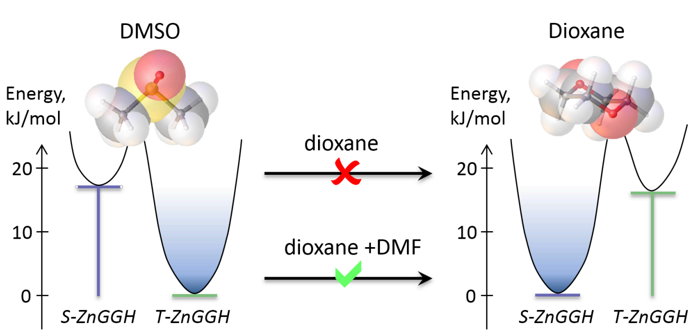

Figure 6. The demonstration of conformational selection and chemical triggering in ZnGGH.

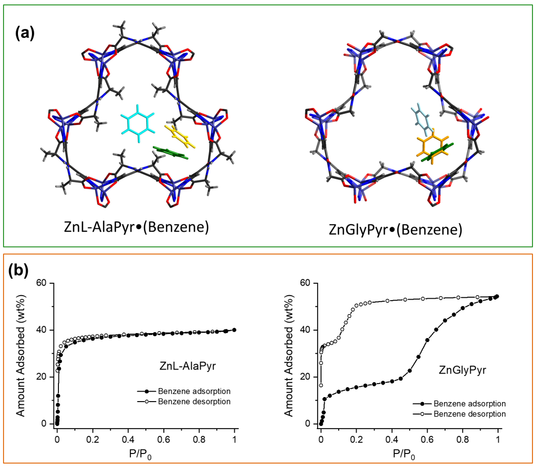

Figure 3. Effect of sidechain functionality on guest response of flexible MOFs

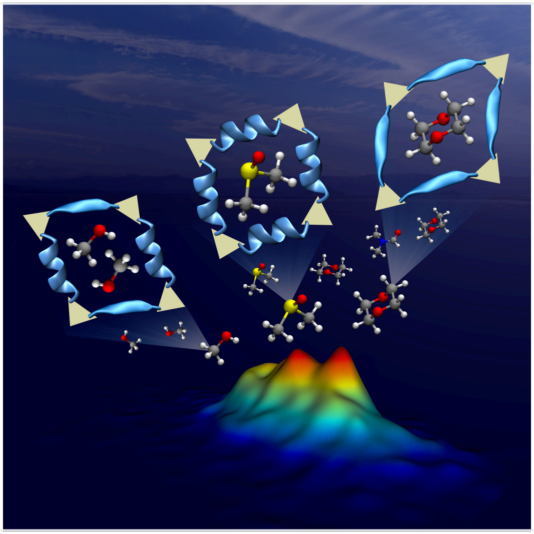

Figure 1. A schematic representation of a flexible metal-organic framework.

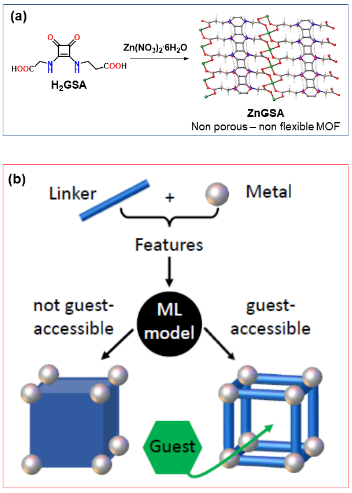

Figure 4. Selection of components for the synthesis of porous and flexible MOFs

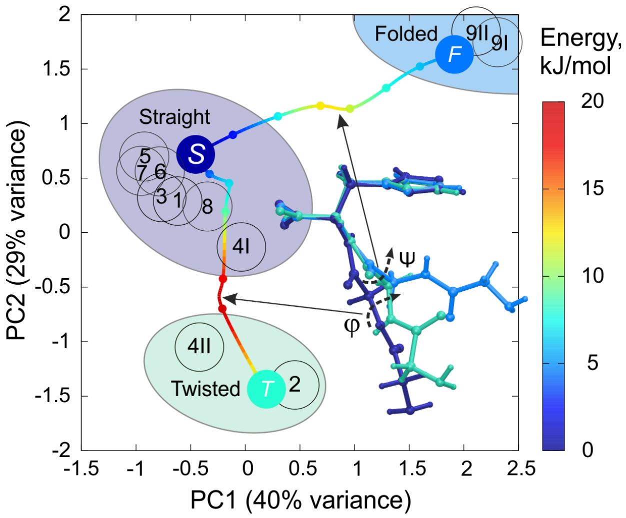

Figure 5. The dPCA of experimental linker conformations and calculated CEL of ZnGGH.

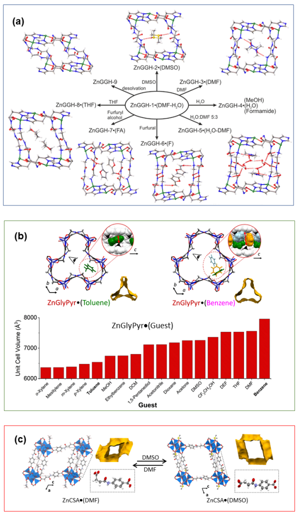

Figure 2. Representation of structural response to guests of flexible MOFs made by different linkers

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